Abstracts

Australian Dementia Forum

Melbourne Convention & Exhibition Centre
15-17 October 2017

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Introduction

NHMRC National Institute of Dementia Research

The number of Australians with dementia is projected to nearly triple by 2050. This will place increasingly significant burdens on our society, healthcare system and economy. At present, there is no known effective therapeutic intervention that will cure or delay the progression of dementia; and not all identified risk factors can be modified (for e.g. age, gender, genetics). The NHMRC National Institute for Dementia Research (Dementia Institute) was established by the Australian Government in 2015 with $200 million in new funding to address this significant health challenge through boosting dementia research.

It is in this context that we welcome you to the Australia Dementia Forum: Progress on the Boosting Dementia Research Initiative, to take place in Melbourne between 15 and 17 October 2017. Timed to immediately precede Alzheimer’s Australia’s 17th biennial conference, Be the change, the Forum will bring together Australia’s dementia researchers who are working to address the challenge of Alzheimer’s disease and other dementias, providing fertile ground for accessing the latest research breakthroughs and exploring collaborations relevant to the NHMRC Dementia Institute Strategic Roadmap for Dementia Research.

Forum speakers include international and national keynote presenters, preeminent researchers, including from the Institute’s Dementia Research Team Grant holders and recipients of International dementia research funding, policy makers, and community and research leaders.

The Forum provides the 73 NHMRC-ARC Dementia Research Development Fellows, who are reaching the mid-point of their four year program of research, an exciting opportunity to highlight their achievements to date. The convening of Special Interest Groups and other networking events round out discussions and provides the catalyst for new collaborations across the dementia research community.

The NHMRC Dementia Institute also takes the opportunity to share knowledge and information about its research activities, providing an initial overview of outcomes from the significant investment that the Boosting Dementia Research Initiative has made.

Programme Committee

Professor Colin Masters, Chair  Florey Institute, The University of Melbourne
Professor Kaarin Anstey  Australian National University
Janice Besch  National Institute for Dementia Research
Professor Michael Breakspear  Queensland Institute of Medical Research (QIMR) Berghofer
Professor Elizabeth Beattie  Queensland University of Technology
Professor Annette Dobson  The University of Queensland
Professor Jürgen Götz  Clem Jones Centre for Ageing Dementia Research (CJCADR), Queensland Brain Institute
Dr Alexandra Grubman  Monash University
Dr Sandra Garrido  Western Sydney University
Professor Glenda Halliday  Central Clinical School, University of Sydney
Joan Jackman  NHMRC Cognitive Decline Partnership Centre
Professor Sue Kurrle  The University of Sydney
Dr Moyra Mortby  Australian National University
Professor David Phillips  National Health and Medical Research Council
Dr David Sykes  Alzheimer’s Australia
Professor Robert Williamson  University of Melbourne
Round Table Sessions
Sunday 15 October – By Invitation

10.00 – 12.00 **Round Table 1**: The long and winding road to prevention: ensuring dementia prevention research makes an impact
Room 106
Dr Helen Macpherson, Flinders University; Professor Kaarin Anstey, Australian National University
This round table event will include dementia prevention researchers to facilitate a high-level discussion regarding research translation and knowledge exchange between research, policy and practice. Clinicians, representatives from relevant government and NGOs including Alzheimer’s Australia and consumer advocacy groups will be invited to participate.

12.30 – 15.30 **Round Table 2**: Safe and effective use of medicines in people living with dementia
Room 106
Dr Lisa Kalisch, University of South Australia; Professor Deborah Rowett, University of South Australia.
This round table will focus on the safe and effective use of medicines in people living with dementia. It will bring together researchers and health professionals who have an interest in better understanding the adverse effects of medicines in people living with dementia. It will provide opportunities for research collaboration and developing new research directions relating to the safe and effective use of medicines in people living with dementia, and the formation of an ongoing special interest group on this topic.

12.30 – 15.30 **Round Table 3**: Understanding mechanisms in dementia, identifying biomarkers and drug discovery using stem cell models
Room 101
Dr Anthony Cook, University of Tasmania; Dr Alexandra Grubman, Monash University; Dr Anna King, University of Tasmania; Dr Rodrigo Medeiros, University of Queensland; Dr Lezanne Ooi, University of Wollongong; Dr Bradley Turner, Florey.

Tuesday 17 October – All Welcome

12.30 – 15.30 **Round Table 4**: Special Interest Group – Expression of interest. Delaying functional decline in people with dementia through rehabilitative therapies
Room 101
Dr Kate Laver of Flinders University invites you to attend a brief session to express interest in the establishment of a special interest group.
This will bring together a multidisciplinary group with industry partners and consumers who have expressed a commitment to further research and knowledge translation efforts dedicated to delaying functional decline in people with dementia.

Programme
Sunday 15 October

08.30 – 17.00 Registration desk open – Poster boards available
16.00 – 17.00 **CONFERENCE OPENING SESSION**
Chair: Professor Colin Masters, Chair of the Program Committee, ADF2017
Welcome to Country
The Honourable Greg Hunt Minister for Health
Welcome
John Quinn
I’m not JUST another statistic
Maree McCabe CEO, Dementia Australia
Our Important Partnership for People with Dementia
Janice Besch Director, NHMRC Dementia Institute
Progress on theBoosting Dementia Research Initiative
Programme

17.00 – 18.00 ADF2017 Keynote Speaker

Chair: Professor Ralph Martins, Edith Cowan University & Macquarie University

Professor Sam Gandy
Mount Sinai Hospital Professor of Alzheimer’s Disease Research

There is no evidence so far to prove that current Aβ-lowering trials will show any meaningful benefit for memory or other brain functions and there is unlikely to be anytime soon a medicine that is administered for decades from midlife to death as a means of preventing Alzheimer’s Disease (AD). A range of new approaches to postponing the symptoms of AD – interventions when amyloid is present in the brain but before the appearance of symptoms must be considered. This is the future challenge for researchers and pharma alike in addressing the burden of dementia.

18.00 – 20.00 Welcome Reception – Performance: Musical Memories Dementia Choir

Monday 16 October

08.00 – 08.30 ADF2017 Opening Addresses

Chair: Janice Besch, Director, NHMRC Dementia Institute

08.00 – 08.15 Professor Anne Kelso, CEO, NHMRC

08.15 – 08.30 Professor Graeme Samuel, Chair, NNIDR Board and President, Alzheimer’s Australia

08.30 – 10.45 Plenary Speakers

Chair: Professor Robert Williamson, University of Melbourne

08.30 – 09.15 Professor Glenda Halliday
Central Clinical School, University of Sydney

Non-Alzheimer’s degenerative dementias: identifying prodromal genetic/familial phenotypes, modifying factors and protein variations involved in progression

Associate Professor John Kwok, Associate Professor Amy Brodman, Professor Olivier Piguet
Research is generating new knowledge necessary for advancing the diagnosis of the non-Alzheimer’s disease dementias. We will identify the preclinical forms of frontotemporal dementia and Lewy body dementia using similar methods to those successfully employed to advance diagnosis of Alzheimer’s disease. Importantly, our team has the capacity to translate these protocols into clinical practice and into further advances in biological knowledge that is necessary for future therapeutic targeting.

09.15 – 10.00 Associate Professor Ian Blair
Australian School of Advanced Medicine, Macquarie University

Developing insight into the molecular origins of familial and sporadic frontotemporal dementia and amyotrophic lateral sclerosis

Associate Professor Julie Atkin, Associate Professor Tim Karl, Dr Leanne Ooi
There is strong evidence that frontotemporal dementia (FTD) and amyotrophic lateral sclerosis (ALS) represent a spectrum of neurodegenerative disease with common origins. A combined study of FTD/ALS patient cohorts will provide greater power to identify these shared molecular origins. We aim to discover gene variants that cause, predispose, or modify onset and progression of inherited and sporadic FTD/ALS, and validate and study our discoveries in new cell and animal models of these disorders.

10.00 – 10.45 Professor Michael Breakspear
Queensland Institute of Medical Research (QIMR) Berghofer

Prospective Imaging Study of Ageing (PISA): genes, brain and behaviour

Dr Christine Guo, Dr Michelle Lupton, Ms Kerrie McAloney, Dr Robert Adam, Dr Olivier Salvado, Associate Professor Gail Robinson
The Prospective Imaging Study of Ageing (PISA) has been designed to identify those Australians at risk of dementia whilst they are still relatively young. PISA leverages a polygene risk score (PRS) to identify healthy mid-life Australians at high future risk of dementia, and follows them longitudinally with a comprehensive battery of imaging, genetics, neuropsychology, lifestyle and clinical assays. In this talk we will present early progress in each of those domains, highlighting the various logistic, governance, ethics and pragmatic
Programme

challenges that we have overcome in order to execute the study according to our overarching vision. We will also highlight the new collaborative links between wet and dry labs, memory clinics, population health, biomedical engineering, psychology and translational imaging that PISA is fostering.

10.45 – 11.00 MORNING TEA
11.00 – 12.30 Plenary Speakers
Chair: Professor David Phillips, Associate Director, National Health and Medical Research Council

11.00 – 11.45
Professor Jürgen Götz
Clem Jones Centre for Ageing Dementia Research (CJCADR), Queensland Brain Institute

From basic pathomechanisms to therapeutic interventions
Dr Dan Blackmore, Dr Victor Anggono, Dr Rodrigo Medeiros
A concise overview of the research activities at CJCADR including: a new mechanism for local Ab-mediated Tau translation in the somatodendritic domain; ultrasound as a new treatment modality for AD; physical exercise for amelioration of decreased neural stem cell numbers, neurogenesis and cognitive deficits; a novel pathway that mediates Aβ-induced loss of AMPA receptors in mammalian central neurons; molecular mechanisms linking inflammation to Aβ and tau pathology as well as cognitive decline.

11.45 – 12.30
Associate Professor Amy Brodtmann
Florey Institute, The University of Melbourne

Vascular mechanisms of neurodegeneration: drivers and determinants of dementia
Dr Sheila Patel, Dr Vanessa Brat, Dr Jess Nithianantharajah, Dr Lachlan Thompson, Professor Louise Burrell
The evidence is compelling: vascular burden is the greatest determinant of late life cognition. The volume of evidence linking vascular risk and dementia is conclusive. All late-onset dementia syndromes, especially Alzheimer’s disease, are driven or exacerbated by vascular brain burden. We aim to examine how vascular burden causes dementia. Understanding the mechanisms means that we can prevent and treat the global epidemic of dementia. An update on animal and human projects will be presented.

12.30 – 13.30 LUNCH
13.30 – 15.00 Plenary Speakers
Chair: Professor Michael Breakspear, QIMR Berghoff

13.30 – 14.15
Professor Henry Brodaty
University of New South Wales

Maintain your brain
Dr Megan Heffernan (UNSW), Dr Maria Fiatarone Singh (USyd), Dr Michael Valenzuela (USyd)
The internet based intervention targets modifiable risk factors for dementia in general and AD in particular, namely physical inactivity, cognitive inactivity, depression, and being overweight or obese, diabetes (type 2), as well as advice regarding high blood pressure and smoking. Our aim is to determine the efficacy and cost-effectiveness of a multi-modal targeted intervention delivered and monitored on the internet to reduce the rate of cognitive decline in non-demented community dwelling persons aged 55-75 years and in the long-term to delay the onset of dementia.

14.15 – 15.00
Professor Rob Sanson-Fisher
School of Medicine and Public Health, University of Newcastle

The ACcoRD Program
The Australian Community of Practice in Research in Dementia (ACcoRD) is a national, multidisciplinary research team dedicated to developing, implementing and evaluating strategies to improve the wellbeing and quality of care provided to people living with dementia and their care partners. Studies underway include: the development of acceptable and robust measures for assessing the unmet needs of people living with dementia and their care partners; the views of consumers, nurses, general practitioners and geriatricians regarding the acceptability and feasibility of the NHMRC guidelines for dementia care; medico-legal impediments to providing high-quality person-centred care; and the application of strong research methodology to test the effectiveness of strategies to improve important outcomes for people with dementia and their care partners.
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15.00 – 15.30  AFTERNOON TEA

15.30 – 17.30  Dementia Centre for Research Collaboration (DCRC)
Chair: Dr Moyra Mortby, Australian National University
Professor Henry Brodaty, Professor Kaarin Anstey, Professor Elizabeth Beattie
DCRC Directors’ Overview

Professor Marita McCabe (ACU)
Consumer Directed Care in Residential Aged Care: Implementation and Evaluation of the Resident at the Centre of Care (RCC) Program

Dr Matt Paradise (UNSW)
An MRI index of cerebrovascular disease burden: development and validation

Dr Maree Farrow (UTas)
Memory performance is associated with exposure to risk factors for Alzheimer’s disease

Dr Kate Stevens (WSU)
Time Travelling with Technology (TTT): Applying and Evaluating Behavioural and Psychosocial Benefits of Liquid Galaxy-Based Reminiscence Therapy for People with Dementia

Dr Cindy Jones (Griffith U)
Sexualities & Dementia: Improve Knowledge, Attitudes & Practices in Aged Care Via Interactive Live Webinars

18.00 – 20.00  COCKTAIL RECEPTION AND POSTER SESSION

Tuesday 17 October

08.30 – 10.30  Cognitive Decline Partnership Centre (CDPC)
Chair: Professor Susan Kurrle, The University of Sydney

Ms Louise Heuzenroeder
Consumer involvement in development of Clinical Practice Guidelines and Principles of Care for People with Dementia and Associated Consumer Companion Guide

Dr Kate Laver (Flinders)
What do members of the public believe regarding efficacy of treatments for dementia? A systematic review

Dr Morag Taylor (UNSW)
Slow gait speed is associated with executive function decline in older people with mild to moderate dementia

Dr Suzanne Dyer (Flinders)
The effects of different built environments in residential care on consumer-reported outcomes and healthcare resource use

Dr Tracy Comans (Griffith U)
Demonstrating value based health care is an essential element of evaluating new and existing services

10.30 – 11.00  MORNING TEA

11.00 – 11.30  Dementia Research Development Fellows: Research Addressing the Challenges of Living with Dementia and Delivering Quality of Care
Chair: Professor Kaarin Anstey, Australian National University

Dr Julia Gilmartin-Thomas (Monash)
Qualitative and quantitative impact of a virtual dementia experience on medical and pharmacy students’ knowledge, attitudes and self-reported behaviour toward people with dementia

Dr Fiona Kumfor (USyd)
Why do patients with frontotemporal dementia misinterpret social cues? The importance of context

11.30 – 12.45  Dementia Research Development Fellows Panel Discussion: New Research to Improve Assessment & Diagnosis
Programme

Chair: Professor Glenda Halliday, The University of Sydney
Dr Loren Mowszowski (USyd)
Detecting subtle functional decline in prodromal dementia
Dr Shaun Frost (CSIRO)
Eye imaging for early detection of Alzheimer’s disease
Dr Mitchell Goldsworthy (Adelaide)
TMS-EEG indices of cortical effective connectivity and physical activity in older adults
Dr Nawaf Yassi (Florey)
Cortical Cerebral Microinfarcts on 3T MRI in Alzheimer’s Disease
Dr Scott Ayton (Florey)
Cerebral quantitative susceptibility mapping predicts β-amyloid-related cognitive decline

12.45 – 14.00  LUNCH

14.00 – 15.00  Dementia Research Development Fellows Panel Discussion: Intervention and Treatment Studies
Chair: Professor Annette Dobson, The University of Queensland
Dr Kylie Radford (UNSW)
Life course social and biomedical factors associated with dementia in Aboriginal Australians
Dr Belinda Brown (Murdoch)
Update on the Intense Physical Activity and Cognition (IPAC) Study
Dr Kathryn Munro (UoM)
Effects of BACE inhibition on synaptic connectivity
Dr Edwin Tan (Monash)
Acetylcholinesterase inhibitors and risk of stroke and death in people with dementia

15.00 – 15.30  AFTERNOON TEA

Chair: Dr Alexandra Grubman, Monash University
Dr Emma Louise Burrows (Florey)
Progressive behavioural flexibility impairments in the APP/PS1 mouse model of Alzheimer’s disease as measured by translatable touchscreen technology
Dr Yen Ying Lim, (Florey)
BDNF Val66Met increases rate of memory decline, hippocampal volume loss and tau accumulation in autosomal dominant Alzheimer’s disease
Dr Shantel Duffy (USyd)
The longitudinal relationship between anterior cingulate glutathione and executive functioning in individuals at-risk for dementia: a magnetic resonance spectroscopy study
Dr Erin McAllum (Florey)
Metalloproteomic changes in dementia with Lewy bodies
Dr Simon James (Florey)
Iron, copper, and zinc concentration in Aβ Plaques in the APP/PS1 mouse model of Alzheimer’s disease correlates with metal levels in the surrounding neuropil
Dr Sarah Rea (UWA)
An ALS-FTLD associated mutation of SQSTM1/p62 attenuates oxidative stress signalling and autophagy
Dr Samamtha Barton (Monash)
Using patient iPS-derived oligodendrocytes harbouring a C9ORF72 mutation to identify disease causing mechanisms in ALS-FTD

17.15 – 17.30  AWARDS PRESENTATION AND CLOSE
Professor Sam Gandy
MD PhD
Mount Sinai Professor of Alzheimer’s Disease Research
Professor Sam Gandy is an international expert in the metabolism of the substance called amyloid that clogs the brain in patients with Alzheimer’s. In 1989, Dr Gandy and his team discovered the first drugs that could lower formation of amyloid. Dr Gandy has written more than 250 original papers, chapters and reviews on this topic. Dr Gandy has received continuous NIH funding for his research on amyloid metabolism since 1986. Dr Gandy is Professor of Alzheimer’s Disease Research, Professor of Neurology and Psychiatry, and Associate Director of the Mount Sinai Alzheimer’s Disease Research Center, and Chair, National Medical and Scientific Advisory Council of the Alzheimer’s Association.

Dr Gandy is a member of the Faculty of 1000 Biology and serves as a Consulting Editor for The Journal of Clinical Investigation. He also serves on the Editorial Advisory Boards for the journals Public Library of Science-Medicine (PLoS), Neurodegenerative Diseases, and Current Alzheimer Research. He is Associate Editor of the journals Molecular Neurodegeneration and Alzheimer Disease and Associated Disorders. From 1996-2006, Dr Gandy was Director of the Cold Spring Harbor Laboratories/Wellcome Trust Annual Summer Course on the Neurobiology of Human Neurological Disorders. In 2000, he became chief organizer for the Cold Spring Harbor Laboratories Bi-Annual Winter Biotechnology Conference on Therapeutic Opportunities in Neurodegenerative Diseases and continued in that role until 2010. Dr Gandy is also the Founding Director of the Mount Sinai Center for NFL (National Football League) Neurological Care.

Professor Anne Kelso AO
Chief Executive Officer (CEO)
National Health & Medical Research Council
Following her PhD at the University of Melbourne, Professor Kelso undertook research in immunology at the Swiss Institute for Experimental Cancer Research, the Walter and Eliza Hall Institute of Medical Research and the Queensland Institute of Medical Research. From 2000 until 2006, she was also Director/CEO of the Cooperative Research Centre for Vaccine Technology. She then returned to Melbourne as Director of the WHO Collaborating Centre for Reference and Research on Influenza from 2007 until she took up her role with NHMRC in April 2015. She was appointed Officer in the Order of Australia in June 2007 for service to science.

Professor Kelso is a member of several Government and international committees, including the Australian Medical Research Advisory Board (advising the Minister for Health on the strategy and priorities for the Medical Research Future Fund), the Board of the Global Alliance for Chronic Diseases and the Board of Trustees of the International Human Frontier Science Program Organization.

Professor Graeme Samuel AC
Chair NNIDR Board and National President Alzheimer’s Australia
Professor Graeme Samuel AC is a Vice Chancellor’s Professorial Fellow in Monash University’s Business School and co-director of the Monash Business Policy Forum. He is also Chair of the Victorian Taxi Services Commission, a Commissioner of the National Rugby League, a Councillor of the Australian National University, President of Alzheimer’s Australia, and Chair of the South Eastern Melbourne Primary Health Network.

Professor Samuel has held a number of roles in public life including former Chairman of the Australian Competition and Consumer Commission. He was appointed an Officer of the Order of Australia in 1998. In 2010 he was elevated to a Companion of the Order of Australia.
Invited Speakers

**Professor Glenda Halliday**  
Central Clinical School, University of Sydney  
Professor Glenda Halliday is an Australian Professor of Neuroscience leading a research program of 70 researchers tackling non-Alzheimer’s neurodegeneration that stems from her work on frontotemporal and motor neurodegenerative syndromes, and Parkinson’s disease. She is also Director of the Sydney Brain Bank. She received her degrees at University of New South Wales, and postdoctoral training at Flinders University prior to an ARC Queen Elizabeth II Fellow and NHMRC research fellowships since 1988, joining NeuRA in 1993. She has published more than 300 research papers and 2 books, and attracted $30m in grant funding. Prof Halliday is on the editorial boards of 5 international journals, on Scientific Advisory Boards for 3 research institutes (one international), and is a committee member for a number of international organizations, including the International Brain Research Organization (a member organization of UNESCO). She was elected president of the Australian Neuroscience Society (ANS 2006-2007), awarded the 2011 ANS Nina Kondelos Prize, and named a high achiever in Australian Health and Medical Research by NHMRC.

**Associate Professor Ian Blair**  
Faculty of Medicine and Health Science, Macquarie University  
Associate Professor Ian Blair’s research career has focused on determining the molecular basis of a variety of neurological disorders including ALS/MND, FTD, hereditary sensory neuropathy (HSN), Charcot Marie Tooth disorder (CMT), the spinal cerebellar ataxias (SCA), Joubert syndrome, and bipolar disorder. At Macquarie University, his team works to unravel the molecular and cellular basis of ALS and FTD. His group has played a key role in several ALS/FTD gene discoveries including identification of mutations in the TDP-43 and FUS genes. These discoveries have opened new chapters in ALS/FTD research and led to effective diagnostic tests for ALS, CMT1A and HSN1.

**Professor Michael Breakspear**  
Group Leader, QIMR Berghofer Medical Research Institute & Coordinator program of Mental Health research  
Professor Michael Breakspear is Group Leader at QIMR Berghofer and coordinator of the Program of Mental Health Research. He trained in Medicine and Physics at the University of Sydney and completed his psychiatry training at the Black Dog Institute, Sydney. He combines computational modelling with advanced neuroimaging techniques to study neurodevelopmental and neurodegenerative disorders. He is a psychiatrist in the Brisbane Prison Mental Health Service.

**Professor Jürgen Götz**  
Inaugural Director, Clem Jones Centre for Ageing Dementia Research, Queensland Brain Institute, Brisbane  
Professor Jürgen Götz is the inaugural Director of the Clem Jones Centre for Ageing Dementia Research at the Queensland Brain Institute in Brisbane. Götz studied biochemistry in Switzerland and earned his PhD in immunology with Nobel Laureate Köhler in Germany. After postdoctoral work at UCSF and at Novartis, he became a group leader in Zürich, before moving to Sydney in 2005, and Brisbane in 2012. A major focus of his laboratory is the generation and analysis of transgenic animal models to gain a better mechanistic understanding of Alzheimer’s disease and to develop therapeutic interventions targeting two key molecules in disease, tau and amyloid-beta.

**Associate Professor Amy Brodtmann**  
Co-Division Head, Behavioural Neuroscience, NHMRC Clinical Career Development Fellow at the Florey Institute for Neuroscience and Mental Health in Melbourne, Australia; Stroke Neurologist, Austin Health; Cognitive Neurologist and Clinic Director, Eastern Cognitive Disorders Clinic, Box Hill Hospital  
Associate Professor Amy Brodtmann is a stroke and cognitive neurologist at Austin Health and director of the Eastern Cognitive Disorders Clinic. She is the recipient of many awards and grants for her work in stroke and dementia, including NHMRC project grants, post-Graduate, post-Doctorate, and clinical Career Development Fellowships, and is CIA on a Dementia Research Team Grant. She sits on the editorial boards of Neurology and the International Journal of Stroke, the board and committee of Alzheimer’s Australia Victoria Dementia Research Grants, is an inaugural member of the Wicking Strategic Review Panel, and is a founding member of the Australian Frontotemporal Dementia Association. Her research focuses on the imaging of brain network degenerations following stroke, post-stroke behavioural
Invited Speakers (continued)

syndromes, and the diagnosis and management of focal onset dementias.

Professor Henry Brodaty
Director Dementia Centre for Research Collaboration, Co-Director of the Centre for Healthy Brain Ageing at UNSW, Scientia Professor of Ageing and Mental Health, University of New South Wales; Consultant Psychogeriatrician, Aged Care Psychiatry and Head of the Memory Disorders Clinic, Prince of Wales Hospital.

Professor Brodaty's research interests include:
i) prevention of cognitive decline with ageing. He is leading Maintain Your Brain, funded by an NHMRC/NNIDR team grant, which will be the world's largest trial of an internet based intervention to prevent cognitive decline and dementia; ii) Cognitive health and ageing: What predicts cognitive decline in older people? CHeBA is conducting a population based study of >1000 older people to discover what are risk and protective factors; iii) how to improve detection and management of dementia by GPs; iv) the effects of dementia on family carers and on how best to help them; iv) ways to improve quality of life in people with dementia; v) reducing behavioural and psychological symptoms of dementia (BPSD); vi) improving care in nursing homes; and, vii) living well to 100, research on centenarians and near centenarians. Henry is on the editorial board of several journals and has been the recipient of a number of awards. Henry's lifetime achievements have been recognised with the award of AO and the 2016 Ryman Prize.

Professor Rob Sanson-Fisher
Director, Health Behaviour Research Group, School of Medicine and Public Health, University of Newcastle

Laureate Professor Rob Sanson-Fisher is Director of the Health Behaviour Research Group, School of Medicine and Public Health, University of Newcastle. An internationally recognised leader in health behaviour research, his work successfully combines behavioural approaches to knowledge translation, health promotion, health service evaluation and chronic disease control. He has published over 470 peer-reviewed journal articles and obtained some 100 competitive research grants, with a total value over $36 million. His research interests include exploring health care provider behaviour and adoption of best evidence practice, and the development, implementation and evaluation of interventions to improve health outcomes for vulnerable population groups.

Professor Kaarin J Anstey
Professor of Psychology and Population Health, Australian National University

Professor Kaarin J. Anstey is a Professor of Psychology and Population Health at the Australian National University and Director of the Dementia Collaborative Research Centre - Early Diagnosis and Prevention. Her research interests focus on the prevention of dementia, and the impact of cognitive impairment on activities such as driving. Anstey led the first online dementia risk reduction intervention called Body Brain Life that is soon to be trialled in Primary Care. Anstey is a Director of the Alzheimer’s Australia Dementia Research Foundation and the Global Council on Brain Health, an initiative of the US AARP and UK HelpAge organisations.

Professor Elizabeth Beattie
Professor of Aged and Dementia Care, School of Nursing, Queensland University of Technology

Professor Elizabeth Beattie, Professor of Aged and Dementia Care, School of Nursing, Queensland University of Technology, is a psychogeriatric nurse educated in Australia, the UK and the US who has been involved in dementia-focused clinical practice, education and research for 30 years. She directs the Dementia Collaborative Research Centre Carers and Consumers and the Queensland Dementia Training Study Centre. Elizabeth has an international nursing leadership profile and a sustained record of competitive research funding and publication. Her research is focused on improving the quality of care and quality of life of people living with dementia and those who support them.

Professor Susan Kurrle
Geriatrician, Ku-ring-gai Hospital, Sydney

Professor Susan Kurrle is a geriatrician practising at Hornsby Ku-ring-gai Hospital in northern Sydney, and Batemans Bay Hospital in southern NSW, and she holds the Curran Chair in Health Care of Older People in the Faculty of Medicine at the University of Sydney. Since 2012 she has led the NHMRC Partnership Centre on Dealing with Cognitive and Related Functional Decline in Older People. This Centre focuses on research and implementation projects dealing particularly with the care aspect of dementia.
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67 Dr Qiao-Xin Li Poster: No.74
67 Dr Yen Ying Lim Poster: No.75
68 Dr Yen Ying Lim Poster: No.76
68 Dr Xiaoping Lin Poster: No.77
69 Dr Michelle Lupton Poster: No.78
69 Dr Margaret MacAndrew Poster: No.79
70 Dr Sean Macdermott Poster: No.80
70 Dr Helen Macpherson Poster: No.81
71 Dr Adam Martin Poster: No.82
71 Dr Melinda Martin-Khan Poster: No.83
72 Dr Karen Mather Poster: No.84
72 Mr Brendan McLare Poster: No.85
73 Dr Rodrigo Medeiros Poster: No.86
73 Dr Chris Moran Poster: No.87
73 Dr Moyra Mortb Poster: No.88
74 Professor Sharon L Naismith Poster: No.89
74 Dr Morgan Newman Poster: No.90
75 Dr Morgan Newman Poster: No.91
75 Dr Tuan Anh Nguyen Poster: No.92
76 Dr Leanne Ooi Poster: No.93
76 Dr Anita Panayiotou Poster: No.94
77 Dr Luke Perimal-Lewis Poster: No.95
77 Dr Christina Perry Poster: No.96
78 Dr Lyn Phillipson Poster: No.97
78 Professor Constance Dimity Pond Poster: No.98
79 Ms Dannielle Post Poster: No.99
79 Dr Sivaraman Purushothuman Poster: No.100
80 Dr Emily Reeve Poster: No.101
80 Mrs Cathy Roth Poster: No.102
81 Dr Joanne Ryan Poster: No.103
81 Dr Joanne Ryan Poster: No.104
82 Dr Theresa Scott Poster: No.105
82 Dr Theresa Scott Poster: No.106
83 Dr Bingyang Shi Poster: No.107
83 Dr Olga Shimoni Poster: No.108
84 Dr Craig Sinclair Poster: No.109
84 Dr Craig Sinclair Poster: No.110
85 Dr Kate Smith Poster: No.111
85 Dr Ashleigh Smith Poster: No.112
86 Professor Velandai Srikanth Poster: No.113
86 Professor Velandai Srikanth Poster: No.114
87 Dr Genevieve Steiner Poster: No.115
87 Dr Brad Sutherland Poster: No.116
87 Dr Ryu Takechi Poster: No.117
88 Dr Ryu Takech Poster: No.118
88 Dr Jeanette Tamplin Poster: No.119
89 Dr Rachel Tan Poster: No.120
89 Dr Jane Thompso Poster: No.121
90 Miss Esther Tiong Poster: No.122
90 Miss Esther Tiong Poster: No.123
91 Dr Bradley Turner Poster: No.124
91 Ms Pippy Walker Poster: No.125
92 Dr Michael Waller Poster: No.126
92 Dr Stephanie Ward Poster: No.127
93 Ms Rochelle Watso Poster: No.128
93 Dr Rachel Wong Poster: No.129
94 Dr Rachel Wong Poster: No.130
94 Dr Paul Yates Poster: No.131
There is no evidence so far to prove that current Aβ-lowering trials (beginning at age 65 or above) will show any meaningful benefit for memory or other brain functions. There is unlikely to be anytime soon a medicine (analogous to statins for cardiovascular disease and insulin for diabetes) that is administered for decades from midlife to death as a means of preventing AD. In the cases of statins and insulin, the FDA and society as a whole have agreed that their risk–benefit ratios are acceptable. Any new medication for AD that is worth the risk of ingestion for decades must be effective and must do no harm anywhere in the body. The Aβ-lowering drugs in the current pipeline fall well short of this goal. Professor Gandy’s talk will be wide ranging, setting the scene for two days of intensive discussions. He will consider the challenges for researchers and drug companies specific to this disease; a range of new approaches to postponing the symptoms of AD – interventions when amyloid is present in the brain but before the appearance of symptoms; promising genes and precision medicine; combinatorial approaches; new interventions aimed at tau and inflammation; and environmental factors and interventions.
Non-Alzheimer's disease degenerative dementias – identifying prodromal genetic/familial phenotypes and modifying factors, and protein variations involved in progression

The University of Sydney

Glenda Halliday, John Kwok, Amy Brodtman and Olivier Piguet for the Team (Halliday, Hodges, Lewis, Piguet, Kril, Kwok, Villedamel, Kiernan, Rowe, McKeith & Als)

Background and Aims – As recently achieved for Alzheimer’s disease (AD), comprehensive data on the preclinical phase/s for the non-AD neurodegenerative dementias are now required to establish new diagnostic criteria. We will identify and characterise a large cohort of asymptomatic inherited forms of the main non-AD neurodegenerative dementias using established methodology and pathologically confirm the disease phenotype in the probands of these families. We will establish differences in protein ‘strains’ between these phenotypes.

Cohort identification – Two types of cohorts are being targeted and ethics has been approved or is in process for the following sites - in Sydney the Brain and Mind Centre, Royal Prince Alfred Hospital, Macquarie University, Woolcock Institute and Concord Hospital; in Melbourne Eastern Health, Austin Health and the Florey.

1) families with underlying TDP-43 pathologies (Sydney and Melbourne). 125 Sydney families with genes associated with the pathology identified prior to funding. Additional 579 Sydney cases now screened and 55 families identified (180 families of the 185 target). 29 postmortem confirmed. Targeted families in Melbourne identified.

2) families with underlying a-synucleinopathy (Sydney only). 23 pathologically confirmed Sydney families identified prior to funding. Completed screening of 45 Sydney cases and 8 families identified (30 families of the 140 target). Awaiting final analyses of 364 Sydney cases from Brain and Mind clinic (~70 families at current rate) and still to screen Macquarie clinic (66 families identified).

New protocols – Neurology trainee and genetic counsellors recruited. Protocols include challenging initial assessment (clinical, psychometrics), brain imaging (MRI, PET), biofluid collections (genetics as above, CSF pathological proteins), and research on modifiable factors (sleep, movement, metabolism).

Protein strains – Assessment of a-synuclein strains for different pathologies (the common neuronal Lewy bodies versus the less common glial cytoplasmic inclusions) has been completed. Significant differences in the properties of the a-synuclein strains from the different pathologies has been identified. In contrast to the pathological a-synuclein strain from neurons, the pathological a-synuclein from glia has been shown to become self-propagating/transmissible in both genetically-modified cells and animal models. Further, the prion-like a-synuclein from glia is resistant to a number of inactivation methods. The characteristics of the less common prion-like a-synuclein from glia are very similar to those of pathological prions, suggesting similar cautions to prevent disease transmission.

Next steps – Determine and assess TDP-43 pathological strains. Collect and assess data to be able to propose new criteria for prodromal TDP-43 pathologies (in association with the Genetic Frontotemporal Dementia Initiative or GENFI) and a-synucleinopathies (in association with the Consortium for Lewy Body Disease Researchers) and validate the new criteria with our international collaborators in their cohorts.
Associate Professor Ian Blair  
Email: ian.blair@mq.edu.au

Research into origins of dementia and related neurodegenerative disease: Developing insight into the molecular origins of familial and sporadic frontotemporal dementia and amyotrophic lateral sclerosis

Macquarie University

Ian Blair 1, Julie Atkin 1, Roger Chung 1, Gilles Guillemin1, Lezanne Ooi 2, Denis Bauer 3, Mark Molloy 4 Justin Yerbury 2, Nicholas Cole 1, Tim Karl 5.

1. Faculty of Medicine and Health Sciences, Macquarie University;
2. Illawarra Health and Medical Research Institute, University of Wollongong;
3. Transformational Bioinformatics, CSIRO;
4. Chemistry & Biomolecular Sciences, Macquarie University;
5. School of Medicine, Western Sydney University.

There is strong evidence that frontotemporal dementia (FTD) and amyotrophic lateral sclerosis (ALS) represent a spectrum of neurodegenerative disease with common origins. A combined study of FTD/ALS patient cohorts will provide greater power to identify these shared molecular origins. We aim to discover gene variants that cause, predispose, or modify onset and progression of inherited and sporadic FTD/ALS, and validate and study our discoveries in new cell and animal models of these disorders. In this presentation, four Ci's will present an overview of the goals and progress for each of the primary themes that comprise our multidisciplinary team strategy.

Genetic and epigenetic basis of disease: We continue to build genetic and genomic resources through whole genome sequencing and methylation typing of ALS and FTD patients. Integration with international datasets has led to the identification of new molecules associated with familial and sporadic disease and consideration of the implications for predictive genetic testing for ALS and FTD.

Validation, in vitro studies: We are examining novel, and more established, mechanisms linked to pathogenicity in neuronal cell lines and primary human and mouse neurons including those expressing known and new ALS genes.

Validation, animal models: Using the zebrafish and mouse, together with CRISPR, somatic brain transgenesis and traditional transgenesis techniques, we continue to develop pipelines to assess the pathogenicity of new candidate disease molecules, as well as assessing new transgenic animals as potential preclinical models of FTD and ALS.

Validation and elucidation of molecular origins using iPSCs and molecular profiling: We are reprogramming somatic cells, donated from our patient cohort, into pluripotent stem cells in order to profile the molecular differences between patient and control cells and identify pathogenetic mechanisms.

Professor Michael Breakspear  
Email: michael.breakspear@qimrberghofer.edu.au

Prospective Imaging Study of Ageing: Genes, Brain & Behaviour

Queensland Institute for Medical Research Berghofer

The Prospective Imaging Study of Ageing (PISA) has been designed to identify those Australians at risk of dementia whilst they are still relatively young. PISA leverages a polygene risk score (PRS) to identify healthy mid-life Australians at high future risk of dementia, and follows them longitudinally with a comprehensive battery of imaging, genetics, neuropsychology, lifestyle and clinical assays. In this talk we will present early progress in each of those domains, highlighting the various logistic, governance, ethics and pragmatic challenges that we have overcome in order to execute the study according to our overarching vision. We will also highlight the new collaborative links between wet and dry labs, memory clinics, population health, biomedical engineering, psychology and translational imaging that PISA is fostering.

Professor Jürgen Götz  
Email: j.goetz@uq.edu.au

From basic pathomechanisms to therapeutic interventions

Clem Jones Centre for Ageing Dementia Research (CJCADR)

Following a concise overview of the research activities at CJCADR, the following will be covered:
What causes proteins such as Tau to accumulate in Alzheimer’s disease (AD) brains is only incompletely understood. Jurgen Gotz will outline a new mechanism that involves local Aβ-mediated Tau translation in the somatodendritic domain. He will present an update on ultrasound as a new treatment modality for AD.

Advanced age typically results in decreased neural stem cell numbers and neurogenesis as well as deficits in cognition. Daniel Blackmore will reveal how an optimal period of physical exercise ameliorates these deficits in rodents. The findings lead to a human exercise trial of which an update will be provided.

Synaptic failure occurs early in AD pathogenesis and is considered to be a major correlate of cognitive impairment. Synaptic depression associated with AD is due to the loss of AMPA-type glutamate receptors and dendritic spines. Victor Anggono will present new data highlighting a novel pathway that mediates Aβ-induced loss of AMPA receptors in mammalian central neurons.

Rodrigo Medeiros discovered that AD promotes defects in fundamental molecular events that limit and resolve inflammation, and demonstrated that this has a major role in AD pathogenesis. He will present animal and human studies aimed at elucidating the underlying molecular mechanisms linking inflammation to Aβ and tau pathology as well as cognitive decline.

Associate Professor Amy Brodtmann
Email: amy.brodtmann@florey.edu.au

Vascular mechanisms of neurodegeneration: drivers and determinants of dementia
Florey Institute of Neuroscience and Mental Health
The evidence is compelling: vascular burden is the greatest determinant of late life cognition. The volume of evidence linking vascular risk and dementia is conclusive. All late-onset dementia syndromes, especially Alzheimer’s disease, are driven or exacerbated by vascular brain burden. We aim to examine how vascular burden causes dementia. Understanding the mechanisms means that we can prevent and treat the global epidemic of dementia. An update on animal and human projects will be presented, with results per project:

Canvas: post-stroke brain atrophy and cognitive decline

Professor Henry Brodaty
Email: h.brodaty@unsw.edu.au

Maintain your Brain
Megan Heffernan (UNSW), Maria Fiararone Singh (USyd), Michael Venezueala (USyd)
University of New South Wales
The internet based intervention targets modifiable risk factors for dementia in general and AD in particular, namely physical inactivity, cognitive inactivity, depression, and being overweight or obese, diabetes (type 2), as well as advice regarding high blood pressure and smoking. Our aim is to determine the efficacy and cost-effectiveness of a multi-modal targeted intervention delivered and monitored on the internet to reduce the rate of cognitive decline in non-demented community dwelling persons aged 55-75 years and in the long-term to delay the onset of dementia.

Professor Rob Sanson-Fisher
Email: rob.sanson-fisher@newcastle.edu.au

The ACcoRD Program
School of Medicine and Public Health, The University of Newcastle
The Australian Community of Practice in Research in Dementia (ACcORD) is a national, multidisciplinary research team dedicated to developing, implementing and evaluating strategies to improve the wellbeing and quality of care provided to people living with dementia and their care partners. Studies underway include: the development of acceptable and robust measures for assessing the unmet needs of people living with dementia and their care partners; the views of consumers, nurses, general practitioners and geriatricians regarding the acceptability and feasibility of the NHMRC guidelines for dementia care; medico-legal impediments to providing high-quality person-centred care; and the application of strong research methodology to test the effectiveness of strategies to improve important outcomes for people with dementia and their care partners.
Cognitive Decline Partnership Centre

**Professor Susan Kurrle**  
Email: susan.kurrle@sydney.edu.au  
Presentation Type: Oral_CDPC

**A collaborative research model to improve care for people living with dementia**

The University of Sydney

The NHMRC Partnership Centre Dealing with Dementia and Related Functional Decline in Older People (CDPC) brings together clinicians, consumers, researchers and industry to translate research into improved care for people and carers living with dementia and associated functional decline. Professor Kurrle will outline how the CDPC is working towards achieving its vision and program of research; and how the CDPC is progressing towards bridging knowledge gaps to inform policy and practice.

**Ms Louise Heuzenroeder**  
Email: louise.heuzenroeder@bigpond.com  
Presentation Type: Oral_CDPC

**Consumer involvement in development of Clinical Practice Guidelines and Principles of Care for People with Dementia and associated Consumer Companion Guide**

The University of Sydney

Consumer involvement in development of Clinical Practice Guidelines and Principles of Care for People with Dementia demonstrates how a successful partnership between consumers, researchers, clinicians and industry may improve the lives of people with dementia and their carers. This overview of consumer involvement in this CDPC project will describe how consumers were major contributors to these guidelines and the associated Consumer Companion Guide.

**Dr Kate Laver**  
Email: kate.laver@flinders.edu.au  
Presentation Type: Oral_CDPC  
Theme: Intervention and Treatment

**What do members of the public believe regarding efficacy of treatments for dementia?**

A systematic review:

Flinders University

NHMRC-ARC Dementia Fellow and CDPC researcher Dr Kate Laver, will present data from a systematic review determining current knowledge and attitudes to availability or efficacy of treatments for dementia. Do people think they should seek professional help for memory problems, believe that effective treatments exist? And how many people believe there is already an effective cure for dementia?

**Dr Morag Taylor**  
Email: m.taylor@neura.edu.au  
Presentation Type: Oral_CDPC  
Theme: Living with Dementia

**Slow gait speed is associated with executive function decline in older people with mild to moderate dementia:**

Morag E. Taylor, 1,2,3 Danielle A. Lasschuit, 3,4 Stephen R. Lord,1,5 Kim Delbaere,1,5 Susan E Kurrle, 2  
A. Stefanie Mikolaizak, 6 Tasha Kvelde 1 and Jacqueline C.T. Close 1,3

1. Falls, Balance and Injury Research Centre, Neuroscience Research Australia, UNSW, Sydney, NSW, Australia.  
2. Cognitive Decline Partnership Centre, Sydney Medical School, The University of Sydney, Sydney, NSW, Australia.  
3. Prince of Wales Clinical School, Medicine, UNSW, Sydney, NSW, Australia.  
4. Department of Geriatric Medicine, Prince of Wales Hospital, South East Sydney Local Health District, Sydney, NSW, Australia.  
5. School of Public Health and Community Medicine, Medicine, UNSW, Sydney, NSW, Australia.  
6. Department of Clinical Gerontology, Robert-Bosch-Hospital, Stuttgart, Germany.

NHMRC-ARC Dementia Fellow and CDPC researcher Dr Morag Taylor, examined changes in neuropsychological, physical and functional performance over one year in older people with dementia living in community or low-level care. The data presented will demonstrate a significant decline in the performance areas over one year and that baseline gait speed is associated with decline in executive function suggesting shared pathways/pathology between gait and cognition.
**Dr Suzanne Dyer**  
*Email: suzanne.dyer@sa.gov.au*  
**Presentation Type:** Oral_CDPC  
**The effects of different built environments in residential care on consumer-reported outcomes and healthcare resource use:**  
Flinders University  
This CDPC supported study examined the impact of design of residential aged care on consumer-reported outcomes. The study included 541 residents residing in care for 12 months or longer across facilities using different models of care. Differences in consumer rated quality of care, quality of life, ED presentations and hospitalisations will be reported in this presentation.

**Ms Tracy Comans**  
*Email: t.comans@griffith.edu.au*  
**Presentation Type:** Oral_CDPC  
**Demonstrating value based health care is an essential element of evaluating new and existing services:**  
Griffith University  
The health economics sub-unit of the CDPC provides advice and support for economic evaluation of projects. This presentation will give an overview of how this support has assisted researchers, and present preliminary findings from a CDPC project measuring the quality of life of people living with dementia and developing a better economic model to evaluate dementia programs.
Dementia Centre for Research Collaboration (DCRC)

The Dementia Collaborative Research Centres (DCRC) were established in 2006 under the Government’s Dementia Initiative, funded by the Department of Health and Ageing after a competitive tender process. The three centres (‘hubs’) based at UNSW, ANU and QUT have many collaborative partners around Australia, working in partnership with consumers and service providers, Dementia Training Australia and Dementia Support Australia in order to progress prevention, assessment, care and translation of knowledge into everyday practice, as well as building the next generation of dementia researchers.

An overview of the DCRC Program will be provided, and three researchers funded by the DCRC in its recent grant round will present outcomes from their projects.

Dr Matt Paradise
Email: m.paradise@unsw.edu.au Presentation Type: Oral - DCRC
An MRI index of cerebrovascular disease burden: development and validation
Dr Matt Paradise, Ass. Prof Wei Wen, Dr Laughlin Dawes, Dr John Crawford, Prof Perminder Sachdev
University of New South Wales

Cerebrovascular disease (CVD) has an increasingly recognised role in the development of cognitive impairment and both Vascular (VaD) and Alzheimer’s dementia. Diagnosing VaD requires determining whether a patient’s cognitive deficits can be explained by the current CVD burden. However, CVD is markedly pleomorphic and its full extent has been difficult to determine as traditional markers of CVD such as white matter hyperintensities (WMH) are inconsistently associated with clinical outcomes. Recent advances in MRI technology permit the visualisation of multiple indicators of vascular pathology, including large and small infarcts, lacunes, dilated perivascular spaces, WMH, diffusivity, microbleeds, and cerebral blood flow. Most investigators have studied these pathologies in isolation but we aim to use data from two longitudinal studies of ageing at CHeBA (UNSW) to develop a composite measure of CVD MRI burden, with different weights assigned to different pathologies. The Sydney Memory and Ageing Study (MAS) and Older Australian Twins Study (OATS), have multimodal MRI data – T1- weighted, FLAIR, DTI, rs-fMRI, SWI, and ASL – in the same individuals to allow development of a composite measure. We will use contemporaneous neuropsychological data in MAS to develop the MRI CVD Index and test it in the independent OATS cohort. This project is ongoing but pilot data supports our approach. A multiple regression analysis was performed on 310 participants in the MAS, with global cognition as the dependent variables and individual CVD markers as the independent variables. Results showed that Peak Skeletonised Mean Diffusivity (PSMD), a measure of variability of white matter integrity across the whole brain had the strongest association with global cognition (standardised ß = -0.45, p<0.001). When all markers were considered together, compared to PSMD alone, the overall model improved (change in R square= 0.024, p=0.04), supporting the value of a composite index.

Dr Maree Farrow
Email: Maree.Farrow@utas.edu.au Presentation Type: Oral - DCRC
Memory performance is associated with exposure to risk factors
Maree Farrow 1, Shannon Klekociuk 1, David Ward 1, James Vickers 1, Kathryn Ellis 2, Kaarin Anstey 3
1. Wicking Dementia Research and Education Centre, University of Tasmania
2. Academic Unit for Psychiatry of Old Age, University of Melbourne
3. Centre for Research on Ageing, Health and Wellbeing, Australian National University

Previous research found performance on a paired-associate delayed-recall memory task was associated with age, education and histories of cerebrovascular and Parkinson’s diseases in adults aged 50 and over completing an online dementia risk assessment. This study investigated relationships between performance on the same memory task and risk factors measured by the Australian National University Alzheimer’s disease risk index (ANU-ADRI) in participants of the University of Tasmania’s Preventing Dementia Massive Open Online Course.
714 participants aged 50 and older (mean age = 59.08, SD = 6.40) completed the study. The majority were female (88.4%) and well educated (mean years of education = 16.78, SD = 3.97). Memory scores were weakly but significantly correlated with age (rS(712) = -0.11, p < 0.01), education (rS(712) = 0.08, p < 0.05), and the ANU-ADRI total risk (rS(712) = -0.15, p < 0.001).

9.7% of participants reported symptoms above the cut off suggestive of depression, and this was associated with worse memory performance (p < 0.01). 50.4% of participants engaged in protective levels of cognitive activity and this was associated with better memory performance (p < 0.05). These findings support previous research suggesting exposure to dementia risk factors is related to an individual’s level of functioning prior to the onset of any cognitive disorder.

Professor Marita McCabe
Email: marita.mccabe@acu.edu.au Presentation Type: Oral - DCRC
How effective is consumer directed care in residential care
Marita McCabe, Elizabeth Beattie, Gery Karantzas, David Mellor, Kerrie Sanders, Lucy Busija, Kathryn von Treuer, Belinda Goodenough, Michelle Bennett
Deakin University
Introduction: Australia is striving toward a model of care that is both centered on and directed by the consumer. Consumer Directed Care (CDC) is expected to be mandated for Residential Aged Care Facilities (RACFs) in the near future. The aim of this study was to implement and evaluate our Resident at the Center of Care (RCC) staff training program in RACFs. This paper presents information on the facilitators and barriers that we found in relation to the implementation of CDC, as well as the outcomes for residents and staff.
Method: Staff and residents were recruited to participate in the study from six RACFs in Queensland and Victoria. Facilities were randomly allocated into intervention and control conditions. Data were gathered from staff after they had completed the program on the facilitators and barriers to implementing CDC. In addition, resident and staff quality of life (QoL) was evaluated at baseline and three months’ follow-up.
Results: The major facilitators were staff supporting each other, respect and clear processes. The major barriers were the culture of the RACF, resources to implement CDC and communication between other staff and residents. Staff felt pressured, confused and that there was too much change. Residents in the intervention conditions demonstrated improved QoL compared to the control condition. Senior staff, but not junior staff, in the intervention conditions also demonstrated improved QoL.
Conclusions: The implementation of CDC into RACFs is not just a matter of educating staff on CDC and how to obtain resident choices. There is a need for significant changes in the organisational structure of the facility, staff empowerment, time management and communication. This is a process that will take some time to achieve, but the results of our study demonstrate that it is possible to implement CDC in RACFs and improve the wellbeing of both residents and staff.

Professor Kate Stevens
Email: kj.stevens@westernsydney.edu.au Presentation Type: Oral - DCRC
Time-Travelling with Technology (TTT): Google Liquid Galaxy and Reminiscence Therapy
Kate Stevens, Deborah Parker, Andrew Leahy, Janice Stokes, Karen Watson, and Daniel Piepers
Western Sydney University
Reminiscence Therapy (RT) provides an opportunity for people with dementia to talk about memories. Photographs, for example, may elicit recall of life experiences, promoting communication and helping sustain relationships. An experiment investigated whether coupling RT and immersive technology is feasible and beneficial. We hypothesized that if a sense of envelopment and continuity with personally meaningful “landmarks” enriches RT then an experimental group experiencing a full immersive, dynamic experience will show reduced behavioural problems from pre- to post-intervention compared with a control (no envelopment, continuity) condition. Five large immersive displays with participants and facilitator “travelling through” pre-loaded Google Earth and Streetview landmarks formed the 6-week group intervention. Amount of immersion (3 displays) and dynamism were controlled in the comparison condition with landmarks instead presented as static, large ‘postcard-like’ images. The range and mean of MMSE scores from both
groups prior to the experiment were similar and the MMSE used as a covariate. Two experiments have been completed with data from the first analysed. Results from Experiment 1 (N=24) showed a significant decrease in mean scores on the Neuropsychiatric Inventory from pre- to post-intervention in the experimental but not in the control condition. There was no significant difference in Quality of Life scale scores from pre- to post-intervention in either condition. Visual and verbal engagement of participants during sessions showed modest differences in engagement between the groups. It appears that RT combined with immersive technology is feasible and can enhance RT. Experiment 2 is currently being analysed and will increase the statistical power and reliability of results.

Dr Cindy Jones
Email: c.jones@griffith.edu.au Presentation Type: Oral - DCRC

**Sexualities & Dementia: Improve Knowledge, attitudes & practices in aged care via interactive live webinars**

Dr. Cindy Jones 1,2 Prof. Wendy Moyle 1,2 Assoc. Prof. Belinda Goodenough 3

1. Optimising Health Outcomes - Menzies Health Institute (Griffith University, Queensland)
2. School of Nursing & Midwifery (Griffith University, Queensland)
3. Dementia Training Australia (University of Wollongong, New South Wales)

Sexualities, older persons, and dementia is a challenging topic combination for workforce education. Aged care workers and health professionals need training to improve their knowledge and skills towards appropriate responses to the expression of sexuality by older people, including those with dementia. This sequential mixed-methods study evaluated the utility, quality and effectiveness of six, once a week 1.5 hour interactive live webinars focused on the expression of sexuality by people with dementia living in residential aged care facilities.

Average attendance rates of the 104 participants was 75.2%. Most participants were female (95.9%) with a mean age of 42.3 years and an undergraduate qualification (71.9%). Results demonstrated significant improvements in participants’ knowledge (p<.000) and attitudes (p<.000) assessed following the webinars. Not only were the webinars positively received, but practice change was also reported from newly gained knowledge or skills. This study demonstrates the acceptability and effectiveness of interactive live webinars in workforce education for a topic considered ethically challenging for some dementia care philosophies. It is recommended that webinar formats be considered in the suite of education delivery options that may offer equity of access for rural and remote areas of Australia.
Presentation Abstracts

Dr. Scott Ayton
Email: scott.ayton@florey.edu.au Presentation Type: Oral Theme: Assessment and Diagnosis

Cerebral quantitative susceptibility mapping predicts β-amyloid-related cognitive decline
Scott Ayton 1, Amir Fazollahi 2,3, Pierrick Bourgeat 2,3, Parnesh Raniga 2, Amanda Ng 4,5, YenYing Lim 1, Ibrahima Diouf 1,2, Shawna Farquharson 1, Jurgen Fripp 2,3, David Ames 5,6, James Doecke 2,3, Patricia Desmond 7, Roger Ordidge 4, Colin L. Masters
1. Florey Institute of Neuroscience and Mental Health, The University of Melbourne.
2. CSIRO Health and Biosecurity, Australian E-Health Research Centre.
3. Cooperative Research Centre for Mental Health.
4. Department of Anatomy and Neuroscience.
6. University of Melbourne Academic Unit for the Psychiatry of Old Age.
7. Department of Medicine and Radiology, Royal Melbourne Hospital.
8. Austin Health.
9. Cogstate Ltd.

The large variance in cognitive deterioration in subjects who test positive for β-amyloid (Aß) by PET indicates that convergent pathologies, such as iron accumulation, might combine with Aß to accelerate Alzheimer’s disease progression. Indeed, we recently found that elevated CSF ferritin (reporting brain-iron) predicted cognitive decline and risk of developing AD in a 7-year prospective study (Ayton et al JAMA Neurology, 2016; Ayton et al Nature Communications, 2015). Here, we applied Quantitative Susceptibility Mapping (QSM), a relatively new MRI method sensitive to tissue iron, to assess the relationship between iron, Aß load, and cognitive decline in subjects who underwent baseline QSM-MRI and Aß-PET from the Australian Imaging, Biomarkers and Lifestyle study (AIBL). Cognitive function data were collected every 18 months for up to 6-years from 100 volunteers classified as cognitively normal (n=64) or diagnosed with mild cognitive impairment (n=17) or Alzheimer’s disease (n=19). Among participants with amyloid pathology (n=45), higher hippocampal QSM levels predicted accelerated deterioration in composite cognition tests for episodic memory (P= 9.2 x 10^-7), executive function (P=0.004), and attention (P=0.012). Deteriorating performance in a composite of language tests was predicted by higher QSM levels in temporal lobe (P=0.036) and frontal lobe (P=0.006). These findings indicate that iron might combine with Aß to accelerate clinical progression and that QSM could be used in combination with Aß-PET to stratify individuals at risk of decline. Therefore, lowering brain iron with a drug such as deferiprone could slow disease progression, which we will test in a clinical trial beginning in 2017.

Dr Samantha Barton
Email: samantha.barton@ed.ac.uk Presentation Type: Oral Theme: Intervention and Treatment

Using patient iPS-derived oligodendrocytes harbouring a C9ORF72 mutation to identify disease causing mechanisms in ALS–FTD
Samantha Barton1,2,3,4,5, Elaine Cleary 2,3, Navneet Vasishta 1,2,3, Bhuvaneish T Selvaraj1,2,3, Dario Magnani 1,2,3, Karen Burr1,2,3, David Story 1,2,3 & Siddharthan Chandran1,2,3
1. Euan MacDonald Centre for MND Research, University of Edinburgh, United Kingdom.
2. Centre for Clinical Brain Sciences, University of Edinburgh, United Kingdom.
3. MRC Centre for Regenerative Medicine, University of Edinburgh, United Kingdom.
4. Hudson Institute of Medical Research, Melbourne, Australia.
5. Monash University, Melbourne, Australia.

Hexanucleotide repeat expansions (HRE) in the C9ORF72 gene remain the most common genetic abnormality in frontotemporal dementia (FTD) and amyotrophic lateral sclerosis (ALS). Whilst neuronal loss is the hallmark pathology associated with ALS-FTD, accumulating evidence from experimental and pathological studies implicate a role for non-neuronal cells in disease causation. More specifically, MRI and DTI in patients with ALS-FTD has shown altered myelination suggesting a role for oligodendrocytes (the myelin producing cell) in disease progression. Whether this myelination impairment is a result of neuronal death or is intrinsic to the diseased oligodendrocyte remains unknown. Given the importance of oligodendrocytes to not only myelinate neurons but also to provide metabolic support, this remains an important gap in dementia research. Thus, the aim of this project was to determine the role of oligodendrocytes harbouring...
a C9ORF72 mutation in ALS-FTD disease using patient-derived induced pluripotent stem cells (iPSC). We have three cell lines derived from patients carrying a C9ORF72 HRE as well as isogenic controls to these mutants (genetically identical to the mutant patient lines but with the C9ORF72 HRE removed via CRISPR-Cas9 genome editing), and also have two unrelated control lines. We have successfully generated oligodendrocytes from all eight lines. Thus, using these patient lines we are in the process of characterising the morphological and functional differences in C9ORF72 patient-derived oligodendrocytes compared to controls, with the aim of elucidating the role of a C9ORF72 mutation in oligodendrocytes in ALS-FTD pathology.

Dr Belinda Brown
Email: B.Brown@murdoch.edu.au Presentation Type: Oral Theme: Intervention and Treatment
Update on the Intense Physical Activity and Cognition (IPAC) Study
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Inconsistent results from previous studies of exercise and cognitive function suggest that rigorously designed randomised controlled trials are urgently needed. The Intense Physical Activity and Cognition (IPAC) study will assess the impact of a 6 month high-intensity exercise intervention on cognitive function and biomarkers of dementia risk, compared with a 6 month moderate-intensity exercise intervention and control group (no study-related exercise).

Cognitively healthy men and women aged between 60 and 80 years are randomised into either a high-intensity exercise, moderate-intensity exercise or control group. Individuals randomised to an exercise intervention undertake six months of cycle-based exercise twice a week, at 50 minutes per session. All participants undergo comprehensive neuropsychological testing, blood sampling, brain magnetic resonance imaging, and fitness testing at baseline, 6 months (post-intervention) and 18 months (12m post-intervention). In addition, at 3 months (mid-intervention), fitness is assessed.

To date, we have completed 70 baseline assessments (target: n = 105), and 5 post-intervention assessments. Our attrition rate is currently 5%, with personal reasons and illness unrelated to the intervention cited as the factors contributing to withdrawal. Preliminary analysis of our baseline and 3 month fitness data (n = 21) has revealed greater increases in VO2max (fitness) in the high-intensity group (23%), compared with the moderate-intensity group (13%; HI vs MI, Cohen’s d = 0.4) and control group (3%; HI vs control; Cohen’s d = 0.8); suggesting our intervention groups are achieving desired exercise intensities. We expect to complete baseline assessments by the end of October 2017 and post-intervention analyses and publication is anticipated by mid-2018. Long-term effects of the intervention (i.e. utilising 18 month data) will be evaluated and published by mid-2019.

Dr Emma Louise Burrows
Email: emma.burrows@florey.edu.au Presentation Type: Oral Theme: Intervention and Treatment
Progressive Behavioural Flexibility Impairments in the APP/PS1 mouse model of Alzheimer’s disease as measured by translatable touchscreen technology
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Cognitive decline is a core feature of Alzheimer’s disease (AD) and there is no cure or treatment. Genetic mouse models are major tools to investigate mechanisms underlying cognitive decline however, to date, assessment of cognition in mice has been unrelated to the clinic. Recently developed touchscreen technology facilitates the assessment of cognitive domains, directly relevant to impairments described in AD patients. We examined mice containing familial mutations in amyloid precursor protein (APP), and presenilin-1 (PS1) using a touchscreen task assessing behavioural flexibility, a component of executive function. Mice were initially trained to discriminate between two visual stimuli projected onto a touch-sensitive computer screen and associate one with a reward. To assess behavioural inflexibility, the rewarded stimulus was reversed. No differences in visual discrimination or in time to complete reversal learning were seen in 12-month old APP/PS1 animals. During reversal however, APP/PS1 mice required significantly more correction-learning trials, indicative of a subtle impairment in behavioural flexibility. Compared to WT littermates, 24-month old APP/
PS1 mice were impaired in both visual discrimination and reversal and required significantly more correction-trials to acquire the new reward-contingency. Given the nature of cognitive assessment, impaired vision may influence deficits in APP/PS1 mice. Clinical analysis of retinal health was assessed with functional (electroretinography) and structural (optical coherence tomography) assays at time-points coinciding with subtle and severe impairments. This is the first report of behavioural flexibility deficits in APP/PS1 mice and the approach of utilising clinical modes of assessment has great potential to facilitate translation from pre-clinical models to the clinic.

Dr Shantel Duffy
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The longitudinal relationship between anterior cingulate glutathione and executive functioning in individuals at-risk for dementia: A magnetic resonance spectroscopy study
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Background: Oxidative stress is characterised by an imbalance in the redox state of cells and has been implicated in pathogenesis of neurodegenerative disease. Our prior work has shown that glutathione (GSH), the brain's major antioxidant and a marker of oxidative stress, in the anterior cingulate cortex (ACC) is associated with executive functioning in individuals with Mild Cognitive Impairment (MCI). This study aimed to extend our prior work and examine the longitudinal relationship between ACC GSH and executive functioning in this cohort.

Methods: Twenty-eight older adults meeting criteria for MCI were recruited from the Healthy Brain Ageing Clinic, University of Sydney. All participants underwent comprehensive psychosocial, medical and neuropsychological assessment at baseline and after >2-years (mean=3.3 years). Magnetic resonance spectroscopy in the ACC was completed within 2-weeks of both assessment time-points. Absolute GSH concentration was calculated using the calibration curve derived from our previously published phantom data. Executive functioning was assessed via the Trail Making Test-Part B (TMT-B).

Results: Overall, greater baseline ACC GSH concentration was associated with a decline in TMT-B performance longitudinally ($r=-0.41$, $p=0.029$). Furthermore, change in GSH between assessments correlated with an improvement in executive functioning ($r=0.39$, $p=0.045$). These correlations remained significant when controlling for age and time between assessments.

Conclusion: This study demonstrates a significant relationship between ACC GSH and executive functioning longitudinally. Importantly, higher baseline GSH was associated with poorer executive functioning, however, an increase in ACC GSH over time was associated with improved performance longitudinally. These findings may suggest a compensatory up-regulation of GSH production in response to oxidative insult as a result of neurodegenerative pathology. Further research examining GSH in other brain regions and continued longitudinal tracking of participants and their clinical trajectory is now warranted.

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Eye imaging for early detection of alzheimer’s disease
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**Objectives:** We are testing multiple modalities of eye imaging for early detection and monitoring of Alzheimer’s disease (AD). Retinal amyloid-beta plaques are imaged in-vivo using oral dosing with curcumin. The retinal microvasculature is also imaged to investigate the vascular component of AD, and the thickness of nerve cell layers in the retina is imaged using optical coherence tomography to evaluate inflammation and atrophy. Additionally, central cholinergic depletion in AD may extend to the anterior eye and present as altered pupil light response.

**Methods:** Retinal Amyloid-beta imaging involves two visits by volunteers for retinal imaging. Between appointments, volunteers take a proprietary Curcumin supplement. Curcumin binds to Amyloid-beta with high affinity and has fluorescence properties that enable Amyloid-beta plaques to be imaged in the retina using a scanning laser ophthalmoscope. The retinal vasculature is imaged using colour retinal photography and retinal inflammation/atrophy is evaluated using optical coherence tomography. Pupil flash response is measured using a pupilometer. Quantitative analysis of ocular data is performed using automated computer assisted techniques.

**Results:** Significantly more retinal Amyloid-beta was found in the AD group (n=22) compared to the healthy control (HC) group (n=137) (p=0.0054), and an index of retinal Amyloid-beta correlated with brain Amyloid-beta burden from positron emission tomography (PET) imaging (R=0.28, p=0.000065). Longitudinal follow-up imaging demonstrated an increase in retinal plaques over 3 months for PET-positive participants. Constriction phase pupil response parameters were significantly reduced in AD compared to HC (maximum acceleration p < 0.05, maximum velocity p < 0.0005, average velocity p < 0.005, and constriction amplitude p < 0.00005). The PET-positive HC subgroup had reduced pupil response cross-sectionally, and also a greater decline longitudinally, compared to the PET-negative subgroup, suggesting changes to pupil response in preclinical AD.

**Conclusions:** The results suggest that ocular changes may occur in the preclinical phase of AD. Hence, eye testing has a potential as an adjunct for noninvasive, cost-effective screening for preclinical AD. Ocular testing is a potential initial screen for AD that could be delivered as part of regular eye checks. Micrometer-level imaging resolution could also allow accurate monitoring of individual retinal plaques within AD therapeutic trials.

Dr Julia Gilmartin-Thomas

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**Presentation Type:** Oral

**Theme:** Care

**Qualitative and quantitative impact of a virtual dementia experience on medical and pharmacy students’ knowledge, attitudes and self-reported behaviour toward people with dementia**

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**Aim:** Quantitatively and qualitatively evaluate the impact of a virtual dementia experience on medical and pharmacy students’ knowledge, attitudes and self-reported behaviour toward people with dementia.

**Methods:** Medical (3rd year) and pharmacy (4th year) university students participated in a non-randomised controlled study (Sept-Oct’16). In addition to standard curriculum, the intervention arm experienced cognitive/perceptual difficulties of dementia via a 1.5 hour virtual simulation, along with facilitator-guided reflection and discussion. The control arm participated in standard curriculum only. All students were invited to complete the 20-item Dementia Attitudes Scale pre/post-intervention (O’Connor M et al. Int J Alzheimers Dis. 2010). The intervention arm were invited to participate in a focus group. Results: Paired pre/post questionnaire responses were received from 64 medical and 214 pharmacy students. The intervention arm (n=80) showed statistically significant improvements in knowledge, attitudes and self-reported behaviour toward people with dementia, compared to the control arm. Participants (n=49) from the 10 focus groups described the utility of the intervention for their future healthcare roles.

**Conclusion:** This study showed that a virtual dementia experience had a positive impact on medical and pharmacy students’ knowledge, attitudes and self-reported behaviour toward people with dementia.
Iron, Copper, and Zinc concentration in Aβ plaques in the APP/PS1 mouse model of Alzheimer’s disease correlates with metal levels in the surrounding neuropil

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The metal ions of iron, copper, and zinc have long been associated with the aggregation of β-amyloid (Aβ) plaques in Alzheimer’s disease; an interaction that has been suggested to promote increased oxidative stress and neuronal dysfunction. Using X-ray fluorescence microscopy, we examined the metal load of plaques in the hippo-campus of APP/PS1 mice to assess how the anatomical location of Aβ plaques was influenced by the metal content of surrounding tissue. Immunohistochemical staining of Aβ plaques colocalized with areas of increased X-ray scattering power in unstained tissue sections, allowing direct X-ray based-assessment of plaque metal levels in sections subjected to minimal chemical fixation. We identified and mapped 48 individual plaques in four subregions of the hippocampus from four biological replicates. Iron, Cu, and Zn areal concentrations (ng cm-2) were increased in plaques compared to the surrounding neuropil. However, this elevation in metal load reflected the local metal makeup of the surrounding neuropil, where different brain regions are enriched for different metal ions. After correcting for tissue density, only Zn levels remained elevated in plaques. This study suggests that the in vivo binding of Zn to plaques is not simply due to increased protein deposition.

Why do patients with frontotemporal dementia misinterpret social cues?
The importance of context

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The importance of assessing social cognition to characterise dementia syndromes is increasingly recognised. Emotion recognition is impaired in both behavioural-variant frontotemporal dementia (bvFTD) and semantic dementia (SD), yet how these impairments manifest in day-to-day life differs. Importantly, most studies have investigated emotion recognition of isolated, context-free faces. Here, we aimed to determine how contextual information (i.e., body language) influences emotion recognition. Thirty-one frontotemporal dementia patients (19 bvFTD; 12 SD) and 20 healthy age- and education-matched controls were assessed on three tasks which varied contextual cues: (i) Face alone; (ii) Context alone; (iii) Face embedded in context. Neuroimaging analyses were employed to examine neural correlates of task performance. Our results demonstrated that both bvFTD and SD performed worse than controls in recognising emotions from Face alone and Context alone, but performance differed when faces were presented in context. While both bvFTD and SD performed similarly to controls on congruent items, bvFTD performed worse than both controls (p < .001) and SD (p = .049) for incongruent items. Neuroimaging analyses revealed that abnormal contextual influence was associated with lower integrity of the right parahippocampal gyrus/amygdala and left precentral gyrus. Together, these results indicate that bvFTD patients are over-reliant on external contextual information, whereas in SD contextual influence is mediated in part, by the facial expression. The profile in bvFTD is reminiscent of the “environmental dependency syndrome” described in frontal lesion patients. Clinically, these results offer new potential for therapeutic intervention of social impairments in dementia.
**Dr Yen Ying Lim**  
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**Presentation Type:** Oral  
**Theme:** Assessment and Diagnosis

**BDNF Val66Met increases rate of memory decline, hippocampal volume loss and tau accumulation in autosomal dominant Alzheimer’s disease**

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**Background:** The brain-derived neurotrophic factor (BDNF) Val66Met polymorphism (rs6265) is implicated in synaptic excitation and neuronal integrity. In autosomal dominant Alzheimer’s disease (ADAD), mutation carriers (MC) who also carry the Met66 allele show worse memory and higher levels of cerebrospinal fluid (CSF) tau, but equivalent amyloid levels compared to MC Val66 homozygotes at baseline. The aim of this study was to determine the extent to which the BDNF Val66Met polymorphism affects changes in memory, brain volume, tau and Aβ in ADAD prospectively.

**Methods:** Prospective neuropsychological, biomarker and neuroimaging data collected from the Dominantly Inherited Alzheimer Network (DIAN) over ~2 years were analyzed in 81 preclinical mutation carriers (MC), all with a clinical dementia rating (CDR) score of 0 and estimated to be 11 years prior to clinical symptom onset, and 78 matched mutation non-carriers (NC). BDNF genotype was obtained for MCs (58 Val66 homozygotes, 23 Met66 carriers).

**Findings:** Compared to MC Val66 homozygotes, MC Met66 carriers showed greater decline in episodic memory (p<.001), loss of hippocampal volume (p=.005), and increase of CSF tau (p<.001). Cortical Aβ accumulation was equivalent between MC Val66 homozygotes and MC Met66 carriers (p=.427). Compared to NCs, MC Val66 homozygotes showed greater increase in cortical Aβ accumulation (p<.001) but equivalent rates of change in episodic memory decline (p=.700), loss of hippocampal volume (p=.215), and accumulation of CSF tau (p=.266).

**Interpretation:** ADAD is associated with pathologically increased rates of Aβ and tau accumulation, loss of hippocampal volume and decline in episodic memory. The results of the current study show that for MCs who also carry the BDNF Met66 allele, decline in episodic memory, loss of hippocampal volume and increase in CSF tau is substantially greater than for MCs who are Val66 homozygotes, despite equivalent rates of Aβ accumulation. This is consistent with findings in preclinical sporadic AD, where amyloid positive Met66 carriers also show faster deterioration in episodic memory and hippocampal volume, but not Aβ accumulation, when compared to Aβ+ Val66 homozygotes. Together, these data suggest that the BDNF Val66Met polymorphism modifies the contributions to the neurodegenerative process in ADAD.

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**Dr Erin McAllum**  
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**Presentation Type:** Oral  
**Theme:** Intervention and Treatment

**Metalloproteomic changes in Dementia with Lewy bodies**

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Biologically-relevant metals have been implicated in neurodegeneration, stretching back nearly 100 years to when iron was first identified to be abnormally distributed in the Parkinson’s disease brain. Metals have subsequently been associated with multiple neurodegenerative diseases, yet most studies have focussed primarily on measuring changes in metal levels and not the relationship between metals and the biochemical factors that determine their neurological function. Thus, understanding the relationship between metals and their protein ligands is essential to elucidate how metal imbalances participate in neuropathology. Chromatographic separation of proteins prior to metal analysis, offers a relatively simple and effective means of assessing metal-protein binding of soluble proteins, allowing identification of discrete changes that may be masked by measurement of total metal levels. We combined chromatography and element-specific detection to profile soluble metalloproteins in dementia with Lewy bodies, the second most common form of dementia. In the disease-affected entorhinal cortex and anterior cingulate cortex, metal levels were not universally altered in dementia with Lewy bodies compared with controls; rather, changes were associated with specific copper-binding metalloproteins. No changes were observed in unaffected brain regions. Identification of these metalloproteins will allow investigation of how their altered binding of metals may contribute to disease, potentially leading to targeted therapies correcting aberrant metalloprotein function.
Detecting subtle functional decline in prodromal dementia

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There is increasing recognition of mild functional decline even in those ‘at risk’ of dementia; however this is infrequently assessed and difficult to capture with gross measures. As such, we aimed to examine the utility of a brief, clinically-relevant self-report tool for functional change. In this study, 229 older adults completed the Healthy Brain Ageing Functional Assessment Questionnaire (HBA-FAQ) in addition to comprehensive neuropsychological, medical and mood assessments. On clinical consensus, participants were categorized as healthy, subjective memory complaints (SMC), Mild Cognitive Impairment (MCI), or dementia. Using one-way ANOVA with planned contrasts, we compared the utility of the HBA-FAQ to that of the clinician-rated Instrumental Activities of Daily Living (IADL) scale (n=138), a widely used measure of gross functional decline for older adults. A subset (n=37) also completed longitudinal cognitive assessment. The HBA-FAQ differentiated between healthy and all clinical groups (t(28.31)=9.46, p<0.05), as well as between those with SMC/MCI and dementia (t(38.45)=-2.04, p<0.05); but there were no differences between SMC and MCI groups (t(100.78)=0.54, p>0.05). By contrast, the clinician-rated IADL scale only differentiated between healthy and clinical groups (t(15.96)=-2.13, p<0.05) and could not detect early functional change in prodromal groups (t(15.24)=1.70, p>0.05). At longitudinal follow-up, the baseline HBA-FAQ total score was predictive of poorer memory (r=-0.364, p<0.05). Compared to a widely used clinician-rated IADL scale for older adults, the self-report HBA-FAQ is better able to detect subtle functional change even in those with SMC and MCI, and importantly is predictive of long-term cognitive performance. This suggests promising clinical utility for this instrument, which now requires further psychometric evaluation.

Effects of BACE inhibition on synaptic connectivity

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Overview: Inhibition of BACE1 (ß-secretase) is a promising treatment for Alzheimer’s disease which aims to decrease production of the amyloid-ß peptide. BACE inhibitors also affect the functions of multiple proteins which are not associated with Alzheimer’s disease pathology including the Seizure-related gene 6 (Sez6) family of proteins, Sez6, Sez6-like (Sez6L) and Sez6-like 2. Sez6 is required for the normal development of dendrites and excitatory synapses. In this study, we are assessing whether long-term BACE inhibition compromises synapse function in mice, focusing on the altered activity of Sez6 family proteins. RESULTS: Sez6, in addition to its involvement in neurodevelopment, plays an ongoing role in excitatory synapse function in the adult mouse brain. Sez6L, which was recently validated as a BACE1 substrate in vivo, is localised widely within the cortex and hippocampus. Preliminary analysis of Sez6L KO mice indicates deficits in motor function. Mice lacking all Sez6 family members (TKO mice) do not perform as well as wild-type (WT) mice in context fear conditioning and the Morris Water Maze, have significant deficits in motor function, and have fewer mature spine types in the cortex. CONCLUSION: Sez6 family proteins are BACE1 substrates that play an important role in synapse formation, maintenance and behaviour. We are currently investigating the effect of chronic BACE inhibition in TKO and WT mice.
Dr Kylie Radford  
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Presentation Type: Oral  
Theme: Prevention

Life course social and biomedical factors associated with dementia in Aboriginal Australians

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**Background:** The number and proportion of older Aboriginal and Torres Strait Islander peoples is increasing rapidly. Recent studies have shown dementia prevalence is three times higher across remote, regional and urban Aboriginal communities; dementia incidence is also high and onset occurs at an earlier age.

**Methods:** We examined potential risk factors for high dementia rates in a cross-sectional study of the total population aged 60 years and older from five NSW regional and urban Aboriginal communities (n=336). Both proximal (standard biomedical factors and mid-life social factors) and early life factors, including childhood trauma and education, were measured.

**Results:** As expected, a number of standard biomedical risk factors (e.g. head trauma, stroke) were associated with late-life dementia in Aboriginal Australians aged 60 to 92 years; childhood trauma was independently associated with all-cause dementia and Alzheimer's dementia, as well as being partially mediated by an association with proximal biomedical factors. Opportunity for skilled employment (linked to education) was also significantly associated with dementia in multivariate models.

**Conclusions:** A life course approach to understanding dementia risk and prevention in Aboriginal Australians is critical and greater focus on the social determinants of health likely needed to reduce the rates of premature cognitive decline.

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Presentation Type: Oral  
Theme: Intervention and Treatment

An ALS-FTLD associated mutation of SQSTM1/p62 attenuates oxidative stress signalling and autophagy

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**Background:** In recent years, the genes implicated in ALS-FTLD pathogenesis have expanded to include SQSTM1, which encodes the autophagy receptor and signalling scaffold protein SQSTM1/p62. Knowledge of the different mechanisms underlying pathogenesis in these familial cases is incomplete. A missense mutation affecting the LC3 interacting region (LIR) of SQSTM1/p62 (p.L341V) impacts on incorporation of the protein into acidic autophagic vesicles. Further, two mutations affecting the Keap1 interacting region (KIR, residues 347-352) of SQSTM1/p62 (p.P348L and p.G351A) impede activation of the oxidative stress transcription factor Nrf2, due to reduced ability to bind to the Nrf2 regulatory protein Keap1.

**Objectives:** Our objective was to define the molecular basis of the pathogenic effects of an ALS-associated missense mutation (p.R110C) affecting the N-terminal PB1 domain of SQSTM1/p62, as mutations affecting this region of the protein have not yet been investigated.

**Methods:** For Luciferase reporter assays, NSC34 cells were transiently transfected with expression vectors for wild type or p.R110C FLAG-tagged SQSTM1/p62 (or p.P348L control) along with a luciferase reporter for the NQO1, Nrf2 responsive gene and a renilla reporter. Cells were treated with Luperox 24h post transfection, or left untreated and dual luciferase readings obtained. For co-immunoprecipitations, NSC34s were transfected with FLAG-tagged expression constructs. 48h post-transfection cells were lysed in RIPA buffer and FLAG-SQSTM1/p62 immunopurified with anti-FLAG. After washing co-bound endogenous Keap1 was detected by western blot. The effect of mutation status on Ser403 phosphorylation was determined by western blot.

**Results:** Although located outside of the KIR, the p.R110C-SQSTM1/p62 mutation was associated with decreased activation of Nrf2, compared to wild type protein. In these assays p.R110C and p.P348L expression activated Nrf2 ~2-fold compared with control cells, whereas wild type activated Nrf2 3-fold. These results were observed in cells treated with Luperox, and untreated cells. In the case of both variants reduced Nrf2 activation correlated with reduced Keap1 phosphorylation.
binding in immunoprecipitation experiments. We also observe that p.R110C mutant also exhibited reduced TBK1-mediated phosphorylation of SQSTM1/p62 at Ser403, a modification that is important for SQSTM1/p62 mediated autophagy.

**Discussion and Conclusions:** The p.R110C variant lies outside of the region (KIR) required for Keap1 interaction, instead affecting the PB1 domain which mediates SQSTM1/p62 oligomerisation. We also find that p.R110C led to a reduction in phosphorylation of Ser403. Thus, we hypothesise that this variant may result in subtle changes to signalling complex formation, with downstream detrimental effects on the oxidative stress response and potentially autophagy.

**Dr Edwin Tan**  
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**Presentation Type:** Oral  
**Theme:** Intervention and Treatment  
**Acetylcholinesterase inhibitors and risk of stroke and death in people with dementia**

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**Background/Objective:** Cardiovascular disease is a major cause of death worldwide, including in people with dementia. Previously, we found an association between acetylcholinesterase inhibitor (AChEI) use and reduced risk of myocardial infarction and death (Nordström et al 2013). In the present study, we investigate whether a similar association exists between AChEI use and risk of ischaemic stroke and death in people with dementia.

**Methods:** This was a cohort study based on 44288 people diagnosed with dementia who were registered in the Swedish Dementia Registry (SveDem) from 2007 – 2014. Data on AChEI use was linked to diagnosed ischaemic strokes and death using national registers. Propensity-score matched competing risk regression models were used to compute hazard ratios (HRs) and 95% confidence intervals (CIs) for the association between time-dependent AChEI use and risk of stroke and death.

**Results:** During a mean follow-up period of 941 (range 1 – 3470) days, 2084 people had a stroke and 11276 died. In comparison with matched controls, people who used AChEIs had a lower risk of stroke (HR: 0.87, 95%-CI: 0.77 – 0.98) and all-cause death (HR: 0.77, 95%-CI: 0.73 – 0.81). After considering death as a competing risk, high doses of AChEI remained significantly associated with reduced stroke risk (Subdistribution HR: 0.78, 95%-CI: 0.66 – 0.93). Subgroup analyses in those with Alzheimer’s Disease produced similar findings.

**Conclusions:** The use of AChEIs in people with dementia may be associated with reduced risk of ischaemic stroke and death. These results call for a closer examination of the cardiovascular effects of AChEIs.

**Dr Nawaf Yassi**  
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**Presentation Type:** Oral  
**Theme:** Assessment and Diagnosis  
**Cortical Cerebral Microinfarcts on 3T MRI in Alzheimer’s Disease**

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The prevalence of cortical cerebral microinfarcts (CMI) on neuropathological studies of Alzheimer’s disease (AD) is reported at approximately 40%, and they are associated with cognitive impairment. Recent studies have validated the detection of CMI in vivo using both 7T and 3T MRI. We aimed to investigate the prevalence of CMI in patients with AD, mild cognitive impairment (MCI) and healthy controls (HC) from the Australian Imaging, Biomarkers and Lifestyle Study of Ageing (AIBL), and to examine their association with vascular risk factors.
### Poster Abstracts

**Dr Alaa Abdul-Ridha**  
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**Theme:** Intervention and Treatment  
**Targeting GPCRs for the treatment of Alzheimer's Diseases**

Alaa Abdul-Ridha and Daniel James Scott  
Florey Institute of Neuroscience and Mental Health

Alzheimer’s disease (AD) is a devastating, multifactorial neurodegenerative disease clinically featured by cognitive impairment and progressive memory loss. The AD brain is characterised by accumulation amyloid-beta (Aβ) plaques and neurofibrillary tangles (NFTs) of tau proteins. Current AD treatments are inadequate and do not prevent or slow down the progression of the disease and fundamentally new treatment approaches are required. Much of the research has focussed on amyloid and tau proteins which have not been very successful to date. The current project aims to develop novel drug candidates for the treatment and prevention of AD and other neurodegenerative disorders by targeting G protein-coupled receptors (GPCRs). GPCRs comprise the largest family of cell-surface receptors and play critical roles in brain neurotransmitter systems that are disrupted in AD. GPCRs also affect the major hallmarks of AD pathology, regulating the formation Aβ plaques and NFTs. Currently, there are no approved GPCR targeting drugs for AD and other dementia causing conditions. Amongst the numerous GPCRs implicated in AD, the α1A- and α1B-adrenoceptors are emerging as important therapeutic targets. While these receptors are targeted clinically by non-selective α1-AR blockers in cardiovascular disease, their role in the cardiovascular and central nervous systems remains poorly understood due to the lack of subtype selective ligands. We have identified several subtype selective compounds from a trail fragment screen which are currently being characterised and have a therapeutic potential for AD.

**Dr Sophie Andrews**  
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**Theme:** Prevention  
**High-intensity interval exercise enhances neuroplasticity in people gene-positive for Huntington’s disease and healthy adults**

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**Background:** Similar to findings in other neurodegenerative diseases, there is evidence that exercise may delay symptom onset in Huntington’s disease (HD). Research using HD mouse-models indicates that this benefit may be via exercise-induced changes to neuroplasticity, however, this has not yet been examined in people gene-positive for HD. One way to measure changes to neuroplasticity in humans is via changes to cortical inhibition and facilitation using Transcranial Magnetic Stimulation (TMS). The aims of the current study were to determine 1) whether a single session of exercise increases neuroplasticity responses to theta-burst stimulation in people gene-positive for HD using TMS, and 2) the optimal exercise intensity (high- versus moderate-intensity) required.

**Methods:** To date 19 healthy adults and 8 HD gene-positive individuals have completed the study. Participants attended three sessions, at each they undertook 20 mins of either high-intensity interval cycling, moderate steady-state cycling, or rest. TMS was applied to the motor cortex pre and post exercise, and post theta-burst stimulation, to measure changes to short-interval cortical inhibition (SICI) and intracortical facilitation (ICF), as markers of neuroplasticity.

**Results:** In the healthy control group, two-way repeated-measures ANOVAs revealed a significant main effect of exercise intensity for both SICI and ICF, and an exercise*time interaction for ICF, where a larger neuroplasticity response was seen following high-intensity exercise compared to rest, and moderate-intensity exercise showed an intermediate effect. A similar trend was seen in the HD group, but this was not significant, likely due to the small sample size.

**Conclusions:** These findings indicate that high-intensity interval exercise, and to a lesser extent moderate-intensity exercise, enhances neuroplasticity in healthy adults. This same effect is likely to also be seen in people gene-positive for HD. If confirmed with a larger sample of HD participants, high-intensity interval exercise could be an effective intervention to enhance neuroplasticity and slow disease progression in HD.
**Glua1 ubiquitination mediates amyloid-beta-induced loss of surface AMPA receptors**

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AMPA-type glutamate receptors (AMPARs) mediate fast excitatory neurotransmission in the mammalian central nervous system. Excessive levels of amyloid-beta (Aβ) levels disrupt excitatory synaptic transmission by promoting the removal of synaptic AMPARs, dendritic spine loss and synaptic depression. Earlier work from our laboratory has shown that the ubiquitination of GluA1 subunit regulates the intracellular sorting of AMPARs toward late endosomes for degradation. Here, I will present data demonstrating that the same ubiquitin signalling pathway mediates Aβ-induced loss of surface AMPARs. We found that acute exposure of neurons to soluble Aβ oligomers induces AMPAR ubiquitination concomitant with the removal of AMPARs from the plasma membrane. Importantly, expression of ubiquitin-deficient GluA1 mutants fully rescues the adverse effects of Aβ on AMPAR surface expression. Furthermore, we identified a cross-talk between GluA1 phosphorylation and ubiquitination in this process, particularly on the phosphorylation of Ser-845 on the GluA1 subunit, which is crucial for AMPAR recycling and is known to be dephosphorylated in the presence of Aβ. Our data showed that the GluA1 ubiquitin-deficient mutant enhances GluA1 phosphorylation on Ser-845 and conversely, the GluA1 S845D phospho-mimetic mutant reduces the binding with Nedd4-1, and hence the ubiquitination of AMPARs. Importantly, the GluA1 S845D mutant also prevents Aβ-induced removal of surface AMPARs. Altogether, these findings demonstrate the importance of dynamic cross-modulation of GluA1 ubiquitination and phosphorylation, a process that is perturbed by Aβ, in regulating membrane sorting decisions that determine the number of AMPARs on the cell surface.

**A comparison of autobiographical memory cues in people with different types dementia**

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**Background and Aim:** Previous research documenting the preservation of ‘music evoked autobiographical memories’ (MEAMs) in people with dementia (PWD) has been limited to Alzheimer’s Dementia (AD). Furthermore, there has been no comparison of music with other stimuli, precluding any examination of whether music is a more effective cue for autobiographical memories. We explored MEAMs compared with photo (PEAMs) and object (OEAMs) evoked autobiographical memories in people with various types of dementia.

**Methods:** 12 PWD, including 9 AD, 1 vascular dementia, 1 vascular/AD, 1 probable behavioural variant frontotemporal dementia (bv-FTD), 2 with mild cognitive impairment (MCI), and 8 aged matched healthy controls reported memories following exposure to 16 songs (number one in Australian music charts) and 16 photos (of famous events), 2 from each decade 1930 - 2010. A subset of 5 PWD also reported memories in response to 16 objects (iconic household objects).

**Results:** MEAMs were more frequent than PEAMs in the majority of PWD and MCI (9/14; 32.6% versus 22.3%). There was no difference between PWD and healthy controls in the mean frequency of MEAMs (p > .05). There was no significant relationship between severity of dementia (mini Addenbrooke’s Cognitive Examination score) and frequency of memories evoked by music, photos or objects (p > .05). In the 5 PWD who completed the OEAM task, the majority (4/5, including the person with bv-FTD) showed more OEAMs than MEAMs or PEAMs (mean frequency 54% OEAMs versus 34% MEAMs and 19% PEAMs), and the mean frequency of MEAMs and OEAMs was in keeping with healthy controls. The person with bv-FTD had no MEAMs and relatively fewer PEAMs, but his OEAMs were in keeping with other PWD and healthy controls.

**Conclusions:** This is the first study to compare autobiographical memories evoked by music with other stimuli, specifically photos and objects, in people with different types of dementia. Our findings indicate that preservation of music, photo and object evoked memories is not related to the severity of dementia, but may be dependent on the type of dementia. Further, preliminary results suggest that objects may be more efficient than music or photos at evoking autobiographical memories in PWD.
Understanding the factors influencing health professionals’ use of supported decision-making in the context of Dementia care

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Do we all make the best decisions for our current circumstance, physical and emotional wellbeing and the future? Human rights-based approaches have led to growing recognition of respecting a person’s will and preference, and supporting decision-making capacity. Emerging research recognizes that even ‘autonomous’ decision-making is influenced by the person’s environment and social relationships. Individuals with dementia, however, face unique challenges, with changes in their environments, social networks and decision-making capacities. The changes can be sudden or slow, making it more difficult to determine when and what type of decision-making capacity is impaired.

Our study examines the experiences of health and legal professionals in facilitating decision-making among people with dementia, and the factors relating to use of supported decision-making in the context of dementia care. Practitioners in medical, allied health, nursing, legal and aged care were selected based on their roles and experience in supporting individuals with dementia in community and residential settings. Semi-structured interviews using an Interpretative Phenomenological Analysis (IPA) approach focus on detailed cases, and explore factors influencing the use of supported decision-making.

The cases described by health professionals have illustrated broad support for the importance of supporting the decision-making of people living with dementia, along with a range of complexities in practice. These findings will contribute to broader recommendations relating to the use of supported decision-making among people with dementia. The interviews will also assist in the development of a factorial survey method to investigate healthcare professionals’ attitudes to, and self-reported use of, supported decision-making approaches, in vignette scenarios.

Learning in preclinical Alzheimer’s disease: Repeated administration of the International Shopping List Test

Florey Institute of Neuroscience and Mental Health

Objective: Recent meta-analyses suggest episodic memory impairment associated with preclinical Alzheimer’s disease (AD) equates to performance on neuropsychological measures approximately 0.15-0.24 standard deviations below that of cognitively healthy older adults. This estimate, however, obscures important information regarding the nature of the dysfunction in episodic memory in this early phase of the disease. The study aimed to investigate the nature and extent of impairment in verbal learning and memory that could be detected at a single assessment if consideration to acquisition of information as well as recall, was given. The second aim was to understand how verbal learning and memory deteriorates in preclinical AD.

Method: Participants were recruited from the Australian Imaging, Biomarkers, and Lifestyle Rate of Change sub-study (AIBL-ROCS). Three groups were included: amyloid-negative healthy older adults (controls; n = 50); amyloid-positive healthy older adults (preclinical AD; n = 25); and amyloid-positive individuals diagnosed with Mild Cognitive Impairment (MCI; n = 22). A verbal list learning task, the International Shopping List Test (ISLT), was administered multiple times over an 18-month period, in addition to the standard AIBL neuropsychological battery.

Results: At baseline, there was no significant difference between the preclinical AD and control groups in rate of acquisition of words, or total and delayed recall. The preclinical AD group showed a significantly greater change over the 18 months on the total score of the ISLT, compared to the control group, with the magnitude of this difference moderate (Cohen’s d = -0.55[-1.04, -0.07]. The control group significantly improved their performance over time. The preclinical AD group did not.

Conclusions: While no significant dysfunction in rate of acquisition associated with preclinical AD was seen at baseline, individuals with pathology suggestive of preclinical AD do show a significant separation of performance compared to those without pathology, over an 18-month period on the ISLT. Interestingly, this may stem from a lack of learning, or practice effects, over time.
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The ORCA experiment: Using online repeated cognitive assessment to identify amyloid-related learning impairments in preclinical Alzheimer’s disease
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Objective: Elevated levels of beta-amyloid (Aß+) in otherwise cognitively healthy older adults increases risk for cognitive decline and progression to a clinical diagnosis of Mild Cognitive Impairment or Alzheimer’s disease (AD), and is therefore considered to be a preclinical phase of AD. Longitudinal studies consistently report that Aß+ is associated with decline in episodic memory in the preclinical stages of AD, while Aß-related memory impairment has been less consistently found. Assessment over several days may increase the likelihood of detecting learning and memory dysfunction in individuals with preclinical AD compared to those without, effectively replicating longitudinal findings over a much shorter period.

Method: The current study developed the Online Repeated Cognitive Assessment (ORCA) to elicit learning of Mandarin character-English word associations over a series of days, using an implicit learning paradigm. Healthy participants aged 18-40 were recruited for the pilot phase to complete ORCA under either a three-trial single-day (n = 10), five-trial five-day (n = 13), or ten-trial five-day (n = 10) condition.

Results: Participants learnt the correct associations in all three conditions. Average accuracy after three sessions reached 62%, whereas learning was more reliably seen when completed over five consecutive days (approximately 80% accuracy).

Conclusions: ORCA is now ready to be used in the preclinical population, where it is expected that compared to cognitively healthy older adults, those with preclinical AD will have slower learning rates and reduced accuracy by day five. This would greatly decrease the time and cost of identifying at risk individuals.

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Spontaneous speech patterns in progressive supranuclear palsy
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Reductions in spontaneous speech output have been documented in patients with the neurodegenerative condition of progressive supranuclear palsy (PSP). Severely reduced spontaneous speech is the hallmark of dynamic aphasia, a language disorder that has been documented in the context of PSP. Recently, an impairment in the “executive” attentional process of energization accounted for the paucity of spontaneous speech in a patient with PSP and dynamic aphasia. Energization is the process of initiating and sustaining a response over time, in the absence of an external cue. This study aimed to investigate spontaneous speech patterns in patients with PSP without dynamic aphasia, and the role of energization. Patients with PSP (n = 6) and healthy older adults (n = 29) were assessed on cognitive baseline tests of attention, language and executive function, alongside narrative tasks for spontaneous speech and an experimental energization task. PSP patients were reduced on some cognitive baselines (e.g., executive function and attention), which is consistent with known deficits in PSP. The spontaneous speech output of the subjects with PSP showed a clear pattern whereby speech rate decreased significantly after the initial time period, indicative of an energization deficit. On the experimental energization task, the PSP patients showed a similar pattern such that responding slowed significantly after the initial time period, but then continued to fluctuate. Overall, executive attentional mechanisms like energization appear to play a key role in spontaneous speech production. Understanding how these underlying processes operate in healthy and pathological ageing, such as in PSP, has theoretical and clinical implications.
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Three way benefits: Dementia and Delirium Care with Volunteers Program
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In 2009 a dementia and delirium care hospital volunteer program was established and piloted at a rural New South Wales (NSW) hospital in partnership with Alzheimer's NSW. The program aimed to address the emotional vulnerability, risks and adverse events experienced by patients with cognitive impairment. Volunteers provided person centred emotional support and practical assistance with eating and drinking. The outcomes demonstrated high acceptance by staff and volunteers with perceptions of improved care, safety and nutrition.
In 2015 grant funding was secured to implement and further evaluate the outcomes of the program in another seven rural acute facilities. This mixed method, non-randomised, controlled intervention study measured patient (n=290), family carers (n=85), staff and volunteer outcomes. A medical record audit compared patient outcomes and adverse events and interviews were conducted with family carers. Preliminary patient outcomes show a reduction in behavioural incidents (p=.010), reduced readmission rates (p=.038) and reduction in the use of one to one specials (p=.000). Of the families interviewed 92% of rated the program as helping “a lot” and 98% of staff agree that the program is supportive in their care of patients. Families indicated a sense of relief that someone was able to sit with the patient and in particular assist with their eating and drinking. ‘For me, knowing someone was there … I can’t even tell you what a benefit that was’.

Associate Professor Sally Bennett
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Translating research into practice: Occupational therapy for people with dementia and their carers.
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Background: An ever-increasing number of randomised controlled trials have demonstrated the benefits of occupational therapy for people with dementia and their carers. In addition, the recent Clinical Practice Guidelines and Principles of Care for People with Dementia specifically highlighted occupational therapy interventions and related interventions such as training carers in the use of pleasant and meaningful activities, amongst the priorities for research translation. However to enable research translation it is first necessary to understand the nature of the gap between current occupational therapy practice and the evidence. We therefore sought to understand Australian occupational therapists’ current practice with people with dementia and their carers, and to compare it with existing research evidence and guideline recommendations.
Methods: A cross-sectional online survey was undertaken with Australian occupational therapists who work with people with dementia and their carers within any practice setting. The questionnaire asked about current practice patterns, knowledge and confidence for supporting people with behavioural and psychological symptoms of dementia and their carers, awareness and enactment of existing evidence and guideline recommendations, and barriers and enablers to research translation.
Results: Results of this survey will be presented and compared with existing evidence. A program of research that has been funded by the NHMRC Boosting Dementia Research Grants Scheme to address critical research-practice gaps will also be described.
IU1, a selective inhibitor of deubiquitinating enzyme USP14 inhibits Aβ toxicity in neuronal cells

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Autophagy is a vital intracellular catabolic pathway for misfolded proteins and an attractive therapeutic target for neurodegenerative diseases including Alzheimer’s disease (AD). We have previously shown that enhancing autophagy reduced Aβ accumulation and toxicity in cells and improved cognition in an AD mouse model. A wide range of small molecules targeting multiple cell functions have now been developed to modulate autophagy. Assessing the neuroprotective effects of modulators against Aβ toxicity would further our understanding of their protective mechanisms and aid development of novel treatments for AD. Therefore, the main aim of this project is to identify potent autophagy modulators that protect against Aβ induced neuronal cell death.

In this study, we used the MC65 cell line to model Aβ accumulation and toxicity. MC65 is a well-established human CNS derived cell line that generates Aβ by γ-secretase cleavage from a stably transfected C99 fragment of the amyloid precursor protein (APP). Using this cell line as a platform, we screened an autophagy compound library containing 156 small molecules for inhibition of Aβ toxicity. We observed inhibition of Aβ induced cell death by the ion channel blockers carbamazepine, omeprazole and IU1, a selective inhibitor of deubiquitinating enzyme USP14. Overall, IU1 was identified as the most potent compound showing a marked 40% increase in cell survival in MC65 cells producing Aβ. Recent studies show that IU1 regulates autophagy and degradation of prion aggregates in cells. This suggests that its protective effect in MC65 cells is possibly through the upregulation of Aβ protein clearance. Our findings demonstrate a novel role for IU1 in reducing Aβ induced toxicity. Further investigation of its protective effects will be essential in determining its therapeutic potential in AD.

AMPK activator PRKAG2 is elevated in AD and is associated with increased autophagy and Aβ accumulation in the brain

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Previous studies of AD brain shows a marked up-regulation of lysosomal activity, including extensive involvement of various acid hydrolases such as cathepsins B and D with Aβ protein deposits. In addition, the AD brain also shows abnormal activation of nutrient sensing kinase AMP-activated protein kinase (AMPK), which is an important regulator of autophagy. AMPK is a heterotrimeric protein complex composed of a 3 subunits including a noncatalytic regulatory gamma subunit PRKAG2. Recent findings show that PRKAG2 has an important role in regulating stress induced autophagy by AMPK and polymorphisms in PRKAG2 are associated with cognitive impairment and metabolic dysfunction in old age. The main aim of this study was to determine the expression levels of PRKAG2 and whether it correlates with increased autophagy and Aβ levels in the AD brain.

Gene and protein expression analysis of PRKAG2 was conducted in post-mortem brain tissues of patients with AD, FTD (Frontotemporal dementia), LBD (Lewy body dementia) and in healthy controls. Autophagy markers LC3B-I, BECLIN1 and ULK3 were significantly elevated in the AD brain as compared to healthy control and other dementias showing the abnormal activation of autophagy. Gene transcription and protein levels of PRKAG2 was significantly increased in hippocampus and frontal cortex in AD. More importantly, PRKAG2 protein levels were associated with increased Aβ accumulation and BECLIN1 in all brains. In summary, our findings suggest that increased PRKAG2 may be an important contributing factor to lysosomal dysfunction and Aβ accumulation in AD brain.
Lipid alterations in frontotemporal dementia, a distinct profile from Alzheimer’s disease

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Lipid dysregulation has been identified as a common factor in various neurodegenerative disorders including Alzheimer’s disease, Parkinson’s Disease and Huntington’s disease. Frontotemporal Dementia (FTD) is the third most common form of dementia and lipid alteration in FTD brain has not been studied previously. Hence, we performed a nontargeted lipidomics analysis of the superior frontal region of post mortem human brain tissue from control (n=11), FTD (n=10) and AD (n=7) cases using high resolution mass spectrophotometry. The levels of individual lipid species across 19 subclasses were analysed and we found that there are differential changes in lipid subclasses in FTD and AD. When compared to controls, overall, AD cases had a greater number of changes than FTD. Sphingolipids were the most affected class in FTD while glycerolipids were most affected in AD. Ceramide levels were significantly increased both in FTD and AD. Interestingly, the levels of significantly altered phosphatidylcholine lipid species depict a contrary trend in FTD and AD. In conclusion, this is the first study to analyse the lipid changes in FTD post-mortem brain and provides information about differential lipid alterations in FTD and AD that suggest the cellular structures targeted by these dementia syndromes differs significantly.

Improving residential dementia care through staff: Two systematic reviews of the evidence

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Common sense suggests and research indicates relationships between staff in residential dementia care and the quality of life for residents, with poor care increasing unnecessary resident suffering. Two systematic literature reviews were conducted to assist with gaining a coherent picture of which (adjustable) aspects of residential care staff experience, practice, belief, or deployment it would be profitable to address (Review 1-Predictor) and which interventions with staff have a sustained impact on quality of care and consequent resident quality of life (Review 2-Interventions).

**Review 1- Predictor:** From published peer-reviewed literature from the last 20 years, 34 studies were included, only 3 of which were longitudinal and comprehensive. There is collective evidence that: Where staff treat and interact empathically and humanely in care, there is a relationship with better affect for residents, delayed functional dependence and better food intake; and where staff are more skilled and educated there are better outcomes for residents, such as less use of sedating medications.

**Review 2- Interventions:** Only 44 studies met the inclusion criteria; a quarter of these failed to measure effects on residents and half failed to measure longer term outcomes. However, there are high quality interventions that improve the way staff interact with residents, including during personal care, with effects maintained post intervention. However, in some areas, like reducing physical restraint, unlimited empathy is not enough; staff also need to know about dangers of restraint. Interventions with staff aimed at improving resident mood have produced vastly different results – so it is impossible to say whether they are worthwhile. Further longitudinal studies on appropriate targets for staff intervention are required.
Investigating LINE-1 mobile DNA involvement in Parkinson’s disease aetiology

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Abstract. Parkinson’s disease (PD) is a complex neurodegenerative condition, characterized by both motor and non-motor symptoms. About one-quarter of affected individuals, experience PD associated dementia. The main hallmark of PD is the selective degeneration of dopaminergic (DA) neurons, which control voluntary movement. Despite recent advances, current PD treatments only ameliorate symptoms but do not prevent neuronal loss and cannot cure the disease. PD aetiology is multifactorial, with genetic and environmental factors interacting via as yet unclear mechanisms to induce PD pathology. Recent studies have proposed that environmental and genetic factors may trigger hyperactivation of DNA mobile elements. These elements can alter the genome by insertional mutagenesis, recombination and deletion, potentially contributing to the susceptibility and pathophysiology of neurological disorders. Long interspersed element-1 (LINE-1) is the only active and autonomous mobile element in the human genome, and accounts for about 17% of human DNA. L1 is active in neurons and can ‘jump’ from one place in the genome to another by first copying itself into RNA and then reversing the process, thus potentially altering the activity of genes were they relocate. Our preliminary data show that L1 mRNA is present in murine DA neurons throughout life. Furthermore, L1-encoded ORF1p protein, necessary for L1 mobility, is abundantly expressed in DA neurons of aged mice. To establish the core parameters of L1 mobilisation in PD, we are currently assessing changes in L1 expression and activity in a neurotoxin mouse model of PD. We will further test whether L1 driven mutations are likely to alter DA neuronal phenotype, and whether chemical modulation of L1 activity could ameliorate PD phenotype.

Baseline amnestic severity in mild cognitive impairment predicts incident Alzheimer’s disease dementia at 3 years

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Mild cognitive impairment (MCI) has varying definitions that are inconsistently applied. Baseline severity of memory impairment in MCI has not been shown to predict incident dementia due to Alzheimer’s disease (DDAD) in a clinically useful heuristic. As part of the Australian Imaging, Biomarkers and Lifestyle Flagship Study of Ageing, 725 nondemented individuals were recruited and followed up at 36 months. Participants were classified according to Petersen criteria and Winblad criteria at baseline and also stratified into grade 1 or 2 severity based on degree of memory impairment at baseline. Incident diagnosis of DDAD was established by expert panel consensus. At 36 months, 54 (7.4%) participants developed DDAD. Subjects with amnestic MCI according to Petersen criteria were more likely to develop DDAD (PPV 25.5%; 95% CI 19.8-32.4) than healthy controls (PPV 12.0%; 95% CI 0.5-2.6). Winblad criteria were also useful, with multiple domain amnestic MCI being most accurate at predicting AD dementia (PPV 53.1%; 95% CI 39.1-66.1). Finally, grade 2 memory impairment was useful for predicting the development of DDAD in amnestic MCI single domain (PPV 27.3%; 95% CI 17.1-40.6) and in amnestic MCI multiple domain (PPV 69.8%; 95% CI 51.9-83.0). Memory impairment, impairment in multiple cognitive domains and severity of memory impairment are all associated with greater risk of progressing from MCI to DDAD. Classification of MCI should be expanded to include amnestic severity, as this provides important prognostic information.
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Theme: Living with Dementia  
Poster: No. 17  

Reminiscence with music produces more smiles than reminiscence with photos in people with Alzheimer’s Dementia.

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**Background and Aims:** Despite memory impairment in Alzheimer’s Dementia (AD), music evoked autobiographical memories (MEAMs) may be preserved. Studies in healthy populations have found that songs evoking positive emotions are more likely to elicit MEAMs, but this has not yet been explored in AD, and music has not been compared with other stimuli (e.g. photos). We compared positive emotions (smiles) elicited by songs and photos in people with AD.

**Methods:** 8 participants with AD reported personal memories following 16 famous songs (longest duration at number one in Australian music charts) and 16 famous photos (headline events from news sources) from 1930-2010. Facial expressions were analysed by two independent raters using a coding system to detect the presence of smiles.

**Results:** Only 2/8 participants experienced more smiles during the photo task than in the music task. In the remaining participants (6/8), there were significantly more smiles during the music task (p < 0.05), with 56.3% of songs and 26.4% of photos triggering smiles. There was a very strong positive association between smiles and the presence of MEAMs ($\chi^2=26.02$, p<0.001, $\phi = .43$) and a strong positive association between smiles and the presence of PEAMs ($\chi^2=14.10$, p < 0.001, $\phi = .32$).

**Conclusion:** Findings suggest that music is more effective than photos at eliciting positive facial expressions. Further, the presence of autobiographical memories evoked by music or photos is positively associated with smiles.

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Poster: No. 18  

Vascular mechanisms of neurodegeneration: drivers and determinants of dementia

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The evidence is compelling: vascular burden is the greatest determinant of late life cognition. The volume of evidence linking vascular risk and dementia is conclusive. All late-onset dementia syndromes, especially Alzheimer’s disease, are driven or exacerbated by vascular brain burden. We aim to examine how vascular burden causes dementia. Understanding the mechanisms means that we can prevent and treat the global epidemic of dementia. An update on animal and human projects will be presented, with results per project:

Vascular mechanisms of neurodegeneration: drivers and determinants of dementia

There are 3 major streams to this DRTG: post-stroke animal network degeneration with imaging, cognitive testing and histology; human network degeneration in models of vascular disease using cognitive testing, and advanced MRI; and exploring mechanisms for trial development.

Post-stroke animal network degeneration

Our post-stroke animal models are examining the trajectory and site of brain volume changes after stroke, and their correlation with cognitive and functional outcomes, in an attempt to identify factors that exacerbate and protect against degeneration. There are 2 cohorts of both mice and Long-Evans rats, allocated to serial MRI and cognitive training and testing (7 weeks prior to stroke and then serial testing) to examine for post-stroke cognitive decline. All cohorts have histological analysis and ex-vivo brain imaging following sacrifice.

Update and early findings: In a preliminary investigation of remote brain atrophy following middle cerebral artery occlusion (MCAO) in mice, we found significant atrophy in the ipsilateral cortex at 4, 12, 24, 36 and 48 weeks post-stroke compared with sham-operated mice. We also found significant atrophy in the ipsilateral hippocampus at all time-points, but only when the hippocampus was directly affected by the infarct. Cognitive impairments were seen early post-stroke and persisted over time. Our preliminary findings suggest no overt changes in volume in the contralateral cortex or hippocampus post-MCAO.

Human network degeneration in models of vascular disease
Canvas: The Cognition And Neocortical Volume After Stroke study is a longitudinal study correlating cognitive performance and brain volume changes in the five years after ischaemic stroke. Sixty-month testing was facilitated by the DRTG. We expect all participants to have completed their five-year review sessions by mid-2020 at the finish of DRTG funding. Two participants have died and donated their brains to the Victorian Brain Bank Network.

Update and major findings:

- **80** of **135** stroke participants and **25** of **40** healthy controls have completed three-year review sessions.
- **13** stroke participants and **2** controls have completed five-year review sessions.
- Stroke patients have smaller hippocampi and total brain volume around time of stroke suggesting both vascular risk factors and stroke ictus contribute to vascular brain burden and cognitive impairment (Werden, et al. Neurology, 2017)
- Attention networks are impaired after stroke with evidence that increased physical activity is associated with better attention performance (Veldsman, et al., NNR, 2016)
- Brain atrophy occurs across major hubs in the default mode network in the first 3 months after stroke, suggesting network-driven effect (Veldsman, et al., JNNP, 2017)
- Amyloid PET imaging on 23 participants has yielded 6 positive scans – around expected for age – and recruitment continues.

D2: In the Diabetes and Dementia study, we are examining whether people with type II diabetes mellitus (T2DM) and left ventricular hypertrophy (LVH) have increased rates of brain atrophy and cognitive decline compared to people with T2DM but without LVH. Participants complete a neuropsychological assessment, MRI scan and a range of cardiovascular investigations at two time-points over two years.

Update and early findings:

- Forty-five participants have completed their baseline assessments.

**Theme:** Our report of the association between increasing daily physical activity levels and improved performance on cognitive testing contributed to the development of the Post-Ischaemic Stroke Cardiovascular Exercise Study (PISCES). We have recruited 8 participants for this pilot study. The ASPREE-AF study, the final study in the DRTG, will commence in 2018, following completion of the ASPREE 5 year follow-up. Here we will examine effects of incident AF on brain volume and cognition in group of subjects with cognitive testing preceding clinical AF diagnosis, in around 200 participants ASPREE participants who develop AF during 5-year study.

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Preparing carers of community-dwelling people with dementia for natural disasters: The Carer Ready Guide

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Australia regularly experiences natural disasters such as floods, bush fires and cyclones. People with dementia are especially vulnerable and rely heavily on their carers and emergency services to keep them safe. There is a lack of resources that may assist those with dementia living at home to better prepare for and respond to natural disasters. This project aimed to develop an evidence-based guide that supports the disaster preparedness of this vulnerable population. Existing evidence/knowledge concerning the emergency preparedness of community-dwelling people with dementia was synthesized via a systematic literature review. Findings were incorporated into the draft guide which was reviewed by an expert panel of carers of people with dementia and emergency services workers (n=13) using a structured communication method. There was a high level of consensus on the content validity (relevance, likely effectiveness and appropriateness) of the draft guide. Suggestions for improved content, language and formatting of the guide were
incorporated into the final version. An implementation plan outlining strategies to accomplish widespread awareness of the Carer Ready Guide and successfully adopt it into the community has been developed based on the awareness, agreement, adoption, adherence knowledge translation model.

**Dr Jamie Bryant**

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**Planning ahead for future care: A randomised controlled trial to examine the effectiveness of interventions to increase the completion of Advance Personal Planning Instruments**

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Advance Personal Planning (APP) is the process whereby a patient, together with healthcare providers, family, and important others, discuss and document their preferences if they become incapable of participating in health and financial decision making in the future. If sensitively approached and handled, APP can have significant benefits for the person with dementia and their family. However, less than half of patients with dementia have an advance care plan. A web-based resource, Start2Talk, has been developed by Alzheimer’s Australia to support both persons with dementia and their carers to engage in APP; however usage is low. It is timely to examine whether promoting the use of Start2Talk can increase rates of APP. A three-arm randomised controlled trial will be conducted. Individuals with dementia and their carers will be recruited through participating geriatricians and randomly allocated as a dyad to receive: (i) usual care, (ii) a tailored geriatrician-based intervention consisting of a letter from the geriatrician outlining the benefits of APP and available tools and resources to support APP (including Start2Talk), SMS prompts to encourage use of Start2Talk, and a follow-up telephone call to problem solve any issues with APP; or (iii) an invitation to attend group-based shared skill-building workshops that aim to provide a core set of evidence-based skills and techniques to manage dementia-related challenges. The workshops will be facilitated by an individual with expert knowledge of APP and a component of the workshops will include discussion of the importance of APP and tools and resources available to assist with APP, including Start2Talk. Rates of completion of APP instruments (advance directive, Enduring Power of Attorney, Enduring Guardian, and a Will) will be compared between intervention and control groups at 3 and 6 months post-recruitment. This trial will provide evidence about the effectiveness of two different methods of increasing rates of APP for individuals with dementia.

**Dr Sam Buckberry**

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**Profiling the genome regulatory landscape of Alzheimer's Disease at single cell resolution**

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Epigenomic approaches are offering new insights into the role of epigenetics in neurodegenerative disorders, with recent studies revealing differences in gene expression and DNA methylation in AD affected brains. Although these approaches have identified disruption of genome regulatory processes that may play a role in AD, previous work has been performed using whole tissue biopsies. However, the extensive cellular diversity in brain tissue is likely a major confounding factor in understanding cellular changes that may be highly distinct between different brain cell types.

Our initial objective was to profile the epigenome during ageing and the progression of AD in pure populations of neurons, which was until recently the most feasible method of avoiding the pitfalls of bulk tissue molecular profiling. However, in the last 12 months the landscape of what is possible in genomics has changed drastically, with the emergence of high throughput single nuclei genomic techniques, which are ideally suited to investigation of human brain. With single cell gene expression and DNA methylation profiling now possible, overcoming the confounding effect of cell type heterogeneity in these investigations will be critical for understanding how the brain is changing in ageing and AD.

We are currently working towards obtaining single cell gene expression profiles of thousands of cells in healthy and AD affected brains to identify the brain cell types that exhibit the greatest differences in gene regulation. To date, we have optimized isolation of high quality and purity nuclei and genomic library preparation techniques on archival frozen human brain, an essential prerequisite for high quality data production at the single cell level. More recently,
we obtained our first brain single-cell gene expression dataset allowing us to begin identifying molecular markers of distinct cell subpopulations. Given the vast amounts of data we will obtain from thousands of individual cells from each brain sample, and the complex analytics required, I have also been concurrently developing computational methods and algorithms for integrative analysis of these gene expression, DNA methylation, and chromatin accessibility datasets. The methods employed in this project are at the absolute cutting-edge of molecular profiling. We anticipate our results will allow us to define subpopulations of neuronal and glial cells in individual samples, identify which cell populations show abnormal gene regulation in AD, and identify distinct neuronal and glial cellular subtypes in AD affected brains.

Dr Rachel Buckley
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Cognitive reserve relates to greater functional connectivity, independent of amyloid, in clinically-normal older adults

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Background: We recently found that higher baseline resting-state functional connectivity MRI (rs-fcMRI) in cognitive networks predicted less longitudinal cognitive decline in clinically-normal older adults. This finding was observed across varying levels of global amyloid burden, suggesting connectivity may reflect a neural reserve mechanism underlying resilience to cognitive decline. The objective of the current study was to investigate relationships between cognitive reserve (CR) and functional connectivity, and whether an interaction existed between CR proxies and functional connectivity to predict cognitive maintenance in clinically-normal older adults.

Methods: 250 clinically-normal older adults (61–90 years, Clinical Dementia Rating=0) underwent baseline Ab imaging with Pittsburgh compound-B (PiB)-PET, and resting-state-fcMRI. Seven networks were chosen for analysis, including four cognitive networks (default, salience, dorsal attention, and frontoparietal control) and three non-cognitive networks (motor, extrastriate and primary visual). Additionally, longitudinal cognitive performance was measured yearly over 5 years. The CR composite combined proxies of education, occupational attainment, cognitive activity and AMNART verbal IQ. Linear regressions examined the relationships between whole-network rs-fcMRI and CR, after accounting for age, sex and Ab burden. Linear mixed models examined baseline rs-fcMRI and CR to predict longitudinal cognitive performance.

Results: Greater rs-fcMRI across cognitive and non-cognitive whole-networks was associated with greater cognitive reserve after accounting for Ab and covariates, bs=0.13-0.24, p=.002-.04 (Fig 1A). Among examined whole-networks, default, dorsal attention and control exhibited the strongest relationships with cognitive reserve. While connectivity and cognitive reserve relationships were consistent and statistically significant across analyses, these associations were relatively weak. When we investigated the combined influence of CR and functional connectivity at baseline to predict cognitive change, we found subtle, yet significant, interactive relationships between high functional connectivity and cognitive reserve to predict better cognitive outcomes in clinically normal older adults. This was particularly salient when considering AMNART verbal IQ in isolation (see Fig 1B).

Conclusions: Greater functional connectivity in cognitive networks was associated with greater cognitive reserve, independent of Ab burden. These results support the hypothesis that these connectivity measurements reflect neural reserve capacity. Coupled with prior findings that higher connectivity predicts less cognitive decline over time, these results suggest higher connectivity in individuals with higher cognitive reserve may partly underlie their resilience to AD-related cognitive decline.

Dr Emma Louise Burrows
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Absence of task learning in the APP/PS1 mouse model of Alzheimer’s disease as measured by translatable touchscreen technology

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Cognitive dysfunction appears as a core feature of Alzheimer’s disease (AD). Over 300 therapeutics have been identified based on their ability to ameliorate cognitive deficits in mouse models, however all have failed to translate in clinical trials. One reason for this may be that traditional testing of animal behaviour differs greatly from clinical practice. Touchscreen testing in rodents enables assessment of cognitive domains that are directly relevant to patient impairments. We aimed to characterise cognitive changes in the APP/PS1 mouse model of AD, expressing familial mutations in the amyloid precursor protein (APP) and presenilin-1 (PS1) genes. Touchscreen technology, in which mice were trained to nose-poke stimuli on a touch-sensitive computer screen, was used to assess clinically-relevant cognitive tests to APP/PS1 and wild-type (WT) mice. Mice were assessed for deficits in attention using the 5-choice serial reaction task (5-CSRT). 9 month old APP/PS1 mice showed no impairment in the 5-CSRT, in training or across probes assessing multiple modalities of attention. When mice were reassessed for attentional impairment at 12 months of age, WT animal performance significantly improved. This task-learning effect was absent in APP/PS1 mice. These results indicate that APP/PS1 mice may be resistant to cognitive training after 12 months of age. This work is the first characterisation of the APP/PS1 mouse model of AD utilising translational touchscreen technology and is an essential step to enhance drug translation from preclinical studies to the clinic.

Ms Esa Chen

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Development and validation of the Medication Regimen Simplification Guide in Residential Aged Care (MRS GRACE)

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Background: Residents of aged care facilities (ACFs) use increasingly complex medication regimens with many medications, formulations, administration times and dosing instructions. Over half of ACF residents have diagnosed dementia. Reducing unnecessary medication regimen complexity may benefit residents and staff administering medications. There are currently no tools available to guide medication regimen simplification.

Method: A purposively selected multidisciplinary expert panel used modified nominal group technique to identify and prioritise factors that determine whether a medication regimen can be simplified. The five prioritised factors were formulated as questions, pilot-tested and refined by panel members. The final tool was validated by two clinical pharmacists who independently applied the tool to a random sample of 50 residents. Inter-rater agreement was calculated using Cohen’s kappa.

Results: The Medication Regimen Simplification Guide for Residential Aged Care (MRS GRACE) comprised five questions: 1) Is there a resident related factor that precludes simplification?, 2) Is there a regulatory or safety imperative that precludes simplification?, 3) Is simplification likely to result in any clinically significant drug-drug, drug-food, or drug-time interactions?, 4) Is there an alternative formulation that can support less complex dosing?, and 5) Is simplification likely to result in any unintended consequences for the resident or facility?. Two independent pharmacists used the tool with moderate agreement: opportunities to simplify 29/50 and 30/50 residents, respectively, were identified (unweighted Cohen’s kappa 0.38, 95% CI 0.120-0.640). Changing an administration time comprised 75% of the two pharmacists’ recommendations (n=45/60 and 34/46 recommendations).

Conclusion: MRS GRACE is a promising new tool to guide medication regimen simplification for residents of ACFs.
Quantitative simultaneous MR-PET imaging of the brain for application to ageing and dementia research

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Hybrid Magnetic Resonance Imaging (MRI) and Positron Emission Tomography (PET) enables simultaneous acquisition of images from the two modalities. Simultaneous MR-PET imaging opens new opportunities for novel multidimensional imaging and investigations of the mechanisms of the brain ageing, neurodegenerative diseases and dementia. For example, one can use a simultaneous dynamic 18F-fluorodeoxyglucose (FDG) PET and functional MR imaging protocol to investigate metabolic efficiency of the brain and its relationship with functional cognitive impairments in ageing and dementia. The idea of a fully integrated MR-PET system scanner was constructed started a couple of decade ago following advances in PET detector hardware, and since then researchers have spent great effort to physically integrate the two modalities in a robust and efficient manner. After the success in hardware integration, much of recent efforts have been directed towards software developments to implement and validate brain imaging applications.

Where we will report our recent work towards enabling quantitative PET imaging applications in the simultaneous system.

Brain enriched miRNA exosomal biomarkers associated with Alzheimer’s disease are detected in serum exosomes

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Several blood-based tests have been explored to detect Alzheimer’s disease (AD) however, evidence is required to determine whether blood sampling is an appropriate specimen to diagnose brain diseases. Exosomes are small extracellular membrane vesicles packaged with RNA and protein cargo. Previously we isolated serum exosomes from AD patients which displayed an abnormal composition of 16 specific microRNA (miRNA) biomarkers compared to controls. To provide evidence that our serum exosomal miRNA biomarkers are suitable for the detection of a brain condition, we also profiled exosomes isolated from post-mortem human AD (n = 8) and control (n = 8) brain tissues using Next-generation sequencing. Brain derived exosomes (BDEs) were found to contain a unique profile of small RNA, including miRNA, compared to whole tissue. Furthermore, all 16 serum biomarkers, identified in our previous study, were detected in BDEs. This work has identified a highly specific panel of miRNA that is both present in the brain and blood of AD patients. The miRNA candidates can be used to develop a blood-based diagnostic test highly relevant to a brain disease, equivalent to non-invasive brain biopsy.
Miss Xin Yi Choo
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Limiting Neuroinflammation through Delivery of Novel Copper Complexes

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Altered biometal homeostasis has been implicated in several neurodegenerative diseases, including Alzheimer’s disease (AD). Meta-analysis of biometal levels in human AD demonstrated copper (Cu) deficiency in important regions of the AD brain, such as the neocortex. Thus targeted Cu delivery using organic ligands is a potential strategy to restore biometal homeostasis. The Cu complex, CuII(gtsm), has been shown to reduce Aβ load and tau phosphorylation, and improved cognitive performance in the APPswe/PS1δE9 mouse model of AD. However, due to its toxicity in vitro, unraveling its mechanism of action is challenging. We are currently studying novel derivatives of neuroprotective Cu-complexes, differing in the ligand backbone to facilitate subtle but important variations in lipophilicity, cellular uptake, subcellular localisation and metal release. We demonstrate that specifically designed thiosemicarbazone-pyrdylhydrazone Cu complexes (CuTSPH), which are able to increase copper content in multiple brain cell types, reduce cytokine release in an in vitro model of neuroinflammation. We aimed to identify compounds of improved efficacy compared to our prototype compounds. By quantitative real-time polymerase chain reaction (qRT-PCR), anti-inflammatory properties of both prototype and novel Cu-complexes were associated with increased intracellular Cu content and increase in microglial expression of metallothionein 1 (Mt1). Demonstrated by ELISA and qRT-PCR, a novel amyloid-targeting Cu-complex, CuL1, reduced expression and secretion of damaging factors from astrocytes and microglia including pro-inflammatory chemokines MCP-1 and TNFα. CuL1 also mediated changes in expression of AD risk variant genes including Trem2 and Cd33 in TNFα- and IFNγ-stimulated murine microglia. Oral delivery of CuL1 delivered L1 into the brain and altered the proportion of Aβ phagocytosing microglia as shown by flow cytometry analysis (FACS) of acutely isolated microglia. Understanding of how Cu-complexes mediate anti-inflammatory actions through regulating cellular metal content will provide valuable insight into pathogenic and protective mechanisms in neurodegeneration and may aid in development of novel therapeutics for neurodegeneration.

Professor Lindy Clemson
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COPE: Implementing an evidence-based program in Australia: A summary of the planning and implementation phase

Professor Lindy Clemson and Dr Kate Laver
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Consumers want a stronger focus on restorative care to maximise independence and support to help carers support people with dementia to remain at home. There is strong evidence to suggest that dyadic interventions improve outcomes for both the person with dementia and the carer. However, these programs are not widely available in the community as translation of evidence-based programs into clinical practice has been limited.

The Care of People with Dementia in their Environments (COPE) program is an innovative intervention developed in the US and found to be effective in a randomised controlled trial (RCT). It involves occupational therapists (OTs) and nurses conducting comprehensive assessment, stress reduction for the carer, identification of key challenges and difficulties, problem solving (training the carer in how to apply strategies) and activity prescription.

The COPE (Australian) project is examining: (1) to what extent the COPE intervention can be translated into existing services, (2) the costs associated with delivery; and, (3) when implemented into existing services, whether COPE is as effective as initially demonstrated.

To date we have: adapted COPE to the Australian context and recruited and trained 40 OTs and 15 nurses from 12
partner organisations. We’ve completed a case note audit to describe current practice and conducted interviews with health professionals and management to gain an understanding of how organisational context and the current policy environment contribute to the adoption of innovation.

Dr Sean Coakley
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Discovering and studying novel molecules that regulate axonal degeneration.
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Maintenance of neuronal integrity is essential for the preservation of correct neuronal function. The disproportionate length of the axon, and its highly specialized function, makes it extremely vulnerable to damage and maintenance defects that can result in axonal degeneration. Axonal degeneration is an active process and a key early pathological hallmark of several neurodegenerative diseases including Alzheimer’s disease; it often precedes the death of the neuronal cell body and is a critical determinant of disease development and progression. However, a full understanding of the molecular mechanisms and genetic causes of axonal degeneration are lacking. Using the powerful genetic tools available in C. elegans, and focusing on a specific subset of sensory neurons, we have isolated a novel mutant strain with enhanced axonal degeneration. Using classical genetic mapping, combined with deep sequencing, we have identified the mutated gene that causes this phenotype. This conserved molecule functions non cell-autonomously in the epidermis of the animal, in which the axon is embedded, to protect it from spontaneous axonal degeneration. The characterization of this conserved molecule, and its previously unknown functional role in protecting the axon from degenerating will be crucial in expanding the role that non-neuronal tissue plays in protecting the nervous system.

Dr Timothy Couttas
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Ceramides, associated with insulin resistance, increase with age in the human hippocampus
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Alzheimer’s disease (AD), the most common form of dementia, affects 1 in 10 Australians over the age of 65. Age is the major risk factor associated with AD, and with an increase in life expectancy, and an ageing population, the number of individuals affected by AD will continue to increase. The major genetic risk factor for AD is the ε4 allele of the APOE gene, encoding the major lipid transport protein of the brain, apolipoprotein E (ApoE). Ceramides, which belong to a group of lipids termed sphingolipids, have been shown to be altered in human brains affected by AD. Ceramides with different carbon chain lengths have different physiological functions. C16:0 ceramide is a metabolic sensor that drives the development of insulin resistance in liver and adipose tissue. Very long chain ceramides such as C24:1 are major constituents of myelin and are protective in the context of insulin resistance. We investigated how age and APOE genotype influence levels of important signalling lipids in post mortem human brain tissue (n = 81), obtained from neurologically normal subjects aged 65 years or older. Lipids were quantified using liquid chromatography-tandem mass spectrometry. Levels of C16:0 ceramide increased with age significantly according to Spearman correlation analysis (r = 0.3019, p = 0.0065). Gender separation revealed C16:0 ceramide in males (r = 0.4492, p = 0.0012), not females (r = 0.08025, p = 0.6624) showed strong correlation with age. No significant association was observed between APOE genotype and hippocampal ceramides. Recent findings have demonstrated that AD progression is associated with a decline in cerebral glucose utilisation, potentially caused by a loss of insulin receptors at synaptic membranes of the cerebral cortex and hippocampus. Increasing levels of C16:0 ceramide with age may promote an insulin-resistant phenotype in the brain, making a significant contribution to AD pathogenesis.
Ms Amanda Cross

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Potentially inappropriate medication and mortality in people attending memory clinics

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Aim: To examine whether use of medications considered potentially inappropriate for older people with cognitive impairment (PIMcog) was associated with mortality in people attending Australian memory clinics.

Methods: Cross-sectional and longitudinal analyses of data from the Prospective Research In MEmory clinics (PRIME) study. PIMcog was defined as any medication considered potentially inappropriate for an older person with cognitive impairment according to the Beers criteria or Screening Tool of Older Peoples Prescriptions (STOPP).

Results: Of the 964 participants, 360 (37.3%) used a PIMcog at some point during the study, the most common being anticholinergics and sedatives. Using time-dependent Cox proportional hazards regression, adjusted for relevant covariates, PIMcog use was significantly associated with all-cause mortality over a three year follow-up period (adjusted hazard ratio: 1.42, 95% confidence interval: 1.12-1.80).

Professor Maria Crotty

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New evidence that design and organisation impacts of Australian aged care residents’ quality of life and their use of healthcare.

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Objective: To examine the consequences on resident reported outcomes of living in domestic cluster models in comparison to typical Australian models of residential aged care.

Design: A cross-sectional study with 12-month retrospective linked health service usage data

Setting: 17 residential care facilities in 4 Australian states providing either domestic clusters or typical Australian models of residential aged care.

Participants: Those residing in care for 12 months or longer, not in immediate palliative care, including those with cognitive impairment, having a family member willing to participate on their behalf. 901 residents were eligible and 541 consented (24% self-consent, 76% proxy).

Main outcome measures: Quality of life (EQ-5D-5L), hospitalisations. Statistical adjustments to control for baseline socio-demographic and clinical characteristics of participants were made

Results: All residents in a cluster model of care had either a dementia diagnosis or a PAS-Cog of five or more indicative of cognitive impairment in comparison to 79% of those in traditional facilities. After adjustments, individuals residing in cluster models of care had better quality of life (EQ-5D-5L difference 0.107, 95%CI 0.028,0.186), lower hospitalisation rates (rate ratio [RaR] = 0.318, 95% CI: 0.128-0.786) and lower Emergency Department presentation rates (RaR = 0.273, 95%CI: 0.142-0.526), in comparison to those residing in usual Australian aged care facility models.

Conclusions: This analysis suggests the built environment and associated models of care have significant effects on health and quality of life outcomes for people with and without dementia. More information is needed on financial, attitudinal and regulatory barriers to expansion of cluster housing models in Australian residential aged care.
 Associate Professor Joanne Curry  
Email: jcurry7@csc.com Theme: Living with Dementia  
**Understanding the Journey Better: An exploration of the current “state of play” of the health care journey experienced by people living with cognitive decline and their carers**

DXC Technology

Around the world, dementia related illnesses are on the increase. Dementia is a bigger killer than cancer and is second only to heart disease in Australia (Australian Bureau of Statistics, 2016). In Australia, the prediction is that by 2050 more than one million people will be living with dementia. This is a 375% increase since 2011 (Deloitte Access Economics, 2011). The increased numbers of people living with a dementia-related illness will have a significant impact upon the care services that are needed in the future as people living with dementia become increasingly dependent on others for help (Australian Bureau of Statistics, 2012). Whilst care pathways for people living with dementia have been in existence for some time, and guidelines have been developed to improve care significantly (NHMRC partnership centre for dealing with cognitive and related functional decline in older people, 2016), to date little research has focussed on the impact of these interventions on the real life experiences of people living with dementia and their carers from a personal perspective. Research has real impact if we understand what people want. This research asked consumers, people who live with the diagnosis of dementia and their carers, what they want, so that researchers, policymakers and healthcare managers can allocate their efforts appropriately.

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**Anxiety in patients with cognitive impairment and Parkinson’s disease**

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Dementia is observed in 80% of patients with Parkinson’s disease (PD) at advanced stage. PD patients experience cognitive deficits as early as the time of their diagnosis, while mild cognitive impairment (MCI) is detected in 45%. Anxiety is common in PD and the average prevalence is 31%. A recent study demonstrated that anxiety is 3 times more common in PD patients with MCI compared to those without MCI.1 The present descriptive study further examines the link between anxiety and cognitive impairment in PD. Fifty PD patients (n=50) were assessed for MCI using standardized criteria for PD and were examined for anxiety according to the Diagnostic and Statistical Manual of Mental Disorders 5th edition (DSM-5) criteria. Twenty-six patients (52%) screened positive for MCI and 36% were diagnosed with an anxiety disorder. Anxiety was observed in 18% of PD patients with MCI. Deficits in attention (58%) and memory (28%) were common in PD patients with anxiety disorder. Thus attentional and memory impairment may impact anxiety treatment including response to cognitive behavioral therapy. Research is required to develop targeted interventions with innovative technologies such as virtual reality, which can bypass some of the cognitive demands of conventional psychotherapy, to successfully treat anxiety in patients with cognitive impairment.

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**Variations in mental health assessment and psychotropic prescribing practices in Residential Aged Care**

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Depressive symptoms are frequently cited. Despite the introduction of mandatory depression screening in Australian Resitntial Age Care (RAC) facilities, consistency of use remains an issue. The high use of psychotropic drugs (44-79%) also raises questions as to the appropriateness of pharmacological mental health management practices in RAC and specifically patients with dementia.
A care plan analysis performed in 779 residents across twelve RAC homes (57% with dementia) revealed that the Cornell Scale for Depression (CSD) completion was highly variable (43%-98%), and impacted upon by severe cognitive impairment. Of those residents with a completed CSD, two thirds (61%) displayed depressive symptoms with suicide-related ideation disturbance reported in 11% of residents, double that typically observed in the general community. Analysis of psychotropic treatments revealed that overall half of residents (48%) were prescribed a psychotropic medication. Treatment for depression made up two thirds of all prescriptions (62%). Whilst anxiety (27%), sleep problems (25%) agitation (14%), psychosis (11%) and behaviours (7%), were also frequently cited as reasons for pharmacological intervention. Residents with dementia were more likely to be prescribed with antidepressants (OR 1.50, 95%CI 1.09-2.09, p=0.014) and antipsychotics (OR 1.89, 95%CI 1.23-2.87, p=0.004).

Variation in the completion of the CSD still lingers despite its implementation as a component of the Australian Aged Care Funding Instrument in 2008. Depressive symptoms are extremely high, as well as suicide-related ideation disturbance. Treatment with antidepressants is prevalent, as well as pharmacological treatments for other mental health disorders.

Dr Carol Dobson-Stone
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High-throughput cellular assays for assessment of dementia-related phenotypes
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Recent advances in sequencing technology make it a simple prospect to sequence the entire genome of any given individual with an inherited dementia. What is significantly less straightforward is how to filter this huge amount of data to find the causative variant(s). Even after bioinformatic filtering steps, next-generation sequencing projects often identify dozens of candidate disease variants, which require functional validation. Traditional cellular assays testing the effect of gene variants on pathological pathways are time consuming and examine only one or a few variants at a time. A main aim of my fellowship is to develop an efficient and systematic way to screen multiple variants at once in vitro. Our lab has established several cellular assays of dementia-relevant phenotypes based on common pathological pathways, e.g., mislocalisation of TDP-43 in frontotemporal dementia and increased g-secretase activity in Alzheimers disease. Using microtitre plate cell line cultures and automated fluorescence detection imaging systems, we will adapt these and other assays into a higher-throughput format that can assess dozens of variants simultaneously, thus reducing the time needed to filter variants. We expect to determine pathogenicity for currently ambiguous variants in known disease genes, and identify novel genes with variants that show a significant effect on a pathogenic pathway leading to disease, thus addressing a critical bottleneck in dementia genetics research.

Dr Angela D'Rozario
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Clinical, polysomnographic and neurophysiological correlates of sleep-dependent memory with ageing
The University of Sydney

Sleep spindles and slow waves are important NREM sleep brain oscillations which play a role in learning and memory. Changes in sleep neurophysiology and the presence of obstructive sleep apnoea (OSA) may underlie the decline in sleep-dependent memory consolidation (SDMC) with aging. This study examined clinical, polysomnography and sleep EEG correlates of sleep-dependent memory consolidation (SDMC) in older adults. Thirty-two participants (16 male, age 62±13, ESS 7±3, AHI 22±25,) underwent overnight polysomnography in the sleep laboratory. The sample was comprised of three groups: 8 had a diagnosis of mild cognitive impairment (MCI), 15 had OSA and 9 were controls. A 32 word-pair task was administered 1-2 hours before bed. Following an 8-h sleep opportunity participant’s declarative memory consolidation was assessed 1-h after waking during a morning recall phase. Power spectral analysis was performed on all-night EEG data, and slow wave activity in NREM sleep and spindle density (events p/min) in stage N2 sleep were calculated.
Overnight % retention recall was not significantly different between patients with MCI or OSA and healthy sleepers. Within the entire sample (n=29), higher % memory retention recall was significantly associated with increased overall spindle density at frontal and central brain regions. Clinical and polysomnography variables were not significantly associated with overnight changes in memory scores.

Spindle characteristics were the most strongly associated component of SDMC in this sample of older adults exhibiting cognitive decline and sleep disturbance. These preliminary results highlight the potential of sleep interventions to target memory deficits observed in aging and dementia.

Dr Xin Du
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Investigating the synergistic role of brain-derived neurotrophic factor (BDNF) and estradiol on parvalbumin-mediated cognitive function: relevance to dementia

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Epidemiological evidence suggest women are at higher risk of developing dementia. As the female sex hormone estrogen is neuroprotective, it is proposed that declining estrogen level at menopause increases the risk of women developing dementia. A mediator of estrogen’s beneficial effect is brain-derived neurotrophic factor (BDNF), a neurotrophin found to be significantly reduced in patient blood and brain. Both BDNF and estrogen affect the growth, development and function of parvalbumin (PV) interneurons, a GABAergic interneuron that is vital in mediating cognitive performance. PV loss has been found in the brains of dementia patients, particularly in the hippocampus. However, the mechanism between estrogen, BDNF and PV function in relation to cognition is unclear. To examine this, we used a transgenic mouse model (PV-cre/TrkB-fl) where the BDNF receptor TrkB is knocked out of ~50% of PV neurons via the cre-lox system and submitted mice to a battery of behavioural paradigms in adulthood. Both wild-type and PV-cre/TrkB-fl mice of both sexes exhibited no alterations to baseline locomotor activity level or anxiety as measured by the elevated-plus maze. For cognition, the mice performed equally well in the novel object recognition task and the cheeseboard maze, testing in turn recognition memory and spatial/reference memory. In the Y-maze, a test of hippocampal-dependent short-term working memory, disruption of BDNF signalling in PV cells caused a memory deficit in male mice. In female mice, the PV-cre/TrkB-fl mice did not display a deficit. However this finding is qualified by the fact that female wild-type control mice did not perform the Y-maze. Pending molecular analyses, our novel model already shows a subtle cognitive phenotype with possible sex-dimorphism that invite further examination of PV neuron health in conjunction with risk factors such as ageing, metabolic abnormalities, and stress.

Dr Suzanne Dyer
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Outdoor access and quality of life in residents of Australian care facilities

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Introduction: Quality of life is reduced in residents of long-term care facilities. Outdoor living is highly valued by most Australians and we examined its relationship with quality of life in this frail group.

Methods: INSPIRED is a cross-sectional study of 541 participants residing 12 months or longer in 17 care facilities from 4 Australian states. Data were collected on participant and facility characteristics, quality of life (ED5D-5L) and outdoor access. The association between outdoor use and quality of life was examined using multi-level regression models, adjusting for individual and facility level characteristics.

Results: Participants had a mean age of 85 (SD 8.5) years, 75% were female and 84% had a medical diagnosis of dementia or a Psychogeriatric Assessment Scale - Cognitive Impairment score of ≥5, indicating cognitive impairment. After adjustment for potential confounders, living in a facility with independent access to the outdoors was not
significantly associated with a better quality of life (EQ5D-5L $\beta=-0.059$, 95%CI -0.155 to 0.037, $P=0.23$). Going outdoors one or more times per day was significantly associated with a better quality of life (EQ5D-5L $\beta=0.16$, 95%CI 0.088 to 0.232, $P<0.001$), however going outdoors multiple times per week but not daily was not (EQ5D-5L $\beta=0.048$, 95%CI -0.011 to 0.108, $P=0.1134$).

**Conclusion and implications:** The provision of outdoor and garden areas that residents can access in care facilities is not sufficient to impact on their quality of life. Staffing structures to enable residents to venture outdoors frequently are required to maximise the quality of life impact of providing outdoor areas within care facilities.

**Dr Elizabeth Evans**

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*Theme:* Assessment and Diagnosis  
**Dementia Screeners for People with Intellectual Disability**

Elizabeth Evans, Clancy Black, Julian Trollor.

Department of Developmental Disability Neuropsychiatry, UNSW Australia.

There is a need for cost-effective screening for dementia in people with intellectual disability (ID). However, most dementia screening tools for people with ID have been validated only amongst people with Down syndrome. Further, consensus regarding the best tool is lacking. The current study examined the effectiveness of two low-cost dementia screeners in a sample of individuals with ID of any cause.

**Methods:** The Adaptive Behaviour Dementia Questionnaire (ABDQ) and the Dementia Screening Questionnaire for Individuals with Intellectual Disabilities (DSQIID) were administered as part of a larger survey completed by carers of people with ID over the age of 40 years in Australia. Participants were classified as having normal or non-normal cognitive status by clinician case consensus using all available data for each participant. Sensitivity and ROC analyses compared each screener against case consensus classifications.

**Results:** Data were available for 69 people with ID. Neither of the screeners demonstrated adequate sensitivity to detect non-normal cognition using the recommended cut-off scores. ROC analyses indicated that the DSQIID was the most effective at discriminating normal from non-normal cognition, but that a lower cut-off score would be more appropriate for this sample.

**Conclusion:** Compared with the ABDQ, the DSQIID had greater diagnostic utility in this sample when considering all possible cut-off scores. However, it is unlikely that any single cut-off would be suitable for all people with ID. Further research is needed to determine appropriate thresholds for people with different pre-existing levels of ID.

**Associate Professor Lis Evered**

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**Lis Evered NHMRC Dementia Research Development Fellowship # 1102462**

The University of Melbourne

Cognitive decline is the leading cause of morbidity in Australia for individuals aged 65y or more. It is symptomatic in up to 30% of individuals as either mild cognitive impairment (MCI, 20%) or dementia (10%), and in around 15% of older individuals as postoperative cognitive decline (POCD) 3 months following anaesthesia and surgery. To date there have been no prospective studies investigating any overlap or common pathophysiology between MCI/dementia and POCD. This work utilizes anaesthesia and surgery as a stressor for precipitating cognitive decline in order to define the subtype(s) of dementia observed as perioperative cognitive disorders and to define the profile of healthy ageing versus cognitive decliners; both leading to early diagnosis and updated clinical diagnostic criteria.
**Dr Elaine Fielding**
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**What is a “Good Day Out” for People with Dementia? Perceptions of Family Carers and Managers and Staff of Day Respite Centres**

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An understudied care setting for people with dementia is day respite. Government-funded day respite centres (DRC) provide opportunities for socialisation and activities to people with dementia and respite to family carers. This presentation fills a knowledge gap about what constitutes a “good day out” from three perspectives: DRC managers, DRC staff and family carers of people with dementia. Recruitment occurred via a nationally representative set of DRCs. Carers were also recruited through online newsletters and social media. From a goal of 40 DRCs, 37 participated. Managers (n=37), staff (n=28) and carers (n=43) responded to both closed- and open-ended questions on online or phone surveys. All the responding DRCs were either non-profit or government/community organisations. While the majority (87%) of managers had received dementia-specific training, only 50% of the responding staff members had. Managers named financial constraints and inadequate physical space as their biggest challenges to providing good dementia care. Individual staff members expressed a need for more dementia-specific training and activities. While carers were mostly satisfied with DRCs, they wanted more communication between staff and carers and were concerned that at times the person living with dementia did not enjoy going.

**Mr Peter Fransquet**
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**Blood DNA methylation as a potential biomarker of dementia: a systematic review.**

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Dementia is a significant public health issue. Prevalence rates are increasing but many individuals remain undiagnosed. Accurate and timely diagnosis is key for optimal targeting of interventions, thus driving the search for a diagnostic biomarker. A non-invasive easily measurable peripheral biomarker would have greatest utility in population-wide screening. Epigenetics, including DNA methylation, is implicated in dementia, however it’s unclear whether epigenetic changes can be detected in peripheral tissue. Here we systematically review the evidence for an association between dementia and peripheral DNA methylation. Forty-eight publications were identified, all investigating peripheral blood, and 67% reporting significant associations. Ninety percent were published in the last 6 years and Alzheimer’s disease was the most frequent cause of dementia examined (75%). Almost all studies were small case-control, with little attempt to replicate findings. We emphasise the need for future longitudinal studies on large well-characterised populations, measuring epigenetic patterns in asymptomatic individuals. A biomarker detectable in the preclinical stages of the disease will have the greatest utility in future intervention and treatment trials.

**Dr Sandra Garrido**
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**The Effect of Music on Mood in People with Dementia**

MARCS Institute for Brain, Behaviour & Development, Western Sydney University

Personalized music playlists are increasingly utilized in health-care to reduce the severity of symptoms in people with dementia. However, there is little understanding of how features of the music and individual symptoms and personality interact to influence the affective responses of people with dementia to music. A factorial experiment was conducted to investigate the influence of tempo, mode and lyrics on 99 people with dementia. Both the tempo and the mode of the
music were found to have a significant impact on the affective outcomes of listening to dementia. Severity of cognitive decline as well as a personal history of depression and anxiety also influenced response to the music.

**Ms Caroline Gibson**  
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**Theme:** Care  
**Improving dementia care in primary practice – a nurse-enhanced model of care.**  
Ms Caroline Gibson, Practice Nurse, PA / Prof Mark Yates  
The Memory Health Support Service, Ballarat Community Health (BCH).  
**Aim:** Literature and best-practice dementia care guidelines identify gaps between evidence-based and actual practice in primary care that potentially could be addressed by better utilisation of the Practice Nurse (PN). The aim project was to develop and test a nurse-enhanced model of dementia care, the Memory Health Support Service (MHSS).  
**Methods:** A collaborative quality improvement approach was taken and an iterative Plan-Do-Study-Act methodology used to develop, implement, and evaluate the nurse – enhanced model of dementia care.  
**Results:** The nurse-enhanced model of dementia care in primary practice was developed. 97 MHSS nurse consults were completed. All consults utilised chronic disease management MBS item numbers. Data is being collected on patient outcomes; this requires a longer timeframe. All BCH GPs and PNs reported that the MHSS provides an option to support patients with a cognitive impairment and are likely to refer patients to the service; and to recommend the service to patients and colleagues.  
**Conclusions:** The Practice Nurse role can be enhanced to deliver best-practice dementia care utilising the current MBS. This model of care addresses some of the gaps in dementia care in primary practice and increases the capacity of primary care to meet the health needs of people with dementia and their carers.

**Dr Yifat Glikmann-Johnston**  
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**Theme:** Assessment and Diagnosis  
**‘Real-life’ hippocampal-dependent spatial memory impairments in Huntington’s disease**  
Yifat Glikmann-Johnston*, Anna M. Carmichael*, Emily-Clare Mercieca*, and Julie C. Stout*  
1 Flinders University  
2 NHMRC Cognitive Decline Partnership Centre  
3 University of South Australia  
**Background:** Cognitive assessment research in Huntington's disease (HD) has primarily focused on cognitive domains related to the primary pathology of HD within the striato-frontal brain circuit (e.g., executive functions). The HD animal model literature recently reported spatial memory impairments, which were linked to hippocampal changes. Analogous spatial memory tasks in HD participants (e.g., virtual Morris Water Maze) produced similar impairments seen in HD animals, however, these tasks do not translate well to the range of functions involved in day to-day spatial cognition. The present study used an ecologically valid task to examine ‘real-life’ hippocampal-dependent spatial memory in HD participants.  
**Method:** We studied early HD, premanifest HD, and matched controls with an ecologically valid virtual environment, which demanded spatial memory function on three levels: navigation, object-location, and plan drawing. Performance was compared to a common experimental test, Paired Associates Learning from the Cambridge Neuropsychological Automated Test Battery.  
**Results:** Performance of HD participants on all spatial memory variables was significantly worse relative to the comparison group. Premanifest HD performed better than early HD, but overall showed impaired function.  
**Conclusion:** Aligned with studies in HD animal models, ‘real-life’ spatial memory is impaired in people with HD prior to clinical diagnosis. This alignment has important implications for testing treatments for HD. From the standpoint of neurodegeneration, the dependence of our spatial memory measures on hippocampal function extends the attention of cognitive assessment research in HD beyond the striato-frontal circuit.

**Dr Emmanuel Gnanamanickam**  
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**Theme:** Care  
**Home-like model of residential care is associated with better consumer rated quality of care**  
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Models for the provision of residential aged care are changing, with increasing emphasis on person-centred care and providing care in a more homelike environment.

**Methods:** Data were collected from 5.41 individuals who had lived for at least 12 months in one of 17 care facilities across Australia. Consumer rated quality of care was measured using the consumer choice index (CCI-6D), a 6 dimension instrument to evaluate quality of care received by people living with dementia in residential care, from a consumer perspective. The CCI-6D measures quality of care on a scale of 0 to 1 with higher scores indicating better quality of care. Analyses used multi-level regression models and adjusted for individual and facility level characteristics.

**Results:** Four (120 participants) of the 17 facilities provided the homelike model of care. Overall the mean age of participants was 86 years with 75% females and with 3.7 comorbid disease groups. 84% had a medical diagnosis of dementia or were cognitively impaired. Living in a facility providing homelike model of care was significantly associated with better consumer rated quality of care (Mean Δ: 0.138, 95% CI 0.073-0.203 P<0.0001) after adjusting for potential confounding factors. Additionally, the homelike model of care was also significantly associated with higher proxy (family) ratings of quality of care (Mean Δ: 0.094, 95% CI 0.028-0.160 P<0.01).

Homelike model of residential care is associated with better consumer and proxy rated quality of care for people with dementia. Changes to the way aged care is provided is to better align with a ‘homelike’ model of care can better meet consumer preferences.

Dr Danijela Gnjidic

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**Theme:** Care

**Optimising pharmaceutical care for people with dementia in acute care settings**

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Improving medical care for people with dementia in the acute care setting is a major public health need and of immense importance to consumers, community and stakeholders. In Australia, one in four people living with dementia are admitted to hospital every year. The majority of inpatients with dementia experience significant adverse outcomes including functional disability, hospital re-admission and mortality, and is associated with an immense cost for the health system. Importantly, evidence suggests that some hospital admissions and their complications are avoidable, with up to 30% of admissions among older adults attributed to inappropriate prescribing.

The ultimate aim of this research program is to establish a multi-centre linkage cohort study with pilot knowledge translation activities to improve quality of medical care in people with dementia admitted to acute care settings by providing reliable evidence on the patterns and prevalence of appropriate medicine use. This project will leverage on the existing available data in Australia, national and international collaborations, to establish the first cohort study of older inpatients with dementia in Australia to provide systemic evidence on:

1) Extent and variation in inappropriate prescribing among older people with dementia across hospitals;
2) Relationship of inappropriate prescribing with clinical outcomes;
3) Generate modified medication management resources considering input from caregivers and stakeholders, which may provide evidence for guideline care of people with dementia.
TMS-EEG indices of cortical effective connectivity and physical activity in older adults

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Engaging in regular physical activity is protective against late-life cognitive decline, however, the underlying neural mechanisms are not fully understood. The recent combination of transcranial magnetic stimulation (TMS) with electroencephalography (EEG) has made it possible to measure how activation of a targeted cortical area propagates to the rest of the brain (i.e. effective connectivity). Here, we used TMS-EEG to investigate the association between cortical effective connectivity and physical activity levels in older adults without dementia. 7-days of objectively measured 24-h activity data were captured using GENEActiv wrist-worn tri-axial accelerometers in 14 older adults (age range 56-82 years). TMS was applied to the left lateral prefrontal cortex, and EEG was recorded using 62 channels. The brain-wide response to left prefrontal TMS was determined using the global mean field amplitude (GMFA) area under the curve for two temporal windows: early (20-40 ms; reflecting the local response to TMS), and late (100-300 ms; reflecting propagation of TMS-evoked activity to connected brain regions). We found that time spent in light physical activity was positively associated with GMFA area for the late, but not early temporal window. No relationships were observed for sedentary behaviour or time spent in moderate-to-vigorous physical activity. These findings suggest that engagement in light physical activity promotes cortical effective connectivity in older adults. TMS-EEG is a novel approach that may provide new insights into how physical activity protects against dementia.

A call for age friendly communities: Examining the potential of intergenerational care programs in the Australian setting

Dr Katrina Radford, Dr Nerina Vecchio, Professor Janna Anneke Fitzgerald (Presenting Author), & Dr Xanthe Golenko (Corresponding Author)
Griffith Business School, Gold Coast Campus, Australia

Intergenerational care programs provide care and social support for older adults and children in the same setting. The psychological benefits are well documented in the literature; however, little is known about the business case behind creating an intergenerational care program in Australia. This presentation will address this gap by presenting a summary of research to date that focuses on the sustainability of these models in terms of legislation, workforce, educational programs and funding models that would underpin a program in Australia. This is important to address because creating an intergenerational care program is likely to improve the inclusivity of older adults and improve childhood outcomes, such as reduced delinquency. Some of the findings that will be discussed include that intergenerational programs do fit the current legislative framework in Australia, however some considered thought is needed to match the workforce and building requirements. In addition, there is an opportunity to develop a new educational framework designed specifically to offer meaningful reciprocal interactions between older adults and children, and create new career paths connecting child care and aged care certifications between the two workforces. Furthermore, there is an established demand for intergenerational care among the Australian community. Thus, sustainable business models can exist for intergenerational care. This will provide consumers with a wider range of formal care options that better suit the diverse care needs of Australians.
Dr Leonardo Gollo

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Fragility of structural hubs in the human connectome: A framework to study evolution, neuropsychiatric disorders, and neurodegeneration

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Neurodegeneration in dementia is often studied in isolation, without regard to the broader context of brain structure and function. In this study, we employed computational methods to understand the impact of structural perturbations, as occur early in dementia, on the nature of the connectome – that is, the wiring diagram of the brain. To achieve this, we studied random variants of the connectome that introduce subtle perturbations to network topology while preserving the geometrical embedding of the brain. We first show that the presence of hubs widely distributed throughout cortical regions confers a wiring cost that the human brain minimizes. Although slight perturbations of brain networks reduce the wiring length of inter-hub connections, these perturbations quickly disconnect inter-hemispheric links to prefrontal hubs and yield daughter networks that substantially differ from one another. If the variation in structure is permitted to accumulate, strong peripheral connections progressively connect to central nodes and hubs shift toward the middle of the brain. Progressive randomization of brain networks also leads to a topologically unstable intermediate regime consistent with a phase transition in complex systems. Intriguingly, the fragility of hubs to disconnections shows a significant association with the acceleration of grey matter loss in early adulthood life that occurs in schizophrenia. Together with effects on wiring cost, we suggest that fragile prefrontal hub connections and topological instabilities act as evolutionary influences on complex brain networks whose set point may be perturbed in neurodegenerative and neuropsychiatric disorders. These findings form a basis for understanding the pattern of preferential cortical thinning in dementia, which we are now testing.

Dr Mojtaba Golzan

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The association between retinal vascular changes and neocortical beta amyloid scores in the elderly: results of a two-year follow-up study

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Introduction: The eye offers a natural window to the brain to investigate a series of physiological parameters that may be associated with Alzheimer’s disease (AD). Using non-invasive retinal imaging, we studied the association between dynamic vascular changes and neocortical beta amyloid scores in an elderly cohort over two years.

Methods: 45 participants (79±5 yrs, 12 male) with subjective memory complaints but cognitively healthy (neuropsychological assessment) were recruited. All participants had a baseline and one year follow up Florbetaben positron emission tomography (PET) scan and retinal imaging. PET scans were analysed to measure cerebral amyloid levels based on the standardised uptake value ratio (SUVR). Retinal venous and arterial pulse (RVP & RAP) amplitudes were extracted from retinal videos using custom written algorithm.

Results: The mean neocortical beta amyloid (Aß) SUVR in the first and follow up year were 1.34±0.29 and 1.32±0.26, respectively. The mean RAP and RVP in the first and follow up year were 4.4±1.2, 5.7±1 um and 4.9±1.1, 5±0.8 um, respectively. There were no significant difference in SUVR from baseline to follow up (p>0.05). We observed a significant increase in RAP (p<0.05) and a significant decrease in RVP (p<0.001) values over two years.

Discussion: We did not observe a significant difference in amyloid scores over two years but we found a significant change in retinal vascular indices. This may be suggestive of a retinal pathophysiological manifestation that precedes cerebral amyloid deposition. However, further follow up is required to confirm cerebral amyloid exacerbation with progressive retinal vascular changes.
Dr Mark Greenough
Email: magree@unimelb.edu.au Theme: Intervention and Treatment
Presenilin plays a key role in metalloproteostasis
Mark Greenough, Abdel Belaidi, Adam Southon, Scott Ayton, Ashley Bush
The Florey Institute of Neuroscience and Mental Health, Parkville, Victoria
Australia Presenilin (PS) is the catalytic component of γ-secretase, a multiprotein aspartyl protease, that modulates the function of numerous type-1 transmembrane proteins via regulated intramembrane proteolysis. Presenilin has also been implicated in autophagy, a process that delivers proteins and cytoplasmic debris to lysosomes for degradation and amino acid recycling. Previously, we demonstrated that presenilin is required for normal cellular copper transport and to maintain the activity of superoxide dismutase 1 (SOD1), an antioxidant enzyme that requires copper for its activity. Perturbed copper and iron homeostasis is a feature of several neurodegenerative diseases including Alzheimer’s disease (AD). Ferroptosis is a newly identified oxidative cell death mechanism that is distinct from other cell death pathways such as apoptosis.
It is triggered by iron-dependent lipid peroxidation and can be induced in cell culture using small molecule inhibitors that target cellular antioxidant defence systems. Compounds known to inhibit ferroptosis include liproxstatin-1, ferrostatin-1 and deferiprone. Importantly, the iron chelator deferiprone is about to go into a human trial to test whether it can slow Alzheimer’s disease progression. In the current study, we are investigating a potential link with presenilin function and ferroptosis using a murine presenilin knockout cell culture model as well as cultured fibroblasts from patients harbouring presenilin mutations that cause familial Alzheimer’s disease (FAD).

Dr Alexandra Grubman
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Profiling phagocytic microglia in Alzheimer’s disease model mice
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Microglia are specialist immune sentinel cells in the brain parenchyma that besides removing cellular and extracellular debris, also mediate a plethora of effects regulating synaptic plasticity, maturation and removal, thus their function is vital to normal physiological processes and to pathological processes in the brain. The phenotypic diversity of microglia is progressively becoming recognised, including their rapid and potentially reversible ability to adopt distinct and dynamic phenotypes in ageing and disease, as well as upon removal from their native environment. Although a multi-systems level link between microglia and Alzheimer’s disease (AD) has now been conclusively established, the role of microglia in AD remains highly controversial. For instance does their potential toxicity to neurons in a chronically inflamed environment and their tendency in AD to aberrantly overprune synapses outweigh their protective amyloid clearance function, and how is this regulated on a spatio-temporal scale during AD progression? Our work sought to address these questions by exploring the molecular and functional changes occurring in different subtypes of microglia from healthy and 5xFAD AD model mice. We determined that microglia that were not in direct contact with amyloid plaques in vivo were highly molecularly similar to healthy microglia, even in animals with advanced plaque pathology. On the contrary, we found several hundred differentially expressed genes between amyloid-containing and healthy microglia. These genes were involved, among other functions, in phagolysosome and antigen presentation pathways, which were also confirmed by single cell RNA-Seq. Functional analyses are ongoing to determine whether this microglial subset arises as a direct response to amyloid exposure as well as the functional outcome of these microglia in AD.
Dr Vivek Gupta

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Alzheimer’s disease associated pathways identified in human glaucoma retinal and vitreous proteome

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Both glaucoma and Alzheimer’s disease (AD) are neurodegenerative and chronic disorders. We have previously demonstrated that AD is associated with ocular deficits including retinal thinning and reduced electrophysiological response. However, the molecular basis for this link remains obscure. This study was designed to evaluate the association between glaucoma and AD by investigating glaucoma-associated protein changes in the retina and vitreous humour. The multiplexed Tandem Mass Tag based proteomics was carried out on retinal tissue and vitreous fluid collected from glaucoma patients and age-matched controls followed by functional pathway and protein network interaction analysis. About 5000 proteins were quantified from retinal tissue and vitreous fluid of glaucoma and control eyes. Of the differentially regulated proteins, 122 were found linked with AD pathophysiology. Pathway analyses of differentially regulated proteins indicate defects in mitochondrial oxidative phosphorylation machinery. The classical complement pathway associated proteins were activated in the glaucoma samples suggesting an innate inflammatory response. Majority of the common differentially regulated proteins in both tissues were members of functional protein networks associated with AD neuropathology. Identification of previously reported and novel pathways in glaucoma that overlap with AD promises to provide renewed understanding of the aetiology and pathogenesis of age related neurodegenerative diseases.

Dr Veer Bala Gupta

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Longitudinal effect of Clusterin levels on cortical atrophy in Australian imaging biomarkers lifestyle study of ageing


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Clusterin is associated with Alzheimer’s disease (AD) pathogenesis, and higher level of clusterin correlates with faster cognitive decline in AD. In this study, we investigate the effect of clusterin levels on atrophy as measured by cortical thickness on Magnetic Resonance Imaging (MRI) data. The data of 87 (35 M) healthy subjects aged 68.8 (SD 5.9) years old from AIBL was used in this study. Clusterin levels of each subject was measured at baseline, with 18 months and 36 months follow-ups. We used a linear mixed effects model to model temporal reduction of cortical thickness, with respect to age, gender, APOE ε4 allele status, baseline clusterin level, and amyloid status. Clusterin levels are negatively associated with cortical thickness (p=0.026) at baseline. However, the significant interaction between time-point and clusterin levels (p=0.002) indicates that a higher clusterin level was associated with slower decline in cortical thickness. Although the baseline clusterin levels are associated with thinner cortex, during the course of aging, a higher level of clusterin is associated with slower decline in the cortical thickness. This reinforces our earlier work indicating that increase in plasma clusterin levels may occur as a response to the aging/ disease process.

Miss Karra Harrington

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Cognitive ageing in the context of preclinical Alzheimer’s disease

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AIBL Research Group

The phenomenon of cognitive ageing, whereby multiple cognitive abilities decline with increasing age throughout late life, has been well described. However, many studies of normal age-related cognitive changes do not account for the presence of preclinical dementia or other health factors in their samples. Preclinical Alzheimer’s disease (AD), as indicated by elevated levels of amyloid-β (Aβ), is highly prevalent (10-30%) and associated with substantial cognitive
decline in cognitively normal older adults. Failure to account for the presence of Aβ in normal ageing samples may negatively bias estimates of age-related cognitive decline. The aim of this study was to determine the effect of preclinical AD on estimates of cognitive ageing in individuals aged over 60 years. The effect of increasing age on cognitive composites (verbal memory, verbal fluency, psychomotor speed, fluid intelligence) was estimated from a large robust sample of cognitively normal older adults (n=382) whose Aβ status (+/-) had been classified with PET neuroimaging. The extent to which Aβ status contributed to age-related cognitive decline was then determined from linear mixed models, and the rates of change in cognition between those with high and low Aβ were compared. Over 72 months, age was consistently associated with decline in all four cognitive composites. Aβ status significantly contributed to the linear mixed models for verbal memory and fluid intelligence. The Aβ+ group showed more rapid decline for verbal memory, as well as worse fluid intelligence in general, compared to the Aβ- group.

The results of this study indicate that elevated Aβ is associated with substantial decline in verbal memory and impairment in fluid intelligence. Thus, previous studies may have confounded the effect of Aβ with age in their estimates of cognitive ageing for these abilities.

Dr Amy Heffernan
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Is iron storage impaired in ageing?
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Iron is involved in many essential biological processes, including cell division, neurotransmission and oxygen transport. Perturbed iron homeostasis, such as the accumulation of brain iron with age, can lead to oxidative stress and neuronal damage underlying neurodegenerative processes such as those observed in Alzheimer’s disease. Age is the single biggest risk factor for developing sporadic Alzheimer’s, and iron elevation may be a critical factor in both ageing and neurodegeneration. Ferritin is the protein responsible for safe iron storage, and is conserved across taxa, including Caenorhabditis elegans. This microscopic nematode is a widely used animal model of ageing and is easily genetically manipulated. The C. elegans genome is well characterised, and importantly has homology with higher-order species providing an opportunity to study the relationship between neurodegeneration and iron metabolism.

We are developing new analytical methods to assess ferritin levels in aged tissues, iron load in ferritin, and post translational modifications that alter protein function, to better understand the fundamentals of ageing. I will present an optimized protocol for purification and absolute quantitation of ferritin from cell lysate using stable isotope-labelled peptide standards, and high-resolution tandem mass spectrometry. In addition, I will describe complementary genome editing experiments and data mining of ageing C. elegans transcriptomics. Finally, I will discuss how we may transfer our approaches to other animal systems, such as the mouse, to observe changes in iron homeostasis in ageing animals. When conserved across taxa, these changes present a therapeutic target for age-related neurodegenerative diseases in humans.

Ms Amelia Hicks
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Traumatic brain injury and the risk of Neurodegenerative disease: Review of the literature
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2. Wellcome Centre for Integrative Neuroimaging, Oxford University
Traumatic brain injury (TBI) can be a devastating life-long condition that significantly reduces quality of life. With improvements in critical care and rehabilitation, many individuals survive beyond the acute period; carrying their injury across the lifespan as they develop and grow old. This has led researchers to focus on how the biological aging process may manifest in the context of an already vulnerable and traumatised brain, and how this could affect clinical outcomes for survivors. Foremost within this field of research is the question as to whether a brain injury may increase risk of Alzheimer’s disease (AD). Despite many papers on this topic stating that TBI has been confirmed as an important risk factor for AD, findings from observational studies using clinical samples are significantly mixed and are of low methodological quality. This presentation provides a comprehensive review of previous literature, summarising the research findings to date and highlighting the key limitations common to much of this research. This includes a systematic and critical examination of
study design, sample size and power, use of controls and informants, measurement and diagnosis of both TBI and AD, and statistical analyses used. Recommendations are provided for how to improve the quality of research in this area, a critical next step in answering the question of whether a TBI is indeed a risk factor for AD.

Dr Camilla Hoyos
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Arterial stiffness and executive dysfunction in older adults ‘at risk’ of cognitive decline
Kahala Dixon 1, Haley LaMonica 1, Shantel L Duffy 1,2, Ian B Hickie 1, Craig L Phillips2, Ronald R Grunstein2, Sharon L Naismith 1* , Camilla Hoyos 1,2* (joint last authors).
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2. Centre for Sleep and Chronobiology, Central Clinical School Woolcock Institute of Medical Research, University of Sydney

Background: Cardiovascular disease (CVD) in older people has been linked with cognitive impairment, particularly in the domains of executive function and processing speed. However, prior research examining such relationships in the elderly has largely focused on people with established cardiovascular disease. In this study, older adults without established cardiovascular disease, but at risk for cognitive decline, were investigated to determine whether carotid-femoral pulse wave velocity (PWV), an early marker of vascular integrity and arterial stiffness, relates to subtle changes on neuropsychological measures of executive function and processing speed.

Methods: Individuals with subjective mood and/or cognitive concerns underwent medical, psychiatric, neuropsychological and PWV assessments. Primary outcomes were processing speed as measured by the Trail Making Test Part A, executive functioning as measured by DKEFS (response inhibition) and Trail Making Test Part B (set-shifting). The secondary outcome included of memory, specifically new learning (encoding) and delayed recall (Rey Auditory Visual Learning Test).

Results: In 56 individuals, those with high PWV (≥12.0m/s) had significantly poorer executive function as demonstrated on TMT-B, compared to those with low PWV (<12.0m/s). There was a moderate negative correlation (r=-0.38, p=.004) between PWV and performance. There was no relationship between PWV and tests of processing speed or memory.

Conclusions: Our results confirm that in older adults at-risk for cognitive decline, early markers of CVD are associated with subtle decrements in rapid set-shifting, a component of executive functioning. These findings support efforts for the early detection and management of CVD, as a secondary prevention strategy for cognitive decline in middle-aged and older individuals.

Professor Alison Hutchinson
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Reducing harm, in the acute hospital setting, to people displaying symptoms associated with a neurocognitive disorder
Hutchinson, AM 1,2, Rawson, H 1,2, Richardson, B3, Peel, C2, Tomlinson, E 1, Ockerby, C 1, Bucknall, T 1 4, Chalmers, C5, Campbell, DS 6, O'Connell, B7, Redley, B 1 2
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5. Monash Health, Melbourne
6. Monash University, Melbourne
7. University of Manitoba, Winnipeg, Canada

Background: People displaying behavioural and psychological symptoms (BPS) related to neurocognitive disorders are at high risk of preventable harm during hospitalisation. Tailored interventions can help reduce symptoms and risk of harm. Management in acute hospitals, however, is rarely consistent with best practice recommendations.

Aims: 1. Co-produce a knowledge translation (KT) strategy to promote use of best practice to prevent harm to people displaying BPS. 2. Evaluate acceptability and feasibility of the strategy in two acute hospital settings.

Method: An integrated-KT approach was used to co-produce, implement and examine the acceptability, feasibility and outcomes of the KT strategy (comprising facilitation, education, and a point-of-care decision support tool). A mixed-methods approach was used to collect process and outcome data. We will present findings from the analysis of: naturalistic
observation (n=163 hours), self-report surveys (n=95) and incident data (1-year retrospectively and 1-year prospectively).

**Results:** Significant increases were found in the number of strategies used to manage BPS (pre: M=1.67, SD=1.44, post: M=4.16, SD=1.67), and nurses’ knowledge about neurocognitive disorders. During the intervention, a downward trend in continuous observer hours was observed, as well as in monthly medication error (baseline: M=3 per month; intervention: M=2 per month) and fall (baseline: M=5 per month; intervention: M=4 per month) rates.

**Conclusion:** The KT strategy was associated with improved use of best practice and reduced harm.

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**Dr Sharna Jamadar**

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**Theme:** Assessment and Diagnosis

**Assessment of brain reserve using simultaneous MR-PET imaging**

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The concept of reserve refers to the mind’s resilience to damage to the brain. Brain reserve refers to the capacity of the biological substrate to withstand damage, and cognitive reserve refers to the use of cognitive strategies to adapt to changes to the brain. It is well established that brain and cognitive reserve can delay the onset of functional impairments due to ageing, neurodegeneration and possibly dementia, however the neural mechanisms of the protective effect are poorly understood. Ageing is associated with widespread changes in the metabolic efficacy of the brain, which underpins the functional cognitive impairments seen in older age. Changes in brain metabolism may also be associated with amyloid accumulation and cerebral oxidative stress, and be associated with increased risk of Alzheimer’s disease. In this study, we develop a novel MR-PET simultaneous acquisition of blood oxygenation level-dependent (BOLD) functional magnetic resonance imaging (fMRI) and [18F]-fluorodeoxyglucose (FDG) functional positron emission tomography (fPET) protocol to study the neural bases of reserve. The protocol includes a dynamic acquisition of the FDG-PET data, offering an effective temporal resolution of 1-min, while simultaneously providing a BOLD-fMRI contrast with temporal resolution of 2 secs. We report preliminary results from a study of older (over 65-yrs) and younger (18-25yrs) adults scanned using BOLD-fMRI/FDG-fPET while performing a cognitive reserve task. Brain reserve measures are quantified using structural MRI (grey matter, white matter, tractography), functional MRI (neural activity) and FDG-PET (glucose metabolism) and are linked to neuropsychological profiles of cognitive reserve. This novel approach is a promising development in the study of metabolic determinants of age-related cognitive decline and the relationship between metabolic factors and the development of neurodegenerative changes and Alzheimer’s pathology in the ageing brain.

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**Professor Yun-hee Jeon**

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**Theme:** Care

**Optimising independence of older persons with Dementia - Interdisciplinary Home-Based Reablement Program (I-HARP)**

The University of Sydney

I- HARP is a bio-behavioural-environmental model and integrates proven strategies into a comprehensive, person-centered, interdisciplinary, bundle program. It is delivered over 4 months with a goal to enhance the function of older persons with dementia and other chronic age related conditions, such as pain, incontinence, and polypharmacy. I-HARP consists of 1) 12 home visits of 1.5 hours (5-6 OT, 3-4 RN, plus 2-4 additional options of allied health), tailored to the individual client’s needs; 2) up to A$1000 home maintenance and assistive devices; and 3) working in partnership with the carer throughout the process. Out pilot RCT of I-HARP with community dwelling people with amnestic mild cognitive impairment (MCI) and mild to moderate stages of dementia (n=18 client-carer dyads) showed promising results post intervention in terms of goal attainment, improved mobility and independence, no entry to higher care levels, and both self-perceived and observed client’s wellbeing and confidence. The intervention group showed improvement in self-care and independence using the Disability Assessment for Dementia (DAD) while the control group had a further decline (giving a clinically meaningful effect size of 0.61; Cohen’s d=.36). I-HARP addresses a major gap that exists in ways of providing reablement care for people at early to moderate stages of dementia with multimorbidities where multi and interdisciplinary team efforts would likely have higher impact.
Dr Lisa Kalisch Ellett
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Duration of risperidone use for behavioural and psychological symptoms of dementia is decreasing, but is still longer than recommended

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Background and aims: In June 2015, use of risperidone for the management of the behavioural and psychological symptoms of dementia (BPSD) was restricted to patients with Alzheimer’s dementia for a maximum duration of 12-weeks, due to the risk of serious adverse events. We aimed to determine whether the duration of use of risperidone for BPSD decreased in the aged-care setting following these changes.

Methods: We conducted a retrospective cohort study using Australian Government Department of Veterans’ Affairs administrative claims data. Gold card holders living in aged-care from 1 July 2015 to 30 June 2016, and a comparison cohort living in aged-care from 1 July 2012 to 30 June 2013 were included. We identified the number of people in each cohort dispensed risperidone and calculated their duration of use. We calculated the duration of use of other medicines used off-label for BPSD to determine whether there was inappropriate therapeutic shift.

Results: In 2012/13, the median age was 89 years (interquartile range (IQR) 86-91) and the median duration of risperidone use was 336 days (IQR 176-365). In 2015/16, the median age was 91 years (IQR 88-93) while median duration of risperidone use decreased to 240 (IQR 120-365) days. Median duration of use of other medicines decreased or remained unchanged from 2012/13 to 2015/16, suggesting that there was no inappropriate therapeutic shift.

Conclusions: Duration of use of risperidone in aged-care residents has decreased; however, over 75% of patients were dispensed enough risperidone to last longer than the recommended maximum 12-weeks duration.

Dr Christopher Karayiannis
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A twin study of type 2 diabetes and cognition – the role of central aortic haemodynamics and cerebral perfusion

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Background: The mechanisms underlying the link between Type 2 diabetes (T2D) and dementia are poorly understood. We hypothesized that changes in central arterial haemodynamics and cerebral perfusion may play a role.

Methods: Cross-sectional sample of twins discordant for T2D. Measurements included neuropsychological battery, brain MRI with arterial spin labelling (ASL), and non-invasive 24-hour central BP monitoring. Paired comparisons, voxel-wise comparisons and linear mixed modelling were used to study associations of T2D with cognition, cerebral blood flow (CBF), and central haemodynamics.

Results: There were 23 twin pairs, mean age 63.7 (SD=6.1) years. T2D was independently associated with poorer attentional ability (β=-0.45, p<0.001) independent of age and sex, but not with memory or speed. T2D was not associated with global or regional reductions in daytime CBF. Aortic reservoir pressure (β=0.017, 95%CI 0.0021 to 0.032, p=0.026) was associated with better attention independent of age, sex, and T2D. Aortic excess pressure integral was associated with global CBF (β=-0.78 p=0.04), but other measures of central haemodynamics were not. T2D was associated with reduced nocturnal central systolic BP dipping (β=-3.79, p=0.027). The magnitude of the negative association between T2D and attention was reduced in the presence of greater central systolic BP dipping (p for interaction=0.015).

Conclusion: The association of T2D with cognitive function was not influenced by daytime cerebral perfusion. Aortic reservoir pressure may be relevant to cognitive function, but independent of T2D. The effect of T2D on cognitive dysfunction is dependent on the degree of nocturnal central BP dipping.
**Dr Hannah Keage**  
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**Theme:** Assessment and Diagnosis  

**Objective cardiometabolic risk burden associates with functional brain activity independently of cognitive function in late-life**

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Cognitive Ageing and Impairment Neurosciences, University of South Australia; Alliance for Research in Exercise, Nutrition and Activity, University of South Australia; School of Psychology, University of Melbourne  

Cardiometabolic diseases such as obesity, type II diabetes and hypertension, are primary modifiable risk factors for late-life dementia. A current focus of research is understanding the cognitive and biological trajectories of cognitive impairment with a cardiometabolic origin: from no impairment, to Vascular Cognitive Impairment No Dementia (VCIND), a form of Mild Cognitive Impairment, to dementia. This study aimed to investigate cross-sectional associations between cardiometabolic burden, cognitive performance (Addenbrooke’s Cognitive Examination/ACE-III) and functional brain activity (event-related potentials/ERPs) during an executive function task. A total of n=77 (56% female) adults between 50 and 80 years of age completed a graded difficulty n-back task – 0, 1 and 2-back – from which ERPs were calculated. Cardiometabolic risk was calculated using standard clinical cut-offs for: hypertension, obesity (waist:hip), type II diabetes (fasting blood glucose) and high total cholesterol (blood analysis). Mixed-effects modelling showed that the early P1 and N1 components were not associated with cardiometabolic burden; but the later P3 component significantly attenuated as cardiometabolic burden increased, across all difficulty levels. Increasing age and a lower ACE-III score also predicted attenuated P3 responses, with smaller effect sizes than cardiometabolic burden. Findings indicate that cardiometabolic diseases and risk factors are independently associated with functional brain activity during an executive function task, a domain known to be first affected in VCIND. This work extends previous reports of cardiometabolic risk being associated with structural brain changes, and suggests that ERPs may be a sensitive marker of cardiometabolic burden change during intervention trials.

**Dr Michelle Kelly**  
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**Theme:** Intervention and Treatment  

**Management of the Behavioural and Psychological Symptoms of Dementia in the home: A systematic Review**

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**Aims:** The behavioural and psychological symptoms of dementia (BPSD) are arguably very challenging for family carers to manage. This systematic review aimed to provide a snapshot of the volume and scope of peer-reviewed papers which report on the management of BPSD in the home across three-time points. Methods: Eligible papers were published in English and reported on the management of BPSD in the home for the years 1994, 2004 and 2014. Electronic databases Medline, PsycInfo and CINAHL, were searched using MeSH headings and keywords. Studies meeting eligibility criteria were coded into categories; 1) data-based papers including descriptive and intervention, and 2) non-data-based papers such as commentaries and reviews.  

**Results:** A total of 153 eligible studies were identified. Of these 93 were descriptive, 27 were intervention and 33 were non-data-based. Over the three-time periods examined there has been a significant increase in both the number of studies published overall, as well as the numbers within each category. Of the intervention studies, only nine randomised trials aimed to reduce the impact of behaviours associated with dementia in the home. Conclusions: While the overall number of studies investigating behaviours associated with dementia in the home increased over the three-time points examined, most studies continued to describe the problem rather than rigorously testing interventions to contribute to knowledge that can guide clinical interventions. Funded by: National Health and Medical Research Council Dementia Research Team Grant (Australian Community Of practice in Research in Dementia’ (ACcORD)).
Feasibility and efficacy of computerized emotion recognition remediation in premanifest and early-symptomatic Huntington's disease

Monash University

Social cognitive deficits, including difficulty in the recognition of negative emotional expressions, emerge before clinical diagnosis in Huntington's disease (HD), and may affect patients’ everyday social function. Despite these well-characterized impairments, we are not aware of any available remediation programs to improve emotion recognition in HD. To address emotion recognition deficits we conducted an initial study of the feasibility and efficacy of computerized training of emotion recognition in HD. Twenty-two individuals with premanifest or early symptomatic HD were randomly assigned to either the training or control group. The training group used a self-guided online emotion recognition training program, MicroExpression Training Tool (METT), twice weekly for four weeks. Participants in both the training and control group completed measures of emotion recognition at baseline and post-training time-points. Participants in the training group completed seven of the eight sessions on average. Our results showed a significant group by time interaction which suggested that METT training was associated with improved accuracy in emotion recognition for participants in the training group. Our study demonstrates that emotion recognition remediation using the METT is feasible in terms of training adherence. Although our sample size was small, the evidence also suggests METT may be effective in premanifest or early-symptomatic HD, opening up a potential new avenue for social-cognitive intervention. Further study with a larger sample size is needed to replicate these findings, and to characterize the durability and generalisability of these improvements, and their impact on everyday social function in HD.

Maintaining connectivity in neurodegenerative disease

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2. Central Science Laboratory, University of Tasmania

Axonal and synaptic degeneration are key pathological feature of neurodegenerative diseases, although the mechanisms are yet to be determined. Our research goal is to determine the cause of these degeneration pathways in order to target therapeutic protection. In this project, we have investigated the role of TDP-43, a protein implicated in frontotemporal dementia, in regulating the formation and maintenance of neurites in in vitro and in vivo models. Methods: Primary cortical neurons, were derived from transgenic mice expressing human wildtype (WT) TDP-43 as well as from WT mice. To examine the effect of TDP-43 in vivo, AAV2 virus was used to introduce human WT-TDP-43 and TDP-43 with a mutation in the nuclear localization signal (DNLS) into retinal ganglion cells (RGCs) and the effect on axons examined histologically. Results: Over-expression of TDP-43 in cultured neurons resulted in significantly (p<0.05) more branching and significantly (p<0.05) altered growth cone morphology at 3 days. Label-free quantitative proteomic analysis, followed by functional classification of significantly modulated proteins (t-test, FDR<1 %) revealed that actin-binding proteins were among the most down regulated proteins (DAVID enrichment score 4.1). RGC expression of DNLS-TDP-43, but not WT-TDP-43 resulted in a significant (p<0.05, n=10) loss of visual acuity at 6 weeks post injection. Preliminary studies using electron microscopy suggested that altered TDP-43 induced axonal pathology including swollen axon structures filled with organelles. Conclusion: These data suggest that TDP-43 pathology could result in cytoskeletal changes and neurite dysfunction leading to synaptic disconnection. Targeting the cytoskeleton may be a therapeutic target for FTD.
**Professor Glynda Kinsella**  
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**Translating an Evidence-Based Cognitive-Behavioural Intervention for People with Mild Cognitive Impairment into a Community-Based Organisation: Benefits and Challenges**

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3. Alzheimer’s Australia Vic, Melbourne, Australia

**Background and aims:** People with mild cognitive impairment (MCI), a risk factor for dementia, are seeking interventions for maintaining independence. However, current services are limited. This study investigated translation of a research-evaluated intervention (the La Trobe-Caulfield Hospital [LaTCH] Memory Group) into the early intervention services of Alzheimer’s Australia Vic.

**Method:** Over three years, seven Alzheimer’s Australia Vic staff trained as facilitators of LaTCH Memory Groups for 161 people with MCI and their families. Twelve clients were interviewed regarding experiences from participating in LaTCH groups. The seven trained staff also reported on gains for clients, change in their own practice after running the groups, and factors that assisted or formed barriers in implementing the program.

**Results:** Using qualitative analysis (‘Most Significant Change’ technique), clients and staff highlighted the benefits of shared experience through group participation, which reduced anxiety and increased re-engagement in life activities. Further benefits related to improvement in self-confidence and self-efficacy in managing memory and upskilling in use of compensatory strategies. An additional benefit was that family and social relationships improved. Positive change in staff’s own practice related to increased practical knowledge of everyday memory challenges, leading to greater role-satisfaction and self-efficacy. Staff also identified several challenges in running and sustaining the program.

**Conclusions:** Cognitive-behavioural interventions delivered in a community setting can be effective and increase service access opportunities for older people with memory problems. Preparedness to address the specific challenges in delivering new services within community organisations is necessary to improve the translation and sustaining of these programs.

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**Dr Amit Lampit**  
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**Design of controls in trials of computerised cognitive training is ineffectual: A meta-analysis in healthy older adults**

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**Background:** Computerised cognitive training (CCT) is an efficacious and safe intervention for cognitive enrichment in older adults. However, as effective masking of the therapeutic effect is challenging and blinding of participants is implausible, it is difficult to quantify the contribution of non-specific effects such as expectancy bias (‘placebo effect’) or the importance of trial design choices.

**Methods:** We performed a meta-analysis of control group data from 57 RCTs investigating the cognitive effects of CCT in healthy older adults, encompassing 63 control groups and 2,712 participants. Mixed-effects analyses and meta-regressions were used to determine predictors of control group (‘placebo’) response. All moderator analyses were powered at >90% to detect a 0.15SD difference between subgroups at the alpha=0.001 threshold.

**Results:** There were no statistically significant differences between: active control (k=30, g=0.18, 95% CI 0.12 to 0.24) or passive control groups (k=33, g=0.12, 95% CI 0.08 to 0.16); blinded (k=32, g=0.15, 95% CI 0.09 to 0.20) or non-blinded assessors (k=31, 95%, g=0.16, 95% CI 0.10 to 0.21); adherence to intention-to-treat analysis (k=30 g=0.14, 95% CI to 0.10 to 0.18) or non-adherence (k=33, g=0.14, 95% CI 0.07 to 0.20). Across trials, the effect size in the CCT arm explained most of the variance in their respective control arm (ß=0.22, p<0.01, R2=0.86).

**Conclusions:** Contrary to common practice, supposed ‘gold standards’ of intervention trial design appear to be ineffectual in CCT studies. Given sham controls are costly and do not seem to add rigour to trials in the field, a shift to head-to-head trials is recommended to better inform clinical and community translation.
Prof Simon Lewis  
Email: profsimonlewis@gmail.com  Theme: Assessment and Diagnosis

Predicting Dementia and Parkinson’s in the clinic

Simon Lewis MBCh BSc FRCP FRACP MD, Professor of Cognitive Neuroscience

Brain & Mind Centre, University of Sydney

Transitioning from healthy brain ageing to a neurodegenerative disease is a relatively slow chronic process that must include a prodromal phase with subtle pre-clinical features that if appreciated would lead to earlier diagnostic certainty and a window for intervention. One of the most exciting areas for predicting neurodegeneration relates to our greater understanding of sleep disturbances. For example, patients who are destined to develop Parkinson’s Disease or Lewy Body Dementia (LBD) are likely to experience dream enactment behaviour known as Rapid Eye Movement Sleep Behaviour Disorder (RBD), for several years before their classic diagnostic features emerge. Furthermore, the presence of RBD combined with anosmia, reduced colour vision discrimination and parkinsonism carries a 65% risk of transitioning to a synucleinopathy over the next 3 years. My work is performing detailed phenotyping across patient groups including Idiopathic RBD, Mild Cognitive Impairment (MCI) and Familial LBD and utilises novel investigative techniques including neuropsychological paradigms, functional neuroimaging, neurophysiology, actigraphy, gait analysis, genotyping, chronobiology and polysomnography to explore the neural correlates of specific symptoms. Significantly, my Fellowship has already identified that MCI patients who report RBD have a neuropsychological profile akin to that seen in LBD (J Geriatr Psychiatry Neurol 2017). This suggests that more detailed screening of such patients might allow targeted intervention strategies in at risk cohorts.

Miss Li Li  
Email: li.li4@griffithuni.edu.au  Theme: Living with Dementia

Developing a dementia-specific preference-based measure (AD-5D) in Australia: Valuation study protocol

Centre For Applied Health Economics, School of Medicine, Griffith University,

Introduction: Generic instruments for assessing health-related quality of life may lack sensitivity to detect changes in health specific to certain conditions, such as dementia. The QOL-AD is a widely used and well validated condition specific instrument for assessing health-related quality of life for people living with dementia, but it does not enable the calculation of Quality Adjusted Life Years (QALYs), the basis of cost utility analysis. This study will generate a preference-based scoring algorithm for a health state classification system (the AD-5D) derived from the QOL-AD.

Methods/analysis: Discrete Choice Experiments (DCE) with duration and Best-Worst Scaling (BWS) health state valuation tasks will be administered to a representative sample of 2,000 members of the Australian general population via an online survey and to 250 dementia dyads (250 people with dementia and their carers) via face-to-face interview. A multinomial (conditional) logistic framework will be used to analyse responses and produce the utility algorithm for the AD-5D.

Discussion: This project will develop utility value sets for the new dementia-specific economic analysis tool, the AD-5D, from both a sample of the general population and a sample of dementia dyads using two elicitation techniques: DCE with duration and BWS. The algorithms developed will enable prospective and retrospective economic evaluation of any treatment or intervention targeting people with dementia where the QOLAD has been administered. Additionally, the administration of the DCETTO and BWS tasks to dementia dyads via interview provides an opportunity to collect in-depth information on the elicitation processes of this population, for which dementia interventions are designed for.
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Dr Qiao-Xin Li

Email: q.li@unimelb.edu.au Theme: Assessment and Diagnosis

Affirming the clinical application of CSF biomarkers for diagnosis of Alzheimer's disease and Creutzfeldt–Jakob disease based on Australian cohorts

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Differential diagnosis of Alzheimer’s disease (AD) and Creutzfeldt–Jakob disease (CJD) is supported by biomarkers in the cerebrospinal fluid (CSF). Amyloidβ1-42 (Aß42), Total-tau (T-tau) and phospho-tau (P-tau) proteins, measured by ELISA have been extensively studied and are increasingly used in memory clinics to support the clinical diagnosis of dementia or mild cognitive impairment (MCI) due to AD, as well as in screening of patients for therapeutic trials. T-tau is also widely used to support the diagnosis of CJD. In the absence of international consensus regarding analyte cutoff thresholds, we, as a NATA accredited National Diagnostics Laboratory (NDDL), determined the cut-points of the individual proteins based on an Australian AD cohort defined by positive Aß-amyloid PET imaging (n=120/21/16, Healthy control/MCI/AD), and a definite (neuropathologically verified) sporadic CJD cohort (n=132/123, CJD/non-CJD). Cross-validated accuracy, using all three biomarkers or the ratio of P-tau or T-tau to Aß42 to predict MCI/AD, reached ≥92% sensitivity and specificity. To expand our biomarker armamentarium for sporadic CJD, the utility of T-tau in sporadic CJD was also determined, with the sensitivity and specificity of 84% and 82%, respectively at the cutoff of 1072 pg/ml, and 83% accuracy. In parallel studies, 14-3-3 protein was detected by western blot with a dichotomised (positive versus negative) classification of the protein providing a sensitivity and specificity of 89% and 67%, respectively with accuracy of 79%. Of additional benefit CSF T-tau and 14-3-3 protein detection were complementary for supporting the diagnosis of sporadic CJD, with 10 of the 21 CJD cases with either negative 14-3-3 results or technically unsuitable CSF samples revealing a T-tau above the cut-point providing a combined sensitivity of 92%. Our study offers additional support for the use of CSF biomarkers in the early and accurate detection of AD neuropathology as the explanation for cognitive impairment, as well as enrichment of patient cohorts for treatment trials even at the pre-symptomatic stage, with T-tau also offering utility additional to 14-3-3 protein detection in the evaluation of suspected sporadic CJD.

Dr Yen Ying Lim

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Age increases rate of Aß and ε4 related memory decline in preclinical Alzheimer’s disease

Yen Ying Lim, Robert H Pietrzak, Simon M Laws, Victor L Villemagne, Tenielle Porter, Stephanie Rainey-Smith, Christopher Fowler, David Ames, Ralph N Martins, Pierrick Bourgeat, Christopher C Rowe, Colin L Masters and Paul Maruff, on behalf of the AIBL Research Group

Florey Institute of Neuroscience and Mental Health

Background: In non-demented adults, both high amyloid (Aß+) and carriage of the apolipoprotein E (APOE) ε4 allele increase risk for cognitive decline and dementia. Further, Aß+ related cognitive decline is increased substantially by the presence of at least one copy of the APOE ε4 allele. Despite advances in Aß biomarkers, age remains the greatest risk factor for dementia, particularly Alzheimer’s disease (AD). As APOE ε4 increases risk for Aß+ and older adults are also more likely to be Aß+, it is important to understand the extent to which age influences the effects of ε4 on Aß+ related memory decline. This study aimed to determine the extent to which the APOE ε4 allele influenced Aß related cognitive change in adults aged between 60-74 and 75-90 years old.

Methods: Non-demented adults (n=485) enrolled in the AIBL study underwent Aß neuroimaging and ε4 genotyping. Episodic Memory was assessed at baseline, 18-, 36-, 54- and 72-month follow-ups. Participants were classified as Aß- or Aß+ using PET neuroimaging and into two age groups (<75 and ≥75) according to their age at baseline. Data were analysed using linear mixed model analyses.
Results: In adults aged <75, when compared to the Aß- group, there was a significant rate of memory decline only in Aß+ ε4 carriers (d=1.25). In adults aged ≥75, when compared to the Aß- group, both Aß+ ε4 carriers (d=1.23) and non-carriers (d=0.35) showed significant rates of memory; however, the memory decline in Aß+ ε4 carriers was substantially greater when compared to non-carriers (d=0.82). This faster rate of memory decline in adults aged ≥75 was reflected in a 43% of Aß+ ε4 carriers meeting clinical criteria for dementia at the 72-month assessment, in contrast to just 24% of Aß+ ε4 non-carriers and 10% of Aß- participants.

Conclusions: Previous studies investigating the relationship between ε4 and Aß+ have not accounted for potential non-linear effects of age on memory decline. The rate of Aß+ related memory decline was greatest in adults aged ≥75, particularly in those who were also APOE ε4 carriers. This suggests that the combined effects of Aß+ and ε4 on risk for dementia increases substantially in older adults.

Dr Yen Ying Lim
Email: yen.lim@florey.edu.au Theme: Assessment and Diagnosis
**BDNF Val66Met increases rate of memory decline, hippocampal volume loss and tau accumulation in autosomal dominant Alzheimer’s disease**
Florey Institute of Neuroscience and Mental Health

Background: The brain-derived neurotrophic factor (BDNF) Val66Met polymorphism (rs6265) is implicated in synaptic excitation and neuronal integrity. In autosomal dominant Alzheimer’s disease (ADAD), mutation carriers (MC) who also carry the Met66 allele show worse memory and higher levels of cerebrospinal fluid (CSF) tau, but equivalent amyloid levels compared to MC Val66 homozygotes at baseline. The aim of this study was to determine the extent to which the BDNF Val66Met polymorphism affects changes in memory, brain volume, tau and Aß in ADAD prospectively.

Methods: Prospective neuropsychological, biomarker and neuroimaging data collected from the Dominantly Inherited Alzheimer Network (DIAN) over ~2 years were analyzed in 81 preclinical mutation carriers (MC), all with a clinical dementia rating (CDR) score of 0 and estimated to be 11 years prior to clinical symptom onset, and 78 matched mutation non-carriers (NC). BDNF genotype was obtained for MCs (58 Val66 homozygotes, 23 Met66 carriers).

Findings: Compared to MC Val66 homozygotes, MC Met66 carriers showed greater decline in episodic memory (p<.001), loss of hippocampal volume (p=.005), and increase of CSF tau (p<.001). Cortical Aß accumulation was equivalent between MC Val66 homozygotes and MC Met66 carriers (p=.427). Compared to NCs, MC Val66 homozygotes showed greater increase in cortical Aß accumulation (p<.001) but equivalent rates of change in episodic memory decline (p=.700), loss of hippocampal volume (p=.215), and accumulation of CSF tau (p=.266).

Interpretation: ADAD is associated with pathologically increased rates of Aß and tau accumulation, loss of hippocampal volume and decline in episodic memory. The results of the current study show that for MCs who also carry the BDNF Met66 allele, decline in episodic memory, loss of hippocampal volume and increase in CSF tau is substantially greater than for MCs who are Val66 homozygotes, despite equivalent rates of Aß accumulation. This is consistent with findings in preclinical sporadic AD, where amyloid positive Met66 carriers also show faster deterioration in episodic memory and hippocampal volume, but not Aß accumulation, when compared to Aß+ Val66 homozygotes. Together, these data suggest that the BDNF Val66Met polymorphism modifies the contributions to the neurodegenerative process in ADAD.

Dr Xiaoping Lin
Email: x.lin@nari.edu.au Theme: Assessment and Diagnosis
**Using videoconferencing technology with interpreters in cognitive assessments with people from Culturally and Linguistically Diverse backgrounds: a pilot project**
Xiaoping Lin 1,2, Dina LoGiudice 3, Betty Haralambous 1, Andrew Knight 4, Kerry Hwang 1
1. National Ageing Research Institute
2. Monash University
3. Melbourne Health
4. The University of Melbourne

People from Culturally and Linguistically Diverse (CALD) backgrounds account for a large proportion of people with dementia in Australia. There is evidence that this group often presents to health professionals at a much later stage for diagnosis of dementia. One important contributing factor for this later diagnosis is communication gaps in the
assessment and diagnosis process of dementia, which is often caused by a shortage of qualified interpreters. The aim of the pilot project is to explore the feasibility, acceptability, reliability and cost-effectiveness of videoconferencing technology with interpreters (i.e., e-interpreting) in cognitive assessments with people from CALD backgrounds. It builds on findings from an earlier study funded by the Hazel Hawke Research Grant in Dementia Care, which explored the role of interpreters in cognitive assessments and piloted the use of e-interpreting in the home environment. The current study will explore the use of e-interpreting in memory clinics. It will recruit ten patients from the Melbourne Health Cognitive Dementia and Memory Service (CDAMS). Each patient will receive two brief cognitive assessments, one using face-to-face interpreting and the other using e-interpreting. Results from these assessments will be used to evaluate the reliability of e-interpreting. We will also conduct surveys with patients, clinicians, and interpreters involved in the study to collect data on feasibility and acceptability. Finally, cost data associated with face-to-face interpreting and e-interpreting will be collected to assess cost-effectiveness of e-interpreting. Based on the results, a protocol on the use of e-interpreting will be developed. Recruitment for this project has commenced in August 2017 and the presentation will report preliminary data. This pilot project has potential for more timely diagnosis of dementia among people from CALD backgrounds, which will improve health outcome among this group. The project also has the potential to improve cost-effectiveness of the current health system.

Dr Michelle Lupton
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Theme: Assessment and Diagnosis
Genetic Investigations for Prodromal Alzheimer’s disease
QIMR Berghofer Medical Research Institute, Brisbane, Queensland, Australia
While the burden of dementia occurs late in life, neuropathology accumulates for decades prior to onset of dementia. Interventions to modify the course of the disease have the greatest potential to avert neuronal death and later disease burden if they are introduced during this crucial window, well before the onset of clear cognitive decline.

I will present preliminary work and outline future plans for my Boosting Dementia Research Leadership Fellowship. Throughout three distinct themes my overall aim is to identify markers and understand pathogenesis in prodromal AD. I will investigate genetic risk variants for AD using large cohorts with extensive phenotypic data at different life stages before dementia onset. I will investigate both common and rare AD genetic risk factors and test for associations with neuroimaging phenotypes and blood based methylation markers. For the Prospective Imaging Study of Aging (PISA) I am utilizing APOE genotype and polygenic risk scores (PRS) to identify individuals at high and low risk of AD. By leveraging our extensive in-house cohorts, comprising ~16,000 individuals between the ages of 40 and 70yrs we are generating a genetically enriched cohort for studying the precursors and lifestyle risk factors for AD.

Dr Margaret MacAndrew
Email: margaret.macandrew@qut.edu.au
Listening to preferred music with people with severe dementia who wander: A feasibility study
Dr Margaret MacAndrew 1, Dr Elizabeth Beattie 1, Dr Elaine Fielding 1, Dr Kimberly Van Haitsma 2, Dr Ann Kolanowski 2, Dr Gerard Byrne 3, Dr Nancy Pachana 3, Ms Catherine Wyles 1, Mr Adam Novic
1. Queensland University of Technology
2. Penn State University
3. University of Queensland
Using a modified protocol found to be effective in reducing agitation in people with dementia, we trialled the feasibility of using listening to preferred music with people with severe dementia who wander in residential aged care. Ten residents listened to their selection of preferred music for 20 minutes daily for 3 weeks under two conditions: immediately before unique peak activity periods or at randomly selected times. Of the 150 scheduled interventions, 92 were commenced and 60% of these were tolerated for the full 20 minutes. Sessions did not proceed when the participant refused (n=37), was asleep (n=12) or was not available (n=9). The intervention stopped prematurely when headphones were removed (n=20) or the participant walked away from the speaker (n=12). Despite the relatively high number of interventions that did not proceed, those who participated were observed to express more positive (58%) or neutral (32%) mood, with negative mood only recorded during 10% of the observation time. In addition, while not statistically significant,
participants were observed to walk and enter the private space of others less frequently during the intervention period. These findings were consistent with staff and family member’s views. Further investigations are needed to explore the high refusal rates as well as generalisation of effects beyond the intervention time.

Dr Sean Macdermott  
Email: sean.macdermott@deakin.edu.au  Theme: Care

**National rollout of the Dementia care in hospitals program: Preliminary findings**

Dr Sean MacDermott 1, 2, A/Prof Mark Yates 1,2, Ms Meredith Theobald 1, Ms Michelle Morvell 1, A/Prof Jenny Watts 2.

1 Ballarat Health Services  
2 Deakin University

The Dementia Care in Hospitals Program (DCHP) is an all-of-hospital cognitive impairment (CI) awareness and communication program supported by cognitive screening of all patients aged 65 years and over, a training program for staff, and use of a bedside alert (the Cognitive Impairment Identifier (CII)). The CII has been endorsed as a national symbol for CI in hospitals by Alzheimer’s Australia National.

Over 11,000 patients aged 65+ admitted to four hospitals in different jurisdictions were screened for CI using validated tools. Of these, nearly 40% screened positive for CI. Comparisons revealed that those who screened positive for CI were twice as likely to have one of four hospital-acquired complications (urinary tract infection, pressure injury, pneumonia, and delirium). At two of the four sites implementation of the DCHP was associated with a significant reduction in the levels of hospital-acquired complications. Staff satisfaction was assessed before and after program implementation and showed statistically significant improvements on all metrics measured.

This study provides clear support for the incoming standard requiring screening of all over 65s admitted to hospital. It also provides support for tailored programs of care for those with CI. This project is a good example of both the triumphs and travails of research translation in real-world hospital environments which are in a state of constant change.

Dr Helen Macpherson  
Email: helen.macpherson@deakin.edu.au  Theme: Prevention

**Progress update for a multi-faceted exercise and nutrition intervention to enhance cognition in older people at risk of cognitive decline**

Helen Macpherson

Institute for Physical Activity and Nutrition, Deakin University, Australia

Rapid population ageing is resulting in an increasing number of older people living with cognitive impairment and dementia. Current pharmacological treatments at best reduce Alzheimer’s disease (AD) symptomatology but do not delay dementia onset in those at high risk. The Protein Omega 3 vitamin D Exercise Research (PONDER) study is a randomised, placebo-controlled trial targeting prevention through a novel combination of exercise and dietary supplements in elderly who are at risk of further cognitive decline. Participants are randomised to a 6 month multimodal resistance training and aerobic program, or a stretching and flexibility program conducted twice weekly, in community based gyms. Supplements containing omega 3, vitamin D and protein or placebo are taken daily during this time. Cognition is assessed at baseline, at 6 months after completion of the intervention and at 12 months. Participants are 60 – 85 years of age, with subjective memory complaints, recruited from the South Eastern corridor of Melbourne. To date 617 individuals have expressed interest, 236 people have been screened, 85 have met eligibility criteria and are willing to participate and 83 individuals (15 males, 38 females) have commenced the intervention. Additional study cohorts are scheduled to commence the intervention in October 2017 and March 2018. This presentation will provide an update of study progress and recruitment processes. Challenges and opportunities in the conduct of multi-faceted interventions in community settings will be discussed.
**Establishing neural networks in peptide hydrogels**

Dr Adam Martin,* Dr Yazi Ke, Dr Sook Wern Chua, Professor Pall Thordarson, Professor Lars Ittner

University of New South Wales, Sydney, NSW, Australia

Alzheimer’s Disease (AD) is the most common form of dementia and is projected to affect over half a million Australians by the year 2020. Currently, there is no known cure and limited therapies available. A major factor in the ineffectuality of current treatments is centred on the difficulty in diagnosing AD, which can take years. By the time clinical and behavioural symptoms are established in patients, the disease is at an advanced state, limiting treatment options. Therefore, a strategy is needed to identify early diagnostic markers of Alzheimer’s Disease, either biomarkers or physical changes in the brain. One way to achieve this aim is to design materials which mimic the environment of the brains extracellular matrix (ECM).

The ECM is a fibrous mesh which provides physical and chemical cues for various cellular processes. Hydrogels are composed of cross-linked fibres, and represent an opportunity to mimic the structure of the native ECM. The use of short peptides to form hydrogels allows physical and chemical properties of the gel matrix to be tuned, such as stiffness, chemical environment and mesh size. Here we report peptide hydrogels that support the growth of primary neurons in 2D and 3D systems. Neurons can be cultured for over 40 days on these hydrogels whilst maintaining viability, and show synaptic development and electrical activity. The hydrogel can be controllably disassembled, unlike current 3D gel materials which require mechanical shearing. Such a well-defined, tuneable 3D hydrogel matrix holds significant promise for future applications in early diagnosis for various neurodegenerative diseases.

**Cognitive Impairment cannot be managed in isolation: A whole of system approach is required**

Martin-Khan M, Gray L, Peel N, Hornby-Turner, Y

Centre for Health Services Research, The University of Queensland, Brisbane, Australia

Diagnostic screening is required to identify persons with Cognitive Impairment (CI). This screening should be applied to individuals over 70, but it is relevant to many admitted patients. It is difficult to operate systems of assessment and care planning for sub-groups of patients, particularly when the reason for admission is usually not CI. A strategy designed only for patients with CI adds burden to a workforce that is already unable to fully manage clinical care and documentation. A “universal” system that, within it, deals specifically with the issues related to CI is desirable.

The interRAI Acute Care (AC) was pilot tested in 910 adult patients at admission (N=4 hospitals). 24.3% of patients had short term memory problems, common across all age groups. Delirium is a significant issue in AC, with 4.7% of participants having an acute change in mental status. Self-reported poor health was present in 18.7% of the participants. Finally, pain was present in all age groups (66.2%).

The interRAI AC comprising 56 clinical observations and applications pertaining to CI, including accurate diagnostic screeners for delirium and dementia (and suggestions for care planning), is administered to all adult patients at admission. Completion time is less than 15 minutes including data entry. An electronic nursing assessment system for inpatients reduces nursing admission documentation time, increases identification of patients with cognitive impairment and risk of delirium on admission, supports care planning and increases time for direct clinical care. We will test whether it will also improve the quality of care for patients with dementia in hospital.
Dr Karen Mather

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Dr Karen Mather  Poster: No. 84

Email: karen.mather@unsw.edu.au  Theme: Intervention and Treatment

Investigating the Genetic and Epigenetic Factors associated with Alzheimer’s Disease (AD)

Mather, KA 1, Thalamuthu A 1, Wen W 1, Armstrong NJ 2, Brodaty H 1,3, Sachdev PS 1

1. CHeBA, UNSW Sydney, 2. Murdoch University, Perth, 3. DCRC, UNSW Sydney

Background: The Older Australian Twins Study (OATS) and the Sydney Memory and Ageing Study (Sydney MAS) are partners in 2 European consortia investigating the genetics and epigenetics of AD. The EADB consortium focuses on discovering the missing heritability for AD whilst BRIDGET looks at the genetics and epigenetics of endophenotypes of AD.

Methods: EADB– Will use the largest sample to date to run a GWAS meta-analysis for AD (>39K AD, >40K controls). BRIDGET-Will examine DNA methylation in participants with cerebrovascular disease versus controls. A second project will undertake a GWAS examining a neuroimaging phenotype (DWI). Whole genome sequencing (WGS) on AD cases and controls will also be undertaken on our cohorts.

Results: EADB: Australian samples have genotyping data ready for analyses. BRIDGET: Sydney MAS and OATS samples have been sent for methylC sequencing (N=263). Samples have been sent for WGS from Sydney MAS (N=189) and OATS (N=204).

Discussion: DNA methylation and WGS assays will be completed in 2017. Australian researchers have made visits to our European collaborators in 2016/2017, establishing new relationships between other studies investigating AD.

Conclusions: Participation in these consortia has enabled strong relationships to be built between Australia and our European partners and enables Australia to contribute to large genetic and epigenetic studies necessary to unravel the complex aetiology underlying AD.

Mr Brendan McLaren

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Feasibility of Mobile Clinical and Sensor-Based Outcomes in Huntington's Disease

Brendan McLaren 1, Sophie C. Andrews 1, Yifat Glikmann-Johnston 1 Emily-Clare Mercieca 1, Mark A. Bellgrove 1, Clement Loy 2, Sean P.A. Drummond 1, Julie C. Stout 1

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Large datasets containing rich phenotypic and genetic information are essential for discovering genetic and environmental modifiers of cognitive symptom onset in Huntington's Disease (HD). The aim of our Dementia Collaborative Research Centre project was to determine the feasibility and acceptability of cognitive assessment tools and activity monitoring devices implemented by smartphone to conduct large scale data collection in HD.

We developed an app for iOS and Android smartphones which includes informed consent, prompts through study procedures, three cognitive tasks, questionnaires about sleep and physical activity, and a reminder messaging system. We piloted the app in conjunction with Fitbit One in HD (n = 9; pre-symptomatic = 5, symptomatic = 4) and control (n = 10) participants for 48-hours, followed by phone interviews to ascertain experiences with the app. We also compared groups on cognitive, questionnaire, and activity data.

We found that participants independently completed all aspects of the study. Of 10 possible, the minimum mean confidence rating in using the app was 7.6 and groups did not differ in their confidence levels. Participants with HD had significantly slower reaction time on a visual memory task, and trends for less accurate performance, as well as a trend toward slower performance in a psychomotor speed test. Fitbit data indicated significantly more awakenings and time spent awake in the HD group compared to controls. These findings provide evidence of the feasibility and acceptability of independent app-based assessment in HD, which we will now study in a larger sample.
Dr Rodrigo Medeiros

Email: r.medeiros@uq.edu.au Theme: Intervention and Treatment

Targeting inflammation as a biomarker and treatment for Alzheimer's disease.

Clem Jones Centre for Ageing Dementia Research, Queensland Brain Institute, The University of Queensland

The initiation of an inflammatory response is critical to the survival of an organism. However, when inflammation fails to reach resolution (i.e., repair/remodeling), a chronic inflammatory state may occur, and it becomes a major cofactor of many diseases, including Alzheimer’s disease (AD). Comprehending the biological basis for altered innate immunity and inflammation in AD is a challenge that has substantial clinical importance, as restoration or preservation of immunological responses is likely to have a great importance to the lengthen of healthier lifespan. The discoveries that resolution of inflammation is a highly coordinated and active process controlled by endogenous pro-resolving and anti-inflammatory mediators, and that inflammatory cells undergo classical and alternative activation, highlight new potential molecular targets to regulate inflammation and treat chronic inflammatory diseases. Here, we will present novel findings from studies in human samples that demonstrate a severe impairment in signaling pathways associated with the regulation of inflammatory resolution. In addition, pre-clinical data will be presented to support the idea that restoring the activity of regulatory anti-inflammatory interleukins or pro-resolving lipid pathways can elicit protective immunity and mitigate AD-like pathology. In the future, it may be possible to generate tools to regenerate and/or replace the endogenous inflammatory resolution pathways to diagnose, prevent and/or treat AD.

Dr Chris Moran

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Type 2 diabetes and longitudinal change in brain cortical thickness

Monash University

Aims: Type 2 Diabetes Mellitus (T2DM) is associated with lower cerebral cortical thickness. The longitudinal association between T2DM and cortical thickness is unknown. We aimed to study whether T2DM was associated with accelerated loss of cortical thickness.

Methods: The sample included 817 people from the Alzheimer’s Disease Neuroimaging Initiative (ADNI) with a low burden of cerebrovascular disease who had Magnetic Resonance Imaging (MRI) performed annually for 5 years. We used multi-level modelling to examine the relationship between T2DM and rates of change of cortical thickness adjusting for age, sex and APOE4 status.

Results: There were 124 people with T2DM (mean age 75.5) and 693 in the non-T2DM group (mean age 75.1) at baseline. Baseline presence of Alzheimer’s Disease and lower cortical thickness was associated with sample attrition (all p<0.001). We found a negative interaction between T2DM and age (p=0.045) whereby those with T2DM who were older had lower cortical thickness at each time point than similar aged people without T2DM. However, T2DM was not associated with a greater rate of cortical thinning than those without T2DM.

Conclusions: T2DM was not associated with accelerated cortical thinning in this sample. The detrimental effect of T2DM may occur earlier in life or may be more pronounced in those with a greater burden of cerebrovascular disease.

Dr Moyra Mortby

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Evaluating the efficacy of the BPSDplus Program: A protocol for a stepped wedge trial in residential aged care

Moyra E Mortby 1, Elizabeth Beattie 2, Nicola Lautenschlager 3, Colleen Doyle 4 and Kaarin J Anstey 1

2. School of Nursing and Midwifery, Queensland University of Technology
3. Department of Psychiatry, University of Melbourne
4. Australian Catholic University, Melbourne

The BPSDPLUS program (previously BPSD-CARE) has been developed to provide both specialised training to residential aged care staff engaged in the provision of care and also a structured program to help improve early identification and management of behavioural and psychological symptoms of dementia (BPSD). This study aims to evaluate the efficacy of the BPSDPLUS program to reduce BPSD and antipsychotic medication used to manage behaviours, as well as improve quality of life for individuals living with dementia in residential aged care. Secondary aims include the evaluation of the impact of the program on care staff wellbeing.
The efficacy of the BPSDPLUS program will be evaluated using a stepped wedge design over a two-year period in three participating sites of the same residential aged care provider in Canberra, ACT. Approximately 300 residents and care staff will participate across the three sites. Residents must have a diagnosis of dementia (any type), mild cognitive impairment or cognitive impairment as indicated by a MMSE <27. Care staff must be involved in the daily care of residents and will be paired with a resident and complete all assessments and intervention sessions for that resident.

Primary outcome measures include the Neuropsychiatric Inventory Nursing Home and the Quality of Life in Alzheimer’s Disease. Secondary outcome measure used to determine the impact of the program on care staff wellbeing include the Strain in Dementia Care Scale, Sense of Competence in Dementia Care Staff, Professional Care Team Burden Scale and the Work and Wellbeing Survey.

This presentation will describe the trial protocol for the BPSDPLUS program and discuss the challenges experienced and adaptations made to the intervention during the design phase of this intervention study.

**Professor Sharon L Naismith**

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*Theme: Prevention*

**Reduced spindles in MCI are linked with nocturnal awakening and subcortical brain volumes**

Naismith SL, Lewis SJG, Grunstein R, Duffy S, D’Rozario A

The University of Sydney

While emerging evidence links sleep disturbance to dementia, few studies have examined the specific neurophysiological components of sleep that may be linked to cognitive decline. In this study, we aimed to determine a) if sigma power, a marker of sleep spindles is altered in those with Mild Cognitive Impairment (MCI) relative to healthy controls, and b) how sigma power may relate to volumes of key subcortical nuclei. We recruited 60 participants with MCI and 44 controls, all of whom underwent neuropsychological, medical and overnight polysomnographic (PSG) assessment. Power spectral analyses were conducted on the PSG data for the sigma range generally, and for the slow and fast ranges. A subsample (n=35) also underwent neuroimaging from which volumes of the caudate nucleus, hippocampus and thalamus were quantified. Results showed that the MCI group had significantly reduced power in the sigma frequency range particularly within slow spindle ranges. Reduced spindles in the MCI group were associated with greater nocturnal awakenings, but not with neuropsychological functioning. For the neuroimaging subsample, there was a differential relationship between brain integrity and sigma power; for controls, reduced power was associated with having a larger thalamus. For those with MCI, reduced sigma was associated with having a smaller caudate. Overall, these data suggest that sigma power is altered in MCI and is linked with nocturnal awakening and with alterations in subcortical regions linked to spindle formation.

**Dr Morgan Newman**

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*Theme: Prevention*

**Aged vertebrate brains show a conserved failure to respond to hypoxia – a metabolic foundation for alzheimer’s disease?**

Newman M, Moussavi Nik SH, Lardelli M

University of Adelaide, School of Biological Sciences, Centre for Molecular Pathology

The Alzheimer’s disease (AD) brain is hypometabolic showing reduced glucose and oxygen use. Energy is the fundamental determinant of cellular function but are energy metabolism changes the cause instead of just a consequence of AD? Hypoxia is implicated in many phenomena associated with AD such as increased Amyloidβ production. Therefore, we tested the effects of hypoxia on two quite distinct models of dominant, early onset fAD-like mutations in the zebrafish’s endogenous PSEN1 orthologous gene. Remarkably, we saw that – in a normoxic environment - the brains of young adult mutant fish and older wild type fish show moderate upregulation of hypoxia response genes (thus young fAD-like mutant brains appear prematurely aged by this measure). Nevertheless, under environmental hypoxia, both fish types could raise their hypoxic response further to increase anaerobic glycolysis (lactic acid production) to provide energy. In contrast, older fAD-like mutant brains were unable to make this response to hypoxia. They appeared incapable of upregulating anaerobic glycolysis. This difference in responsiveness of aged
fAD-like mutant brains is apparently due to an inability to stabilise the central regulatory protein HIF1A. Intriguingly, a similar failure to stabilise HIF1A protein was previously observed in aged rat brains (Ndubuizu et al 2009 doi: 10.1152/ajpregu.90829.2008) while human AD brains show significantly reduced HIF1A protein levels (Liu et al. 2008 doi: 10.1016/j.febselet.2007.12.035) suggesting that this is a conserved characteristic of vertebrate brains and may be a fundamental characteristic of AD. We are currently making detailed ‘omics analyses of our fAD-like mutants to investigate this remarkable phenomenon.

Dr Morgan Newman
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Rna-seq analysis of zebrafish familial alzheimer’s disease (fad) mutation-like model brains supports a regulatory “inversion” into an alzheimer’s disease-like state
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University of Adelaide, School of Biological Sciences, Centre for Molecular Pathology1. and Bioinformatics Hub2.*equal first authors
Berchtold et al. 2014 (doi: 10.1016/j.neurobiolaging.2014.03.031) discovered that many genes with relatively increased expression in mild cognitive impairment (MCI) brains show, contrarily, decreased expression in Alzheimer’s disease (AD) brains and vice versa. Other studies have supported increased activity in early MCI brains before these become hypometabolic AD brains (e.g. Ashraf et al. 2015, doi: 10.1007/s00259-014-2919-z). Thus the decades-long progression of brains into AD may not follow a linear path. Instead, brains may “invert” into AD. This phenomenon may have confounded our attempts to understand AD pathogenesis. For genetic analysis in vertebrates, zebrafish offer particular advantages for reducing genetic and environmental noise. Families of over 100 siblings can be raised in a common environment. We have created the first models of dominant fAD-like mutations in endogenous zebrafish genes. We exploited large zebrafish families to make detailed transcriptomic analyses of adult brains from young (6 month) and older, infertile (24 month) heterozygous mutants compared to wild type siblings. This revealed a striking pattern of gene expression inversion: genes (predominantly) relatively upregulated in young mutant brains versus wild type brains are subsequently downregulated in older mutant brains versus wild type brains. Expression of FKBP5 (associated with decreased MAPT degradation) was notably inverted. Gene Ontology analysis suggests the genes with inverted expression are important in circadian rhythm, P13K and insulin receptor signalling, stress responses, and transcriptional regulation. Our results support that: 1) Aged fAD brain changes are not linearly consistent with prodromal changes, 2) the AD brain inverts into a discrete, stable transcriptomic state.

Dr Tuan Anh Nguyen
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Use of medicines with the potential to affect cognition in people with dementia: a retrospective study in a tertiary hospital in Vietnam
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Introduction: This study aimed to examine the use of potentially inappropriate medicines in people with dementia in Vietnam, with a particular focus on medicines that may affect cognition.
Methods: Medical records of out-patients with dementia attending a tertiary hospital in Vietnam between 1st, Jan 2015 and 31st, Dec 2016 were examined. Medicine use was assessed against medications considered potentially inappropriate for patients with cognitive impairment (PIMcog). Concomitant use of cholinesterase inhibitors (CEIs) and anticholinergics, and antipsychotics use was also examined.
Results: Of the 128 patients, 41% used a PIMcog, 39.1% used CEIs concomitantly with anticholinergics, and 18% used antipsychotics of whom a quarter used antipsychotics longer than three months. The initial doses of risperidone were not optimal in treatment of behavioural and psychological symptoms of dementia.
Discussion: This study highlights the high level of use of medicines that can further impair cognition or reduce the effectiveness of CEIs in the population with dementia in Vietnam. Dementia is an emerging area of disease burden in Vietnam and efforts to improve quality use of medicines for this population are warranted, particularly supporting awareness of and reduction of use of medicines that further impair cognition.
Novel nitroxides protect against oxidative stress-induced apoptosis and cytotoxicity in a patient-derived in vitro model of Alzheimer’s disease

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Nitroxides are antioxidants eliciting low cellular toxicity that can prevent oxidation by free radical scavenging. As such, they have been shown to be useful in protecting against β-Amyloid deposition and memory deficits in familial AD mouse models. However, whether nitroxide compounds exhibit neuroprotective capabilities in human sporadic AD neurons remains unknown.

Here we assessed the treatment potential of a newly synthesized nitroxides (1KT123D), generated through coupling the nitroxide tempamine to the nonsteroidal anti inflammatory drug indomethacin, in neurons of individuals with sporadic AD and healthy donors. We differentiated basal forebrain cholinergic neurons from induced pluripotent stem cells in hypoxic conditions (3% O2) and triggered oxidative stress by increasing O2 to 20%. We subsequently monitored cytotoxicity, apoptosis, reactive oxygen species and culture viability after treating with 1KT123D and the known nitroxide CTMIO. Raising O2 triggered an increase in caspase 3/7 activity and cytotoxicity in cultures from sporadic AD patients, while not affecting healthy neurons. Nitroxide treatment reduced the impact of increased O2 in a dose-dependent manner, without affecting viability of healthy neurons.

Our findings show that neurons from sporadic AD individuals have heightened susceptibility to oxidative stress compared to healthy neurons. Furthermore, the antioxidant properties of the two nitroxides reduced the neurotoxic impact of raised O2 in our patient-derived in vitro AD model. In current experiments we are exploring the electrophysiological properties of cholinergic neurons from AD patients and the effect of nitroxides on cell membrane properties.

Strategies for Relatives (START) On-Line

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Carers of people living with dementia (PLWD) experience depression and anxiety at higher rates than any other group in our community. Programs are needed to assist carers to manage their role. The StrAtegies for RelaTives (START) program is an effective intervention for reducing anxiety and depression and improving quality of life (QoL) amongst carers in the UK. START is an 8-week manual-based therapy program delivered face-to-face in a one-to-one format to help carers better manage their caring role. The current project adapted and redesigned the UK START manual for Australian carers of PLWD, and is piloting its delivery via video-conferencing to increase accessibility, particularly for carers living in rural areas. The adapted manual is the result of collaboration between University College London (UCL), Melbourne Ageing Research Collaboration (MARC), National Ageing Research Institute (NARI) and The University of Newcastle. Thirty-five carers of PLWD will be recruited from rural and urban Victoria. Depression, anxiety, and QoL measures will be completed before and after the 8-week program. The main aim is to test the feasibility and acceptability of the Australian START program when delivered on-line via video-conferencing. It is expected that the video-conferencing mode of delivery will be acceptable and feasible to carers of PLWD, and that carers will experience improvements in symptoms of anxiety, depression and QoL.
Dr Lua Perimal-Lewis

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Assistance through personalised online technology for older people with early stage dementia

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Flinders University - Digital Health Research Centre

Background: People with early stage dementia might forget words or names and may be vague in their communication. Mild Cognitive Impairment (MCI) is acknowledged as an indicator of impending dementia; people with MCI exhibit some memory loss, but often do not show other signs of dementia and can function independently. Accessing rich online resources can be a confusing process. This project will allow online resources to coexist in a single artefact, with the choice and complexity level to be customisable to an individual’s needs.

Methods: This project will develop and evaluate an adaptive clutter-free, personalised online solution for mobile tablet and smartphone devices for people with MCI.

Results: The aim of this project will be realised by using participatory co-design principles, with the following main functional categories: ‘Information’, ‘Organisation’ and ‘Wellbeing’. The ‘Information’ functionality will provide collated information relevant to the person’s health condition. The ‘Organisation’ functionality will enable management of daily living independently without reliance on carers. The ‘Wellbeing’ functionality will support memory activities and physical activities at an appropriate level to ensure the individual can cope with the activities and is being appropriately challenged, which offers some defence against rapid cognitive decline.

Conclusion: This project will benefit the ageing in place agenda by providing a simple adaptive technology artefact to support individuals experiencing memory loss to live independently and to continue being part of their communities.

Dr Christina Perry

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Chronic alcohol produces specific cognitive deficits

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Chronic alcoholism is associated with cognitive effects that range from mild impairment to profound and irreversible dementia. Even where mild, these deficits are clinically relevant because they impede the process of behavioural change during therapy. Despite this, addiction therapy frequently fails to account for the cognitive deficits that may be present, and there is poor understanding regarding the mechanisms that underlies this decline. In this project we established a rodent model of chronic alcoholism to measure the cognitive effects and underlying neural changes. Rats had intermittent access to ethanol, or an isocaloric solution, in their home cage under voluntary 2-bottle choice conditions. After 6 months, the animals were divided into two groups, matched by consumption. One group underwent a battery of cognitive tasks using touchscreen technology. The others were perfused and their brains retained for volumetric analysis. Rats consumed on average 6 g/kg/session over the 6 month period. Ethanol-exposed and control rats showed equivalent acquisition of pairwise discrimination, however ethanol rats performed fewer trials (p<.05), and with lower accuracy (p < .05) when the contingencies were reversed, indicating reduced behavioural flexibility. In addition, when tested in a 5-choice serial reaction time task ethanol-exposed rats showed increased attentional bias towards a reward associated over a neutral cue (p < .05). Importantly, the cognitive changes observed - decreased behavioural flexibility and specific attentional bias - resemble those seen in human alcoholics. Going forward we will use this model to describe emerging neuropathology in order to elucidate the mechanism(s) for alcohol-induced cognitive decline.
Dr Lyn Phillipson  
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Are information and supports adequate to support consumer directed care decisions in the Home Care Packages program?

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Many have heralded the potential benefits of consumer directed care (CDC) within the Home Care Packages (HCPs) program introduced in Australia in 2015 to support older people with complex needs to remain living in the community. However limited attention has been paid to whether the conditions for supporting consumer decisions and equitable outcomes have been met. To address this gap, information resources, training and other supports were identified on .au domains using an advanced Google search on May 2 2017. Key word searches included all of the words: ‘aged care’ and ‘home’ and any of the words: ‘support’ or ‘packages’ or ‘guidelines’ or ‘policy’ or ‘program’. The first 100 first page results were reviewed. Snowball searches were also conducted within the Department of Health, My Aged Care and Home Care Today websites. A content analysis was then conducted on 47 identified resources (16 web pages, 30 resources and 1 person support) for: currency, type, content and accessibility. Resources were limited for those who speak or read languages other than English, have low grade level literacy or who have limited capacity for decision making such as those living with dementia. There were no current opportunities for consumer training. The study highlights an urgent need to improve the quality and accessibility of information resources, training and support for CDC decision making to ensure equitable outcomes in the Home Care Packages program.

Professor Constance Dimity Pond  
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Primary Care Guidelines for dementia identification and management

Discipline of General Practice, University of Newcastle

Background: This presentation will describe the development of primary care guidelines for dementia, to complement the 2016 NHMRC Clinical Practice Guidelines and Principles of Care for People with Dementia (NHMRC Dementia Guidelines).

Method: These Guidelines, funded by the Cognitive Decline Partnership Centre, are an adaptation of the 2003 RACGP GP Dementia Guidelines. A range of international GP/Primary Care Guidelines were reviewed and key topics identified. As well as assessment, continuing care, BPSD and carer support, from the 2003 guidelines; the team added specific advice on communication, prevention (not in the NHMRC Guidelines), legal issues, elder abuse, younger onset dementia, intellectual disability and rural and remote issues. Input was received from an Advisory Group of carers and consumers and an international Steering committee.

Narrative reviews were conducted for each guideline topic, using questions developed during the initial review process and refined in consultation with the advisory and steering groups. For each topic, a one page summary, a brief overview and a background literature review was prepared. Flowcharts were used to present a visual summary of most recommendations.

Chapters were also reviewed by primary care focus groups and general practice triallists, and modified according to feedback.

Conclusion: A narrative review process has resulted in the production of Primary care guidelines to complement the NHMRC Dementia Guidelines.
Ms Dannielle Post
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Perceptions of the impact of targeted exercise prescription for older people with dementia in residential aged care
Gaynor Parfitt, 1 Megan Corlis, 2 Alison Penington 2, Dannielle Post 1
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3. NHMRC Cognitive Decline Partnership Centre, University of Sydney, NSW.

Dementia impacts the functionality of older adults. Providing avenues in the aged care environment to maintain physical, cognitive, and behavioural functionality as dementia progresses is one of the roles of Accredited Exercise Physiologists (AEPs). A 12-week exercise program is being delivered to residents in an aged care environment. Evaluation will focus on the impact of the targeted, individually specific, exercise intervention for people who have significant dementia and other chronic health conditions and disabilities. Factors considered include perceptions of the intervention and its impact from the perspective of family members, and care staff, will be analysed through survey and interview data.

Perceptions about who can benefit from AEP-led exercise, from ambulant residents, to residents in ‘princess chairs’, appear to be changing. There were perceived improvements across a range of factors during the intervention, and no perceived deterioration. Care Staff appear motivated by the effectiveness of the program, supporting the value of AEPs as a member of an allied health team, in the care of dementia patients in the residential aged care environment. Objective functional data and the sustainability of the intervention are currently being investigated.

Dr Sivaraman Purushothuman
Email: siva.p@neura.edu.au Theme: Diagnosis/Assessment
Risk factor analysis in pathologically-confirmed dementia with Lewy bodies compared with Alzheimer’s disease
Sivaraman Purushothuman & Glenda Halliday
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Background: Dementia with Lewy bodies (DLB) is the second most common form of clinically diagnosed dementia, but pure Lewy bodies at autopsy occurs in only 32% with many having severe Alzheimer pathology instead (Nelson et al. 2010). Consequently, most research on risk factors and other features identify significant overlap between DLB and Alzheimer’s disease (AD). In clinical cohorts, risk factors for DLB overlap with those for AD and Parkinson’s disease (PD), as may be expected, and include male sex, smoking, education, depression, low caffeine intake and family history (Boot et al. 2013). No study has assessed these risk factors in pathologically confirmed DLB cases.

Objective: To assess risk factors in pathologically confirmed cases of DLB compared with AD.

Study design: Longitudinally followed AD and DLB patients (N=178) who donated their brains to the Sydney Brain Bank for research purposes were selected following ethics approval. All cases with AD (NIA-Reagan criteria) or Lewy body (LB) pathology were included. Chi-square analyses were performed on extracted proforma captured data to determine differences in these key variables between groups.

Results: Twice as many pathological AD cases were misdiagnosed (27% with clinical DLB) compared with pathologically confirmed DLB cases (13% with clinical AD). Most clinical DLB cases had mixed AD with Lewy body pathology (53%). More pathologically confirmed DLB cases were male (81%) compared with AD (46%), whereas more AD cases had some family history of dementia (61%) compared with DLB (40%). There were no differences between groups in the years of education, smoking history, caffeine intake or presence of depression.

Conclusions: Clinical misdiagnosis of DLB is common, but most cases with pathologically confirmed DLB also have AD pathologically. The dominance of male gender as a risk factor for DLB and not AD was confirmed, but no differences in many other risk factors were found to differentiate DLB from AD. Dominant genetic influences appear more likely in AD compared to DLB.
**Evidence-based Clinical Practice Guideline for Deprescribing Cholinesterase Inhibitors and Memantine in People with Dementia**

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**Introduction:** There are currently two classes of medications available to treat the symptoms of dementia: cholinesterase inhibitors (ChEIs) and memantine. The potential benefits and risks of these medications may change over time. The purpose of this guideline is to assist healthcare professionals to determine when it might be suitable to trial withdrawal of these medications.

**Methods:** The Guideline Development Team (GDT) consisted of nine clinicians with experience in caring for people with dementia and two consumer representatives. We followed the process of developing class-specific deprescribing guidelines, which are based on a comprehensive checklist for successful guideline development and the AGREE-II criteria. We also incorporated requirements for Australian National Health and Medical Research Council external guideline approval. The process involved a systematic review and used the GRADE process to assess the quality of the evidence and convert the evidence into recommendations.

**Results and Discussion:** Four recommendations and three practice points were developed to guide deprescribing of ChEIs and memantine. The recommendations take into account the quality of the evidence, the risks and benefits of deprescribing, the risks and benefits of continuation, consumer values and preferences, and economic considerations.

**Conclusion:** While there were limitations to the available evidence, the GDT was able to provide recommendations to guide deprescribing of ChEIs and memantine. The recommendations should be considered in the context of the individual and deprescribing should be conducted as a process with consumer engagement throughout.

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**PALZ-Professionals with Alzheimer’s: Retaining Identity**

PALZ- Professionals with Alzheimer’s

When diagnosed with Alzheimer’s Disease or other dementia, those who have worked in a high-powered, intellectually-stimulating environment, lose not only the mental challenges within the workplace, but the social network, so often built through work relationships. Their loss of a sense of identity, dignity, and self-respect is profound. Yet, in the early years of these diseases, many are still high-functioning, knowledge-seeking, socially adept, and professionally inquisitive individuals, frustrated and saddened that their contributions to professional dialogue are no longer deemed valid.

PALZ – Professionals with Alzheimer’s addresses this by providing a bi-monthly corporate-style social forum, where attendees are part of interactive presentations by leading professionals, and are subsequently able to expand those discussions with peers, over coffee. Alternate months allow industry groups eg: accountants, lawyers, teachers to have industry-based meetings, or may provide an opportunity for board room or site visits. An annual conference fosters recall of conference attendances of past times, with the conference programming tailored for best receptiveness.

From a societal perspective, the longer the brain can be kept active and engaged, the longer a person is able to function within the community – not drawing on community resources. PALZ – Professionals with Alzheimer’s provides an environment that fosters that mental stimulation, but further, is able to do so whilst ensuring the social focus is on the “Who I am” not the “What I have.”
Using the ASPREE Study to advance dementia research

Monash University

Background: Large prospective studies of dementia with deep phenotyping will enable better characterisation of risk factors for cognitive decline and dementia.

Methods: ASPirin in Reducing Events in the Elderly (ASPREE) is a double blinded placebo-controlled randomised trial to determine whether daily ingestion of low-dose aspirin can prolong ‘disability-free survival’ (incorporating onset of dementia or persistent disability and mortality) in older adults when used in a primary prevention setting. Eligible individuals were ≥70 years (≥65 years for US minorities groups) without cardiovascular disease, physical disability or dementia, and with a Modified Mini-mental State Examination (3MS) score <78.

Results: 16,703 Australian and 2,411 US participants were recruited. Participants undergo regular systematic cognitive assessments over an average 5 years. Loss to follow-up has been minimal (<5%). Mean (SD) cognitive scores at baseline were: 3MS (global cognition) 93.4 (4.6), Symbol Digit Modalities Test (attention/processing speed) 36.7 (10.2), Hopkins Verbal Learning Test-Revised (delayed recall memory) 7.7 (2.8), Controlled Oral Word Association Test F (language/verbal fluency) 12.1 (4.6). Dementia diagnosis is adjudicated by an international clinical panel after reviewing the results of cognitive and functional assessments, medical records and clinical diagnosis information, and brain imaging and blood tests (as clinically indicated). We estimate approximately 800 individuals will be diagnosed with dementia by the end of the trial (December 2017).

Conclusion: Given the depth and breadth of high quality data which has been gathered on such a large population, we will describe how the ASPREE study provides a valuable resource to study protective and risk factors for dementia.

A peripheral epigenetic signature of dementia: blood methylation levels of brain derived neurotrophic factor (BDNF)

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Background: Recent research suggests the involvement of epigenetic processes, such as DNA methylation, in dementia. Epigenetics also provides a promising new class of biomarkers with potential clinical utility for early diagnosis. The aim of this study was to determine whether blood DNA methylation of brain-derived neurotrophic factor (BDNF) was associated with the prevalence and incidence of dementia. BDNF is an important regulator of neuronal activity and neurogenesis, and lower serum BDNF levels have been reported in individuals with dementia.

Methods: 1024 participants aged ≥ 65 years were recruited as part of a longitudinal study of psychiatric disorders in France (the ESPRIT study). Dementia was diagnosed at baseline and follow-up according to the DSM-IV revised criteria by a panel of independent neurologists who reviewed the results of neuropsychological examinations, imaging and detailed medical information. BDNF promoter I methylation was measured using the SEQUENOM MassARRAY platform.

Results: BDNF methylation at baseline was associated with both prevalent dementia and incident dementia over the 12 year follow-up period. Among participants without dementia, BDNF methylation was also associated with baseline scores on the Mini-Mental State Examination (MMSE), and the decline in MMSE scores over time. No effect modification (interactions) were observed with sex or the ApoE-e4 allele, and all associations remained after adjustment for age.

Conclusion: Our findings highlight the potential for blood BDNF methylation to be a biomarker of dementia, however further work is needed to determine how BDNF genetic variation could influence these associations. Replication of these findings is also required.
Strategies Used by Primary Care Practitioners to Support People with Dementia with Driving Cessation

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This research addresses dementia and driving cessation, a major life event, and an immense challenge in primary care. In Australia, it is general practitioners (GPs) who identify changes in cognitive functioning and monitor driving issues with their patients. GPs are advised not to base their fitness to drive decisions solely on disease duration, and without clear guidelines or tests, it is a complicated area of practice. We aimed to gain an understanding of the barriers and facilitators that primary care practitioners experience in managing driving cessation with their patients with dementia, and the strategies implemented to address these. A qualitative study was undertaken to understand how GPs transition a patient with dementia to non-driving status. Data were collected through five focus groups with a total of 29 GPs in practices across Queensland, Australia. Discussions were audio recorded, transcribed verbatim and thematically analysed taking a phenomenological approach. Preparation and education were identified as key. Because loss of insight into declining driving abilities exacerbated the challenges of stopping, timing of the discussion was regarded as critically important. However, it was complicated with the difficulty of identifying early dementia; and concern for the negative impact that raising the driving issue had on the doctor-patient relationship. A number of in-room tests were reported as somewhat useful, however no single test satisfactorily predicted fitness to drive, and these lacked face validity with patients. GPs noted that involving supportive family members and providing strategies for accessing alternative transportation were helpful. The findings clarify a need for support programs to support GPs and their patients to manage the complex issues around dementia and driving cessation.

Can Telehealth Deliver Improved Outcomes for Older People with Dementia who are Giving up Driving?

Primary Care Clinical Unit, The University of Queensland

This study examined the feasibility of using telehealth technology to deliver a driving cessation intervention aimed at enhancing independence and wellbeing for people with dementia. Telehealth can improve access to health care for people living in geographically isolated areas, which is highly relevant for Australia’s dispersed population. Its role in the health care management of community-dwelling older Australians with dementia however, is not fully realized. It was important to understand the potential usability and benefits of telehealth for people with dementia from a number of perspectives. This phase involved an expert reference group of multidisciplinary health professionals from neuropsychology, geriatric medicine and telemedicine. Data were collected via semi-structured interviews with a convenience sample (N=6), recorded and transcribed verbatim and analyzed using a phenomenological framework to identify concepts and themes. There was clear recognition of the need for such an intervention. Following diagnosis, driving cessation was the biggest single issue that people with dementia faced according to these experts – often resulting in depression, and less commonly, suicidal ideology. Suggestions to enhance effectiveness were offered, including limiting the amount of time individuals spent in sessions, to reduce fatigue, and having someone in the room, such as a family member, for support. However, there was consensus that older people with dementia could ably manage telehealth technology, and it was noted as ageist to infer otherwise. These experts acknowledged that telehealth has the potential to change the way that dementia is dealt with in Australia, especially in areas where there are no face-to-face alternatives.
Dr Bingyang Shi
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New Strategy for Blood-Brain Barrier Crossing and Brain Disease Therapy
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Abstract Summary: A key challenge for treating neurodegenerative diseases is the delivery of drugs across the blood–brain barrier (BBB). To overcome this, our group has been developing nanoparticles based strategy to transport drugs across the BBB into brain, offering high-performance therapy for brain diseases.

Introduction: The BBB is a natural protective cellular barrier separating the brain and spinal cord from the rest of the body, preventing toxic chemicals and molecules from entering the brain. However, the BBB also stops most therapeutic drugs from reaching the brain.[1] Over many years, various strategies have been proposed to increase BBB penetration efficiency, including chemical modification of compounds to facilitate their membrane permeability across the BBB, and carrier- or receptor-mediated transcytosis.[2-4] Unfortunately, these approaches are relatively unsuccessful, with the best techniques clinically verified taking less than 1% of drugs through the BBB.[5] Nanoparticles (NP) are emerging as a new class of delivery vehicles that can mediate and/or improve transendothelial penetration of drugs to specific regions of the brain.[6] Conventional nanoparticles, including polymeric nanoparticles,[7] gold nanoparticles[8] and silica nanoparticles,[9] have all been reported to improve molecule transportation across the BBB, but face a list of obvious challenges. One outstanding bottleneck is the difficulty in mapping the distribution of nanoparticles and tracking their entry pathways into the deep tissue of the living brain, where high background noise is generated by blood circulation. This issue stops further systematic study of the mechanism of the nanoparticles based BBB penetration, how sizes, shapes, and surface of nanoparticles affect BBB penetration for advanced BBB penetration. Another fundamental problem is how to avoid particle clearance by the immune system, and how to target the delivery of nanoparticles (and controlled release of drugs) to specific cells or tissues in sufficient quantities for therapeutic efficacy. Clearly further multidisciplinary research is needed to identify a robust biocompatible strategy that combines the multiple functions of BBB penetration, excellent biocompatibility and on-demand targeted delivery of compounds.

Most recently, we firstly investigate how nanoparticles with different surfaces and shapes affect BBB penetration using upconversion nanoparticles (UCNPs), because the unique advantages of UCNPs such as fine tuning shape size/surfaces, background free, photo stable, and high deep tissue penetration,[9] results them as ideal model nanoparticles to investigate the underlying mechanisms of how nanoparticles cross the BBB. Furthermore, we also study the strategy that employ the cell membrane of red blood cell to coat the nanoparticles for the fabrication of biomimetic BBB penetrative delivery system, to avoid particle clearance by the immune system. Most importantly, we have discovered that some targeting molecules, for example glucose and transferrin, which can help nanoparticles to pass the BBB. Based on the key information from this study, we further developed a toolbox of efficient BBB penetrable nanoparticles for brain disease therapy and diagnostics.

Dr Olga Shimoni
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Novel nanocrystalline particles for earlier detection of Alzheimer’s onset
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Over the past few decades, there has been a rapid growth in nanoparticles (NPs) discovery and their use for medical therapy and diagnostics [1,2]. Nanoparticles based on crystalline matrix of sodium fluoride have a pronounced ability to host functional ions, such as lanthanide ions. Gadolinium-doped nanoparticles (Gd NPs) have proven to function as enhanced contrast imaging agent for magnetic resonance imaging (MRI) [3]. In this work, we developed ultra-small Gd-doped nanocrystals as a potential MRI sensor. The as-synthesized Gd NPs are generally hydrophobic in nature due to their capping by long-chain hydrophobic ligands (e.g. oleic acid). For application in biomedicine, NPs should be stable
in physiological environment and specifically recognize the target biomolecules. Consequently, we have established a surface functionalization protocol to stabilize NPs in biological media. Furthermore, we demonstrated surface functionalization with molecule that specifically target neuronal cells undergoing apoptosis associated with Alzheimer’s or Parkinson’s diseases. Overall, our results show a great potential as novel MRI sensor for non-invasive detection of Alzheimer’s disease.

Dr Craig Sinclair

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Supported decision-making and dementia: Observations from legislation and case law in three Australian states

Meredith Blake, Pia Castelli-Arnold, Sue Field, Cameron Stewart, Sascha Callaghan, Craig Sinclair

The University of Queensland

This paper addresses the issue of health care decision-making in relation to persons with dementia against the backdrop of the Convention on the Rights to Persons with Disabilities and the subsequent Australian Law Reform Commission Report. It begins by outlining the premise behind recent legal developments promoting the rights of persons with disabilities, and the concept of supported decision-making as a way of securing decisional autonomy for such persons. The paper then examines the legal frameworks which address decision-making for people with impaired decision-making capacity in three Australian jurisdictions, seeking to establish the degree to which these frameworks reflect supported decision-making. This is accompanied by a review of decisions by administrative tribunals in these same jurisdictions as a means of identifying how the legal principles and provisions are operating in practice in the context of persons with dementia. This analysis indicates that, while tribunals regard guardianship orders as a course of last resort, there is little evidence of formal supported decision-making, with the tribunals preferring informal approaches to decision-making in such cases, arguably resulting in a lack of clarity and transparency. By way of comparative analysis, the paper examines the law in British Columbia, Canada, which has in place a statutory framework which provides a formal system for representative agreements as a way of providing decision-making support for persons with compromised capacity. The paper concludes by identifying a number of ways in which Australian approaches to decision-making for persons with dementia could benefit from the Canadian experience.

Dr Craig Sinclair

Email: craig.sinclair@rcswa.edu.au Theme: Living with Dementia

Substitute or supported decision-making? Learning from the lived experiences of people with dementia and their carers to guide practice, policy and law reform

The University of Western Australia

Craig Sinclair (presenting author), Kate Gersbach, Michelle Hogan, Romola Bucks, Meredith Blake, Kirsten Auret, Kathy Williams, Josephine Clayton, Helen Radoslovich, Sascha Callaghan, Sue Field, Meera Agar, Cameron Stewart, Meredith Gresham, Angelita Mart

Recent years have seen growing debate regarding the rights of individuals to make decisions about their own lives, and to have these decisions respected. People living with disabilities have traditionally experienced barriers to the full enjoyment of legal capacity, with substitute decision-making often being the default response for people living with cognitive impairments. International treaties, and a recent report from the Australian Law Reform Commission, have challenged this practice, with calls for people living with disabilities to be supported to enact their own decisions, to the greatest extent possible. The emerging practice of ‘supported decision-making’ has been explored in the disability sector, however there is very little research on this topic in the context of dementia.

This two-phase qualitative study is part of a broader program of research undertaken within the Cognitive Decline Partnership Centre, examining supported decision-making in the context of dementia. The first phase of the study explored lived experiences of decision-making and future planning relating to healthcare, medical treatment and personal or ‘lifestyle’ matters among people living with dementia and their carers. The second phase of the study involves specific consultation with participants regarding the ‘supported decision-making’ approach. The researchers use in-depth semi-structured interviews with individuals and dyads (pairs), aiming to draw on the lived experiences of people living with dementia, and their carers, to understand what types of support might be helpful, who is best placed to
provide such support, and the practical issues and safeguards that need to be considered. To date 30 interviews have been undertaken (17 dyad, 13 individual), with key themes including accommodating cognitive impairment, the role of the supporter, and the relational context in which decisions are made and enacted. In many cases supported decision-making was described as ‘already happening’, although ‘independent’, ‘supported’ and ‘substitute’ decisions could be seen to intertwine in participant decision-making. In some cases supported decision-making was seen as an abstract idea. Participants have expressed strong support for close and trusted people to be in the role of supporters and provided insights into the role of professionals in facilitating this process. Further work will be focused on refining these themes and developing community resources, in collaboration with Alzheimer's Australia / Dementia Australia.

Dr Kate Smith
Email: kate.smith@uwa.edu.au Theme: Care

‘A Moorditj Life’: Development of a quality of life package for older Aboriginal Australians
Centre For Aboriginal Medical And Dental Health, University of WA

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2. National Ageing Research Institute, Melbourne Health
3. Western Australian Centre for Health and Ageing, University of Western Australia;
4. Institute for Choice, University of South Australia

Introduction Despite the need there is no quality of life measure for older Aboriginal Australians with dementia. This project aims to develop such a tool, and a package of recommendations.

Method Qualitative Indigenous research methods were utilised. Aboriginal Australians over the age of 45 years living in Perth completed in-depth interviews using a yarning approach. Thematic analysis was used to identify what is important to have a good (Moorditj) life, utilising a phenomenological approach to make meaning of participant stories.

Result and Discussions 20 interviews were completed, with a participant age range of 47-82 years. The key factors currently important to the quality of life of participants were: strong spirit; access to country; cultural knowledge, identity and activities; language; community (family and friends); health; socio-economic factors; individual factors; Eldership and teaching; security; and recreation. Factors additionally important to participants as they grow older included: end of life planning, aged care services, and healing. Factors impacting on quality of life include racism, service issues, adapting to society, colonisation, missions, trauma, substance abuse, and stolen generation causing loss of: culture, family, identity and language. These results will be discussed in yarning groups with people with dementia and their caregivers to finalise items for the tool and wording of items. Validity testing will begin next year.

Conclusion The final package can be utilised by services to identify and improve the quality of life of older Aboriginal Australians, including those with cognitive impairment.

Dr Ashleigh Smith
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Moderate to vigorous physical activity is associated with EEG global power in older adults
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2. Cognitive Ageing and Impairment Neurosciences (CAIN), School of Psychology and Social Work, University of South Australia, SA.
3. Neuromotor Plasticity and Development (NeuroPAD), School of Medicine, University of Adelaide, SA.

Physical activity is a primary risk factor for late-life Mild Cognitive Impairment (MCI) and dementia. Previous studies have highlighted the potential diagnostic value of resting state electroencephalography (EEG) to discriminate between cognitive states in late-life and the prediction of decline to Mild Cognitive Impairment or dementia. Here we extended this approach by investigating if resting state EEG was associated with individual differences in physical activity levels in older adults without dementia. 7-days of objectively measured 24 h activity data were captured using GENEActiv wrist-worn tri-axial accelerometers in 16 older adults (range 56-82 years, mean age 69.4 ± 6.1, 8 females). Using 60-s epochs, average daily time spent in sleep, sedentary behaviour, light PA and moderate-to-vigorous PA was calculated using pre-defined cut-points using custom COBRA software. In addition, 3-min of resting state EEG (eyes closed) was captured using a 62 channels and global power determined using the (delta + theta)/(alpha + beta) ratio (DTABR); a measure of generalised slowing of
neural activity, previously shown to be sensitive to MCI and vascular burden. When accounting for age and sex, time spent in moderate-to-vigorous physical activity, but not sedentary time, sleep or light physical activity was associated with a lower global DTABR ($p < 0.05$). These findings provide evidence that engagement in moderate-to-vigorous physical activity protects against the typical alterations in brain neural synchronisation associated with MCI and dementia.

**Professor Velandai Srikanth**

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*Theme: Prevention*

**Pilot RCT of multi-modal exercise on cognition in Type 2 diabetes mellitus**

*Peninsula Health & Monash University*

**Background:** Type 2 Diabetes (T2D) is associated with increased risk of dementia. We aimed to determine the feasibility of a randomised controlled trial (RCT) examining the efficacy of exercise on cognition and brain structure in people with T2D.

**Methods:** A 6-month pilot parallel RCT of a progressive aerobic- and resistance-training program versus a gentle movement control group in people with T2D aged 50-75 years (n=50). Assessors were blinded to group allocation. Brain volumes, cortical thickness and white matter microstructure were measured using MRI, and cognition using a neuropsychological battery. Outcomes were changes to protocol, recruitment, time to enrol, randomisation, adherence, safety and retention.

**Results:** The mean age of participants was 66.2 (SD 4.9) years and 48% were women. There were no changes to the design during the study. A total of 114 people were screened for eligibility, with 50 participants with T2D enrolled over 8 months. Forty-seven participants (94%) completed the study (23 of 24 controls; 24 of 26 in the intervention group). Baseline characteristics were reasonably balanced between groups. Exercise class attendance was 79% for the intervention and 75% for the control group. There were 6 serious adverse events assessed as not or unlikely to be due to the intervention. Effect sizes for each outcome variable are provided.

**Conclusion:** This study supports the feasibility of a large scale RCT to test the benefits of multi-modal exercise to prevent cognitive decline in people with T2D.

**Professor Velandai Srikanth**

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*Theme: Prevention*

**Longitudinal associations of Type 2 Diabetes Mellitus (T2D) with Cognitive Decline and Brain Atrophy**

*Peninsula Health & Monash University*

**Background:** T2D is associated with dementia. There are very few longitudinal data describing the longitudinal associations of T2D with cognitive decline and brain atrophy. We aimed to study the longitudinal relationships (1) Between T2D and cognitive decline and (2) Between T2D and imaging markers of brain atrophy.

**Methods:** Cohort study (3 points of measurement, total follow-up ~6 years). T2D sample – from National Diabetes Service Scheme Database in Southern Tasmania, Australia (age >55). Non-T2D sample – randomly selected from electoral roll in Southern Tasmania (age >60). Cognitive Battery - Digit Symbol Coding, Symbol Search, COWAT, Category Fluency, Stroop Test, Digit Span, Hopkins Verbal Memory Test, Rey Complex Figure copy and delay. Structural MRI - 1.5T MRI brain scan, total brain and ventricular volumes measured using automated segmentation. Multivariable linear mixed level regression for longitudinal modelling.

**Results:** Total 705 participants, mean age 71 years, 42% female, 49% with T2D. T2D was associated with poorer cognitive scores, smaller brain volume, and greater ventricular volume at baseline. T2D was associated with greater rate of decline in verbal fluency ($p = 0.05$) and verbal memory ($p = 0.001$) and a greater rate of increase in ventricular volume ($p = 0.04$). T2D was associated with lesser rate of decline in visuospatial skills, possibly due to differential sample attrition.

**Conclusion:** T2D is associated with greater rate of cognitive decline and brain atrophy over 6 years, possibly contributing to the risk of clinical dementia.
Dr Genevieve Steiner

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When life gives you lemons, you make lemonade: validating a phone screening procedure to differentiate mild cognitive impairment from subjective cognitive complaints

Genevieve Z. Steiner, Naomi L. Fagan, Dennis H. Chang
The Western Sydney University

Mild cognitive impairment (MCI) is a heterogeneous syndrome that increases the risk of dementia. One of the difficulties in recruiting people with MCI from the community is that targeted advertising campaigns typically yield a high proportion of potential candidates who have subjective cognitive complaints (SCCs), rather than MCI. SCCs involve the subjective experience of cognitive decline, but the absence of any objective cognitive impairment on standardised neuropsychological tests. In order to save resources and reduce participant burden by unnecessarily inviting people with SCCs in for testing, our team has developed a comprehensive phone screening process to maximise the number of MCI true positives. This process has been facilitated by parallel recruitment for a SCC study. Our phone screening procedure involves: consent, inclusion/exclusion criteria, Telephone Interview for Cognitive Status-Modified (TICS-M), Weschler Test of Premorbid Function (ToPF) Complex Demographics, and a brief clinical interview that probes medical history, subjective premorbid function, evidence of changes in memory and thinking, time course and nature of the changes, potential mitigating situational factors, sleep quality, and mental health concerns (if depression is suspected, the Geriatric Depression Scale is administered). Although this is not the primary aim of the fellowship project, we have found it to be a particularly fruitful exercise with promising results that we hope will aid other groups utilising community-based recruitment strategies.

Dr Brad Sutherland

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Uncovering mechanisms of pericyte contraction and death that reduce energy supply and cause cognitive decline

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Vascular dysfunction, characterised by hypoperfusion and blood-brain barrier (BBB) disruption, can lead to an energy deficit within the brain and could drive pathogenesis of dementia and Alzheimer’s disease (AD). Pericytes are spatially isolated cells on capillaries that actively control cerebral blood flow (CBF) by constricting or dilating capillaries. Mild changes in CBF can cause pericyte death, clamping capillaries shut and limiting oxygen supply to the brain. Therefore, pericyte degeneration could switch a transient vascular insult into a chronic restriction of blood supply. We hypothesise that identifying mechanisms of pericyte contraction of capillaries could provide novel targets to prevent energy deficit and subsequent cognitive decline. A gene microarray of human brain vascular pericytes revealed that compared to endothelial cells, there was greater expression of receptors for both contractile (angiotensin-II type 1, endothelin-1A) and relaxant (adenosine A2b, prostaglandin EP4) mediators. Direct administration of the vasoconstrictor endothelin-1 generated a prolonged contraction of pericytes in vitro. AD and vascular dementia are characterised by enhanced free radical production. We exposed pericytes to hydrogen peroxide in vitro, which dose-dependently caused pericyte death. In order to protect pericytes from free radical damage, we placed pericytes in a hypothermic environment (33°C). Hypothermia reduced pericyte death following hydrogen peroxide exposure showing that pericytes are able to be protected from free radical injury. These results show that pericytes respond to both vascular mediators and free radicals, and can be protected from injury, which suggests that they may provide a novel target to improve blood flow and energy supply thereby restricting cognitive decline.

Dr Ryu Takechi

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Blood-brain barrier dysfunction may be causally associated with cognitive decline and neurodegeneration induced by pre-diabetic insulin resistance in wild-type mice

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**Background:** Diabetic insulin resistance and pro-diabetic diet are reported to increase dementia risk through unknown mechanisms. Emerging evidence suggests that the integrity of blood-brain barrier (BBB) is central to the onset and progression of neurodegeneration and cognitive impairment. Therefore, the current study investigated the effect of pro-diabetic diets on cognitive dysfunction in association to BBB integrity and its putative mechanisms.

**Methods:** C57BL/6J mice were chronically ingested with a diet enriched in fat and fructose (HFF) for 4 or 24 weeks. BBB integrity was measured with cerebral extravasation of plasma IgG and endothelial tight junction expression. Cognitive performance was assessed by Morris Water Maze.

**Results:** Morris water maze test indicated no significant cognitive decline after 4 weeks of HFF feeding compared to low-fat fed control. However, at this stage, BBB dysfunction accompanied by heightened neuroinflammation in cortex and hippocampal regions was already evident. After 24 weeks, HFF fed mice showed significantly deteriorated cognitive function concomitant with substantial neurodegeneration, which both showed significant associations with increased BBB permeability. In addition, the data indicated that the loss of BBB tight junctions was significantly associated with heightened inflammation and leukocyte infiltration.

**Conclusions:** The data collectively suggest that in mice maintained on pro-diabetic diet, the dysfunctional BBB associated to inflammation and leukocyte recruitment precedes the neurodegeneration and cognitive decline, indicating the causal association.

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**Dr Ryu Takechi**  
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**Theme:** Prevention

**Vitamin d, cerebrocapillary integrity and cognition in murine model of accelerated ageing**

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**Background:** Increased use of vitamin-D (vit-D) supplements has been attributed for improved cognitive performance, an important consideration given that vit-D deficiency becomes more common with older age. However, several lines of evidence suggest that chronically heightened plasma vit-D may paradoxically compromise cognitive function. The mechanism(s) for detrimental effects of exaggerated vit-D on central nervous system (CNS) function have not been delineated. However, in animal model studies, we showed that one possibility might be through heightened neurovascular inflammation that occurs in response to changes in cerebral capillary permeability. Senescence-accelerated-mouse-phenotype strains (SAMP) represent lines of AKR/J mice that feature accelerated aging. The SAMP strain-8 (SAMP8) is considered a relevant animal model for human-ageing, because the pathological traits that develop are age-dependent and occur as a consequence of subtle oxidative metabolic aberrations over a prolonged period of time. SAMP8 mice have been comprehensively assessed for behavioural disturbances and have demonstrated spatial learning and memory deficits. Passive and active avoidance disturbances are indicated and object recognition compromised in older age SAMP8 mice. Methods: SAMP8 mice at the age of 6 and 20 weeks were used. The capillary integrity was assessed by the cerebral extravasation of plasma IgG. Cognitive performance was assessed by Morris Water Maze (MWM). Results: In this study, we present studies in SAMP8 male mice and show that serum 25(OH)D progressively increases with ageing in SAMP8 male. However, we also provide evidence that the increase in serum 25(OH)D occurs concomitant with poorer cognitive performance by MWM analysis and increased capillary permeability. Latency time area-under-curve (AUC) to rescue platform in MWM determined over a 3 day trial increased by approximately 50% in SAMP8 mice at 20 weeks of age compared to baseline at 6 weeks of age. Moreover, in these same mice, parenchymal abundance of IgG within HPF and CTX was markedly increased as SAMP8 mice. Conclusions: Strong evidence of causality between endogenous hypervitaminosis D and poorer maze performance is suggested by the finding that maintenance of SAMP8 mice on a diet deficient in vit-D prevented the age-associated decline in maze performance, concomitant with maintenance of capillary impermeability. The findings may explain paradoxical clinical data reporting associations of serum vit-D homeostasis and cognition.

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**Dr Jeanette Tamplin**  
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**Theme:** Living with Dementia

**Musical Memories: Connecting community-dwelling people with dementia and their family caregivers through song**

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Active music participation may offer benefits for people with dementia (PwD) and their family caregivers (FCG) living in
the community. For the PwD, this capacity to respond to music may facilitate reminiscence and social engagement. Consequently, FCGs may experience meaningful and satisfying connection with their loved one. This study investigated the effects of therapeutic singing groups for PwD/CG dyads on: relationship quality; life satisfaction, caregiver satisfaction, flourishing, and depression in CGs; and anxiety, quality of life, agitation, apathy and cognitive function in PwD.

A mixed-methods, single group pre-post design utilised standardised outcome measures and qualitative interviews. 11 participant pairs attended 20 weekly group sessions (attended by PwD and CG together) that incorporated singing preferred songs and opportunities for social interaction. Findings from this feasibility study have informed the design of a randomized controlled trial. Quantitative results indicated that healthy baseline scores for relationship quality and wellbeing were maintained throughout the 20-week intervention period for both PwD and FCG. Qualitative results demonstrated that participants perceived both social and personal benefits from participation. They felt that singing in the choir stimulated cognitive responses including learning, skill development, and memory for both the PwD and FCG, and their participation in the research project was perceived as both a positive and challenging experience. These results suggest that therapeutic singing groups offer a unique combination of social support and opportunity for creative emotional expression that may maintain quality of life and sustain a positive and fulfilling relationship between PwD and FCG living in the community.

Dr Rachel Tan
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β-amyloid in Frontotemporal dementia syndromes
Rachel Tan 1,2, Jillian Kril 3, Yue Yang 1, John Hodges 1,2, Victor Villemagne 4, Christopher Rowe 4, John Kwok 1,2, Lars Ittner 2, Glenda Halliday 1,2
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The clinical distinction between frontotemporal dementia (FTD) and Alzheimer’s disease (AD) remains challenging, with ~25% of patients with an FTD syndrome found to have AD at autopsy, a difficulty likely to be overcome with the use of in vivo β-amyloid imaging. Importantly however, prior to the publication of the updated pathological criteria for AD in 2012, only neuritic plaques were used for diagnostic confirmation of AD. As such, knowledge on the prevalence of β-amyloid deposition in the ~75% of patients with an FTD syndrome that do not fulfil pathological criteria for AD is lacking. To address this, the present study assessed β-amyloid deposition in a large series of 94 autopsy-confirmed FTD cases without pathological AD. We report β-amyloid deposition in 38% of patients with behavioral variant FTD and in 37% of patients with primary progressive aphasia. The presence and topographical progression of β-amyloid was found to increase with age in FTD, as observed in controls. The present study also assessed the pathological accuracy of PiB-PET imaging in a cohort of patients with clinical FTD followed to autopsy (n=15). AD pathology was identified in all cases with high PiB retention (n=4) and in one case with low PiB retention. A strong regional correlation was identified between the volume fraction of histological β-amyloid with PiB standard uptake value ratio scaled to the white matter. Together, the present study has assessed a large pathologically-confirmed series of FTD cases, providing a pathological reference that may aid the interpretation of future in vivo assessments of β-amyloid in FTD syndromes.

Dr Jane Thompson
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Involving patients and the public (‘consumers’) in the NHMRC National Institute for Dementia Research (NNIDR)
Alzheimer’s Australia National Dementia Consumer Network

The NNIDR Strategic Roadmap states an intention “… to involve consumers in every stage of dementia research to ensure consumer driven research and translation priorities and outcomes.” The NHMRC provides guidance on how patients/the public can be involved at various levels of research, at various stages of the research cycle and in institutions conducting research.1 How well is NNIDR meeting these expectations? Patients/the public were involved in the development of the NHMRC National Dementia Research and Translation Priority Framework which underpins the Roadmap. Within NNIDR, they are involved in the Expert Advisory Panel and Board. This is necessary, but not sufficient, to fulfill expected standards of public involvement. We also need to ensure
that all NNIDR funded projects and researchers actively involve patients/the public in their research in whatever way is appropriate. Researchers may need specific guidance on this, particularly in basic science research, and, patients/the public need to be supported to develop knowledge, skills and experience to be involved.

Examples of patient/public involvement include: setting research priorities and questions; informing research design; guiding funding decisions; shaping ongoing research; disseminating research findings; campaigning for implementation.

Patient and public involvement (PPI) is becoming an essential element of publicly-funded research. The NNIDR is ideally placed to provide leadership in PPI in dementia research in Australia, but needs to develop resources and structures for its researchers and the public it serves.

Miss Esther Tiong
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Interactive Visual Cues using Intelligent Technologies to Support Care and Health Monitoring Services

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We initially reviewed the possibility of visual cues against impact of reignite flashbulb memories and retention of their short-term memory [1]. The matter on how memory consolidation and duration of memory retention will determine the severity of memory declination, their attentiveness [2] and neuroplasticity of brains. Effective visual cues also discovered to help diagnosis on cognitive declination and type of dementia [3]. Our research aims on building a computerized intelligent system that extracts video keyframes of significant memories to create a set of multi-modal memory hooks with proposed interactive learning interface. By evaluating existing technologies to seek input as to the precise nature of the system, we have come up with logic of intervention: magic choice of conversation mode, using slow prompting technique, repetitive instructions and emphasized consonants that will provide higher attentiveness and interaction between patients and artificial intelligence system. We involved clinical staff and carers (n=17) to develop a functional definition of the system, considered issues on security, privacy and sensitiveness issues and limitation on data storage on memory hardware [4], and examples of various other forms of non-pharmacological interventions [5]. The survey also collected to identify types of major life events that are crucial for digital memory hooks, and need for technique to distinguish associated features from personal life to inform the extraction of video keyframes. Proposed interventions and device interface should be appraised from actual subjects and care staff from institutional environment, also relatives/families and the home environment in future work to formally evaluate the hypothesis from current work.

Miss Esther Tiong
Email: tion0019@flinders.edu.au Theme: Living with Dementia

Interactive Visual Cues for Dementia

Esther Y. C. Tiong, David M. W. Powers, Anthony J. Maeder
Flinders University, Adelaide

Complex attentiveness and deprived memory is often observed with dementia, which causing them unable to learn and retain new knowledge. The value of visual cues has been recognized e.g. for flashbulb memory reignition, retention of short-term memory and useful in assessment of cognitive decline. Our research aims to construct an intelligent agent system with an information environment based on visual cues that supports teaching and learning information and introduce explicit memory hook on dementia. The system will record personal and environment based events, extract video keyframes of significant memories dynamically, and create a set of multi-modal visual cues for recalling memory and encourage memory consolidation. We conducted survey identifying supportive events that promotes likeness and reviewed technologies with relevant support to bring our design concept together for the base of learning and teaching cues. We will formally evaluate a trial intervention with a co-design process involving home caregivers (n=3) to derive a functional definition of our proposed system to improve its usability and effectiveness. We hope our system will assist-to-improve memory, delay chronic progression, promote well-being and support home care. Extending the system to include facility environment will be future work.
Dr Bradley Turner

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SMN mitigates neurodegeneration and disease progression in a mouse model of ALS/FTD

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Cytoplasmic accumulation and aggregation of TAR DNA binding protein 43 (TDP-43) in neurons and glial cells is a pathological hallmark linking amyotrophic lateral sclerosis (ALS) and frontotemporal dementia (FTD). TDP-43 is a RNA binding protein implicated in regulation of RNA splicing, transport and transcription. TDP-43 shows structural and functional overlap with survival motor neuron (SMN), a RNA binding protein also implicated in RNA processing and splicing. We therefore examined a potential contribution of SMN to TDP-43 proteinopathy. Here, we determined a significant and progressive upregulation of SMN protein, but not mRNA, in cortical neurons and spinal motor neurons in a TDP-43 A315T mouse model of ALS/FTD. A corresponding accumulation of cytoplasmic SMN complexes occurred in cortical neurons and spinal motor neurons in TDP-43 A315T mice. Furthermore, cytoplasmic SMN complexes sequestered both TDP-43 and HuR, consistent with incorporation into stress granules. To address whether SMN can functionally compensate for pathological TDP-43, we crossed transgenic PrP-SMN and TDP-43 A315T mice and examined progeny for motor and cognitive behaviour, survival and neuropathology. We demonstrated that transgenic SMN overexpression attenuated neurodegeneration, astrocyte and microglial activation and significantly slowed disease progression in TDP-43 A315T mice. Our findings highlight novel molecular interactions of TDP-43 and SMN in ALS/FTD, while SMN overexpression may counter disease progression and neuropathology in TDP-43 proteinopathy. Enhancing SMN levels and function using pharmacological and genetic agents may therefore prove therapeutically beneficial for ALS/FTD.

Ms Pippy Walker

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Vitamin D Supplementation to Reduce Falls: An Implementation Study in Australian Residential Aged Care Facilities

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Introduction: There is strong evidence for the effectiveness of vitamin D supplement use in preventing falls in residential aged care facilities. It is one of the few falls prevention interventions that clearly apply to people with dementia. Despite this evidence, there is poor and variable uptake of this guideline in practice. This project aims to increase the uptake of vitamin D supplement use in the aged care setting.

Methods: A multifaceted interdisciplinary approach was employed, including frequently used implementation strategies such as identifying a local champion, using expert opinion leaders, disseminating educational materials, providing educational outreach visits, using audit and feedback, and facilitating quality improvement activities over a 12 month intervention period. A non-randomised stepped wedge design was used.

Results: Forty-one facilities participated. The prevalence of vitamin D supplement use, as per best practice falls prevention guidelines varied between individual facilities and was on average 56%. Changes in prevalence over the duration of the intervention were inconsistent and generally corresponded with identified barriers or enablers to implementation.

Conclusion: Implementation in the aged care setting is complex, with numerous barriers across different stakeholder groups. Key issues appear to be lack of recognition of the issue and its consequences by key decision makers (general practitioners and senior management), fragmentation of health management responsibilities, and the changing role of aged care to provide principally palliative care. In addition vitamin D supplement guidelines should consider older people receiving in home care as an alternative to living in a residential facility.
**Dr Michael Waller**  
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*Theme:* Assessment and Diagnosis  
**Poster: No. 126**  

**Differences in age at death largely account for sex disparity in Alzheimer’s disease and dementia mortality rates in the Australian population**

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The University of Queensland  

**Background** There is conflicting evidence about sex disparities in rates of Alzheimer’s disease (AD) and dementia. We examined this issue using death records for Australia.

**Methods** We used death certificate data for all individuals over 60 years with any mention of dementia (including AD and vascular dementia) as the underlying or an associated cause of death for 2006-14 (n=184562). Death rates for women and men were compared using Poisson regression.

**Findings** The crude rate of all deaths with AD or other dementias was 4.9 per 1000 person-years. For women compared to men, the relative rate of mortality with AD or dementia mentioned anywhere on the death certificate was 1.55 (95% confidence interval: 1.53-1.56). After adjusting for single year of age, this rate was attenuated to 0.99, (95%CI: 0.98-1.00). Dementia of ‘unspecified’ type was most commonly reported as the underlying cause of death (58% of records of death with dementia), and also as an associated cause (76%). AD and vascular dementia were the next most commonly recorded underlying causes of dementia deaths (30% and 12%, respectively). Age-adjusted rates for AD were higher for women than men (1.14, 1.12-1.16), while vascular dementia rates were lower (0.80, 0.78-0.82). Age-adjusted death rates with AD or dementia as the underlying cause increased over the 2006-2014 period, but associated causes decreased; total rates of dementia mortality, on the other hand, remained stable. These patterns across 2006-2014 were similar for women and men, and for all dementia types.

**Interpretation** Women’s older age at death explained most of the sex differences in mortality with Alzheimer’s disease or dementia. Completion of death certificates for people with dementia is often imprecise. As such, in order to obtain valid population estimates from death certificates, it is important to combine records across dementia types and underlying and associated causes of death.

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**Dr Stephanie Ward**  
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**Poster: No. 127**  

**A Pilot Dementia Clinical Quality Registry to improve Dementia clinical care**

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**Background:** Clinical Quality Registries (CQRs) are powerful and cost-effective tools that promote and monitor the implementation of clinical guidelines into practice, benchmark clinical performance, and by providing feedback, can substantially improve patient care. There is growing recognition of the need for an Australian dementia registry that incorporates a CQR component. However, developing a CQR for dementia in Australia presents complex challenges. These are best overcome through a pilot registry that can develop and test methodologies, and address initial feasibility issues.

**Methods:** This is a three-year NNIDR-funded project that commenced in September 2017 with the aim of developing and testing methodologies for a dementia CQR. Key steps will include establishing an overall registry purpose and case ascertainment criteria, identifying an epidemiologically sound minimum data set and key quality indicators, exploring and testing patient recorded outcome measures (PROMS) and data linkage, establishing a governance structure for a functioning CQR and costing out a national expansion. Data from an existing large and well-characterised cohort of participants with incident dementia diagnosed during the ASPirin in Reducing Events in the Elderly (ASPREE) study will be utilised, where indicated, to test various elements of the proposal, including identifying participants for testing of PROMs.

**Discussion:** This project builds on team members’ collective expertise in dementia clinical care and CQR development and operation, whilst efficiently utilising data from a large, well characterised cohort. The outcomes from this pilot will inform the most efficient and effective methods for establishing an Australian dementia CQR.
Ms Rochelle Watson

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What is a ‘timely’ diagnosis? Exploring the preferences of health service consumers regarding when a diagnosis of dementia should be disclosed

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Background: A shift in the field away from early diagnosis of dementia towards timely diagnosis acknowledges the importance of person-centred dementia care. What is considered timely diagnosis disclosure may differ depending on the unique preferences and circumstances of the person with dementia. The perception of ‘timely’ diagnosis disclosure may also differ between the person with dementia, their family members, and the clinician. This research explored the preferred timing of dementia diagnosis disclosure among health service consumers.

Methods: A cross-sectional survey was conducted with outpatients and their support persons attending an Australian hospital. Participants were aged over 18 years and English-speaking. Participants were recruited in the clinic waiting room and provided a web-connected iPad to complete the survey. Data was collected on socio-demographics and experience with dementia. Preferences for timing of diagnosis disclosure were explored via two hypothetical scenarios.

Results: 446 participants completed the survey. Most participants preferred a dementia diagnosis to be disclosed as soon as possible, regardless of whether the scenario described themselves being diagnosed (92%) or their spouse having dementia (88%). Socio-demographics and previous dementia experience were not significantly associated with preferences. Preferences for self and preferences for spouse were strongly correlated (0.91).

Discussion: Findings may assist to overcome some barriers to timely diagnosis by providing clinicians with guidance about consumer preferences. These preferences, along with increasing prevalence of dementia, may have important implications for models of dementia care.

Dr Rachel Wong

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Cerebrovascular resistance is an early biomarker of slow gait and cognitive deficits in healthy older women

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Cognitive difficulties and gait abnormalities both increase with age; all of these are linked to altered cerebrovascular hemodynamics and collectively predict the speed of transitioning to dementia. We have previously shown that impaired neurovascular coupling compromises cognitive performance in healthy older women; others have also linked cerebrovascular dysfunction to slow gait in the elderly. Here, we determined whether cerebrovascular dysfunction is associated with slow gait and poor cognitive function in a sample of healthy, normotensive older women.

During the baseline assessments of a two-year nutrient intervention, 146 postmenopausal women aged 65±7 years underwent a neurocognitive battery assessment of cognitive flexibility, processing speed, verbal, working, and episodic memory. Gait speed was determined by dividing the total distance by the time taken during a 2-min walk test, at preferred speed. Transcranial Doppler ultrasound was used to assess cerebral velocities and vessel stiffness in the middle cerebral arteries at rest and during a 3-min hypercapnia challenge.

With age as a covariate, gait speed was negatively correlated with cerebrovascular resistance (ratio of systemic mean arterial pressure to basal mean blood flow velocity) (r=−0.241, P=0.021). This relationship was partially mediated by BMI, central adiposity and fasting triglyceride levels. After taking into account education levels, slow gait was also linked to poor processing speed (r=0.259, P=0.002), verbal memory (r=0.171, P=0.041) and overall neurocognitive performance to the test battery (r=−0.176, P=0.035). However, cerebrovascular responsiveness to hypercapnia did not correlate with cognitive function or gait speed.

In our cohort of healthy older women, cerebrovascular resistance appears to be the pathological link between slow gait and cognitive deficits. Preventing the onset of metabolic syndrome in adulthood may be a useful target for dementia prevention.
Subjective cognitive decline is associated with cerebrovascular dysfunction in healthy older women.

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Subjective cognitive decline (SCD) complaints, preceding mild cognitive impairment, is emerging as a marker of prodromal dementia. Impaired cerebrovascular function is related with the severity of cognitive impairment, but this relationship has not been explored in SCD. We examined whether SCD is associated with cerebrovascular dysfunction in a cognitively-normal population.

Using the baseline assessments from a two-year resveratrol supplementation intervention in 146 postmenopausal women aged 65±7 years, SCD was determined by a percentage score from a survey of 20 questions relating to everyday memory complaints. Depressive symptoms, obtained using the Center for Epidemiologic Studies Depression Scale (CES-D), were also normalised to a percentage. Transcranial Doppler Ultrasound (TCD) was used to measure cerebral blood flow velocities (CBFV) in the middle cerebral arteries at rest. Resistance in the cerebral vessels or cerebrovascular resistance (CVRi) was calculated as the ratio between systemic mean arterial pressure and basal mean CBFV.

Independent of age, CES-D was related to SCD (r=0.364, P<0.001). However, depressive symptoms were unrelated to CVRi or CBFV. After adjusting for years of education and depressive symptoms, SCD was positively correlated with CVRi (r=0.292, p=0.006) and negatively with basal mean CBFV (r=-0.227, p=0.009).

We now provide the initial evidence that in our cohort of healthy, normotensive older women, those with SCD are likely to report more depressive symptoms and have reduced CBFV and increased resistance in the cerebral vessels. Therefore, maintaining optimal cerebrovascular function is crucial for delaying the onset of cognitive impairment.

Vascular risk measures and longitudinal Aβ accumulation: results from the AIBL study of ageing

Dr Paul Yates

Interventions to delay or prevent the onset of dementia have potential to considerably reduce its future prevalence. Hence, the interface between risk factors for vascular disease and development of dementia is of great interest, because many vascular risk factors (VRF) are amenable to intervention. We used longitudinal Aβ PET imaging to identify whether VRF factors were associated with increased accumulation of Aβ over six years’ follow-up.