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Centre for Healthy Brain Ageing (CHeBA)
Annual Report 2016

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DIRECTORS' REPORT

"The year 2016 saw an upscaling of our efforts at national and international levels to meet the growing challenge of dementia."

Dementia continues to pose an ever-growing challenge to our society. While there has been good news that the incidence of dementia may be reducing somewhat in high income countries, this will not be enough to prevent a continuing increase in the total number of persons with dementia. The many advances in neuroscientific research have not yet delivered an effective drug treatment. The research at CHeBA therefore continues to focus on the prevention of dementia, or delaying its onset. The year 2016 saw an upscaling of our efforts at national and international levels to meet this challenge. The two most noteworthy efforts of 2016 were continued expansion of **The Dementia Momentum** and development of **Maintain Your Brain**.

In 2015, CHeBA launched its major philanthropic initiative, The Dementia Momentum, to create new funding partnerships between researchers and corporate Australia, and raise community awareness about risk and protective factors for the disease. One year on, the initiative has lived up to its name exceeding its first year target of raising $2 million as part of its larger goal of $10 million over 5 years. This could not have been achieved without the indefatigable efforts of Spokesman Richard Grellman AM in driving awareness for the cause, as well as the generous on-going support of KPMG, ARIA Restaurant Sydney and Queenscliff Surf Life Saving Club in hosting events throughout 2016. A number of philanthropic groups, including the John Holden Family Foundation, Vincent Fairfax Family Foundation, Yulgilbar Foundation and Roth Charitable Foundation, have committed multi-year funding to The Dementia Momentum which has enabled CHeBA to establish more ambitious projects seeking to delay or prevent dementia.

As part of The Dementia Momentum, our international consortia – COSMIC, ICC-Dementia, PROMOTE and STROKOG – grew thanks to the support of donors and the tireless work of CHeBA researchers. In 2016, we continued to produce ground-breaking research around early diagnosis, intervention and possible preventative strategies for the dementias. Dr Nicole Kochan found that reaction time tests predicted the likelihood of older adults developing dementia within the next four years. Our collaborative SMART trial with the Universities of Sydney and Adelaide showed building muscle strength can improve the brain function of people aged over 55 with mild cognitive impairment. Dr Nady Braidy published findings about the effect of a pomegranate-rich diet for improving brain health of mice with Alzheimer's disease. He is to be congratulated for receiving an Australian Research Council/Discovery Early Career Researcher Award for his research into the role of sirtuins in age-related cognitive decline.

We extended our community outreach in 2016, exploring new channels to raise awareness about dementia and modifiable risk factors. In addition to our successful **Wipeout Dementia** campaign, which we ran again in May and November 2016, we established the **Better Brain. Better Life** corporate seminar series thanks to the generous support of platinum sponsor Genworth. Our goal with these campaigns is to educate corporate leaders about protective factors for brain health, who will spread awareness through their extensive networks and establish wider communities of change. This builds on our highly successful **CHeBA Champions** initiative, established in 2012, with our fitness ambassadors in their 20s, 30s and 40s spreading the message in 2016 about healthy lifestyles from an early age for better brain health in late life. We continued to contribute to public discussion about dementia research and policy with media coverage in *The Conversation, Studio 10* and *Channel 9 News.*

Our achievements are made possible through the determined work of our colleagues and supporters. In particular, we would like to thank Ms Heidi Mitchell, CHeBA's Marketing & Communications Officer, who drives CHeBA's outreach through innovative avenues each year. We would also like to thank our Centre Manager, Ms Angie Russell, our administrative team and the Advisory Committee for their support in 2016. We thank all the research staff and welcome the new staff and students who joined us in 2016.

We have ambitious goals again for 2017. Following our 2016 recruitment drive, in 2017 we will launch the website for Maintain Your Brain, the world's largest clinical trial testing online tools to reduce dementia risk in people aged 55-75. Projects from our international consortia will also increase in 2017, following extensive work establishing protocols and harmonising data.

We look forward to providing the community and policy makers with a strong evidence-base for cognitive health factors, diagnosis and intervention strategies.

Sincerely,

Scientia Professor
Henry Brodaty

Scientia Professor
Perminder Sachdev

ABOUT THE CENTRE

The Centre for Healthy Brain Ageing (CHeBA) is a premier research institution in Australia, investigating brain ageing. CHeBA was established within the Faculty of Medicine at UNSW Sydney (The University of New South Wales) in October 2012. It is headed by internationally acclaimed leaders in the field, Professors Henry Brodaty and Perminder Sachdev.

OUR PURPOSE

CHeBA is an international centre of excellence in multidisciplinary research into the ageing brain and various aspects of cognitive disorder, including dementia. Its work extends from molecular work in the Genetics and Proteomics laboratories, to tissue culture and cell-related work in the Molecular Biology & Stem Cells group, to neuronal systems and networks in the Neuroimaging Laboratory, to clinical, epidemiological and sociological research, to research on ageing health policy using its strong links with teaching hospitals, aged care providers, state and federal governments and its established ageing cohort studies. Its work strongly emphasises implementation, capacity building and translational research.

OUR VISION

Our vision is to achieve, through research, healthier brain ageing and better clinical care of age-related brain diseases.

OUR MISSION

Our mission is to enhance the evidence base in relation to prevention, early detection, and treatment of age-related disorders, in particular brain diseases, and improve the health care of individuals affected by these diseases.

OUR AIMS

The Centre aims to conduct multidisciplinary research into ageing in health and disease, and be involved in knowledge dissemination and translational research. The Centre focuses in particular on the following aims:

- Determine the pathways of normal and abnormal brain ageing in the community.
- Identify risk factors for and protective factors against abnormal brain ageing.
- Determine the prevalence of age-related neurodegenerative and cerebrovascular disorders.
- Identify biomarkers for brain disorders.
- Investigate the pathophysiology of brain diseases so that novel treatments can be discovered.
- Conduct treatment trials of novel drugs and non-pharmacological strategies.
- Conduct educational activities for a workforce involved in the care of the elderly, especially those with dementia.
- Design models of assessment and care using the latest research evidence.
- Develop research programs in special populations, e.g. young-onset dementia, dementia in intellectual disability.

OUR FUNCTIONS AND GOALS

The functions of the Centre are to:

- Build capacity and research capability for age-related research, in particular brain research.
- Support the development and sharing of infrastructure for research across different Schools and Faculties of UNSW.
- Build relationships between the Centre and other similar centres in Australia and overseas.
- Build relationships between the Centre and the industry involved in the treatment and care of the elderly.

This will be achieved through:

- Strengthened collaborative research programs among staff and partners locally, nationally and internationally, supported by increased peer-reviewed grants and commissioned research.

- Development of specialised research facilities and laboratories that place the Centre at the forefront of brain ageing research nationally and internationally, to achieve the highest quality research and advance the Centre's attractiveness to prospective researchers of excellence.
- Extensive linkages with practitioners and policy makers at local, state and national levels to improve relevance and impact of research.
- Increased numbers and quality of skilled researchers undertaking research and evaluation activities in this field.
- Enhancing numbers of postgraduate research students.
- Exercising enhanced influence via dissemination and transfer of research findings through publications, presentations and forums with a focus on academic, practitioner and policy maker audiences.

Professor Terry Campbell

Professor Philip Mitchell

GOVERNING STRUCTURE

Centre Steering Committee

The Centre Steering Committee is the major decision making group for CHeBA. Centre Steering Committee members provide leadership across the Centre, are responsible for developing the Centre's strategy, advise on the Centre's operations and financial position, new partnership and funding opportunities. The founding Co-Directors of CHeBA are Professor Perminder Sachdev and Professor Henry Brodaty, who report to the Dean of Medicine, UNSW.

The Centre Steering Committee Members are:

- Professor Terry Campbell, Deputy Dean, Chair of CHeBA Steering Committee
- Professor Philip Mitchell, Head of School of Psychiatry, UNSW
- Professor Henry Brodaty, Co-Director of CHeBA
- Professor Perminder Sachdev, Co-Director of CHeBA

2016 MEETING DATES: 5 December

ADVISORY COMMITTEE

CHeBA's Advisory Committee made outstanding individual contributions to support our research and outreach in 2016. Professor Roger Layton AM became a Silver Member of The Dementia Momentum after donating $25,000 in honour of his wife Dr Merrilyn Layton who was diagnosed with Alzheimer's disease in 2002. A $40,000 grant from Dr Sudarshan Sachdev's personal Foundation allowed the Genetics & Genomics group to plan undertaking methylation assays to provide a comprehensive picture of both the genetic and epigenetic factors associated with successful ageing. This provides a unique resource for our exceptional longevity studies both in Australia and worldwide. Both Chairperson Dagmar Schmidmaier AM and John Thomas continued to contribute as a Friend of The Dementia Momentum. HWL Ebsworth Lawyers, where Deputy Chairperson John Gray is a senior partner, gave pro bono legal assistance which allowed us to trademark CHeBA, The Dementia Momentum and Wipeout Dementia. Throughout 2016 the members of the Advisory Committee members also generously gave their time to attend CHeBA's major events including The Dementia Momentum anniversary, our annual ARIA luncheon and Better Brain. Better Life forums.

The CHeBA Advisory Committee is a group of senior academic and business leaders. Their role is to assist and guide the Directors on matters of strategy, fund-raising, policy, marketing and media.

Members of the CHeBA Advisory Committee are:

- Dagmar Schmidmaier AM – Chairperson
- John Gray – Deputy Chairperson
- Roger Layton AM
- Richard Matthews AM
- Imelda Roche AO
- Dr Sudarshan Sachdev
- John Thomas

2016 MEETING DATES: 22 February and 8 November

DAGMAR SCHMIDMAIER AM
Chairperson, Chief Executive Women Leaders' Program

Dagmar has held senior executive positions for the past 30 years, the last as CEO and State Librarian of the State Library of NSW from 1995-2006. Prior to that Dagmar was director of OTEN and held senior positions in the fields of technology, education, and librarianship. She has worked in the university, government and private sector and has been a director on a number of not for profit boards. Dagmar has worked as a consultant to national and international organisations and was awarded a Fulbright Scholarship in 1988/89. She has published widely and has been guest speaker at conferences both in Australia and overseas.

JOHN GRAY

Deputy Chairperson, Partner
HWL Ebsworth Lawyers

John is one of Australia's leading technology, media and telecommunications (TMT) practitioners, and has worked in the area of TMT for over 19 years. John has been the principal legal advisor on some of the most complex and strategically important TMT projects in the Asia Pacific region, including major system and network roll-outs, outsourcings, the procurement of cross-border IT services and innovative online transactions. He is listed on the 2012 Financial Review's Best Lawyer list.

ROGER LAYTON AM

UNSW Emeritus Professor of Marketing

Roger has been published widely in the research literature and is the joint author of several books including Fundamentals of Marketing and Contemporary Hospitality Marketing – A Service Management Approach. His current research interests centre on the nature and role of marketing systems and the interplay of function and structure in the evolution of such systems.

ASSOCIATE PROFESSOR RICHARD MATTHEWS AM MBBS

Director, Neuroscience Research Australia (NeuRA)

Richard is the Director of NeuRA, Nominee SESLHD, Member of the NeuRA Building Committee and was the Deputy Director-General, Strategic Development of UNSW Health; Chief Executive, Justice Health; Acting Chief Executive Officer, Corrections Health Service; Director of Clinical Services, Corrections Health Service; Director of Drug and Alcohol, Corrections Health Service. He is also on the Board of Alzheimer's Australia NSW, Chair of the Board of General Practice Education and Training (GPET), and Director of Calvary Healthcare.

IMELDA ROCHE AO

Co-Chairman
Roche Group Pty Ltd

Imelda Roche is internationally recognised for her outstanding achievements in business, which include an appointment by Prime Minister Paul Keating as Australia's representative to the Business Forum of the Asia-Pacific Economic Co-Operation (APEC) and subsequently by Prime Minister John Howard as representative to the successor organisation, the Business Advisory Council to APEC.

JOHN M THOMAS

KSS FAICD FIFS JP

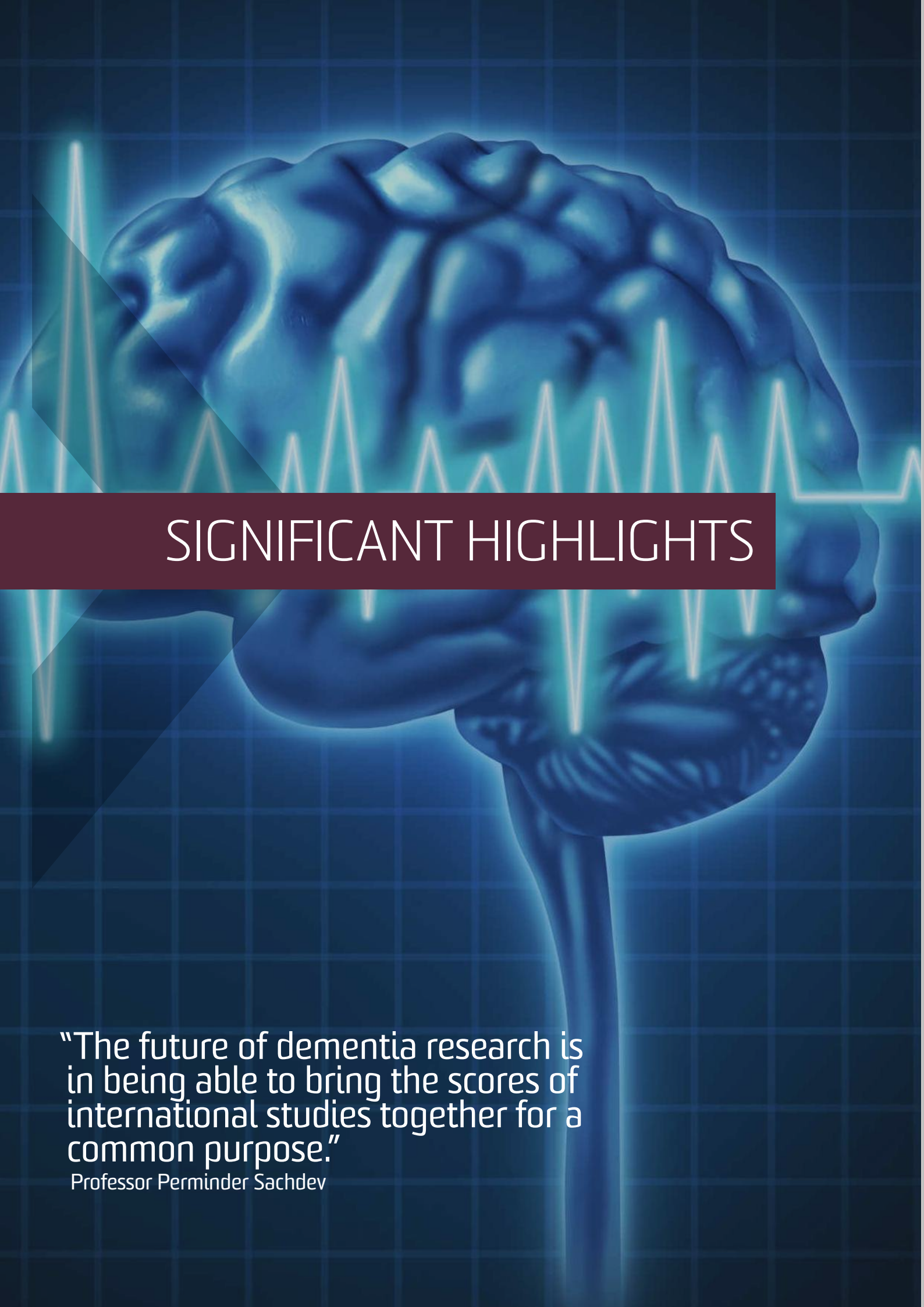
Principal, JT Consultancy

John has been involved in banking, finance and funds management activities for over 35 years. John began managing the Howard Mortgage Trust in 1987 with assets of $8 million and oversaw its growth to $2.6 billion by 2003. Under John's leadership, Howard Mortgage Trust won the Money Management Magazine "fund manager of the year award" on 7 occasions.

DR SUDARSHAN SACHDEV

Ophthalmologist

Sudarshan is an ophthalmologist who has had his own private practice in Sydney for over thirty years. He has a keen interest in healthy ageing and prevention of dementia having lost his mother to Alzheimer's disease. He has supported medical researchers in various disciplines of medicine.



SIGNIFICANT HIGHLIGHTS

"The future of dementia research is in being able to bring the scores of international studies together for a common purpose."

Professor Perminder Sachdev

PROFESSOR HENRY BRODATY WINS RYMAN PRIZE

Professor Henry Brodaty, CHeBA Co-Director and world-class researcher, clinician, advocate and pioneer, won the 2016 Ryman Prize as recognition of his three decades of tireless work into ways to combat dementia.

"Professor Brodaty is a pioneer in diagnosis and treatment of Alzheimer's and dementia in Australasia and his influence has been felt around the world."

Dr David Kerr, Ryman Prize Juror

The Ryman Prize is a $250,000 international prize which rewards the best work in the world that has enhanced quality of life for older people. It is the world's richest prize of its type and was established to create the equivalent of a Nobel Prize for people working in the field of the health of older people.

Ryman Prize Juror Dr David Kerr said Professor Brodaty was a worthy winner.

"We had an incredible field this year and there were some strong contenders from all over the world. Professor Brodaty's nomination was a standout, his dedication and achievements are truly world-class. He is a pioneer in diagnosis and treatment of Alzheimer's and dementia in Australasia and his influence has been felt around the world.''

Professor Brodaty said it was a wonderful honour.

"We are all ageing. Older people are the fastest growing sector of our population and mental health is the largest contribution to disease burden as we age,' he said. "I'm absolutely thrilled to receive this award. The Ryman Prize highlights the importance of enhancing the profile of research to improve the quality of life for older people."

Professor Brodaty is a psychogeriatrician who has spent his career working on ways to enhance the quality of life of older people with dementia and their families. He has also been a strong advocate for their rights. As well as treating thousands of patients at his clinic, he has been a pre-eminent researcher into ways to improve diagnosis and treatment of dementia.

"Age care is core business for health care and dementia is central to aged care," Professor Brodaty said. "I hope this will advance the profile of dementia research globally. Research feeds innovation and improvement."

He was a founding member and president or chair of the NSW and Australian Alzheimer's Associations and Alzheimer's Disease International. He is immediate past president of International Psychogeriatric Association and has been a member of numerous Australian and international committees aiming to advance the mental health of older people globally.

MAINTAIN YOUR BRAIN

Media icon and long-standing champion of Alzheimer research, Ita Buttrose AO OBE, is the patron of CHeBA's Maintain Your Brain study.

"Most people mistakenly believe that memory loss and cognitive decline are normal parts of ageing. But they are not," said Ms Buttrose.

"There is a growing body of research that shows seven modifiable risk factors account for about 30% of the cause of Alzheimer's disease. Since Alzheimer's disease is mostly a disease of late life, there is scope for us to intervene through simple lifestyle changes and delay the effects of the disease until after we've died.

I am proud to be the patron of Maintain Your Brain and look forward to working with CHeBA and participants to help change the future of brain health for our next generation."

The study is based on addressing modifiable risk factors for dementia in general and Alzheimer's disease in particular, namely physical inactivity, cognitive inactivity, depression, overweight and obesity, diabetes (type 2), high blood pressure and smoking. Intervention modules delivered over the internet will be customised to individual risk profiles using modified tools developed by our team to assess the risk of developing the disease. The study aims to determine the intervention's cost-effectiveness and efficacy in reducing the rate of cognitive decline in people aged 55-75 years.

MAINTAIN YOUR BRAIN

Ita Buttrose: Patron of Maintain Your Brain

> "Most people mistakenly believe that memory loss and cognitive decline are normal parts of ageing. But they are not."
> Ita Buttrose AO OBE

TOP RESEARCHERS ADVOCATE UNITED ACTIONS TO FIGHT ALZHEIMER'S DISEASE

> "This is the largest grouping of pre-eminent researchers and clinicians to collaborate in developing a blueprint for tackling the challenge that dementia presents to an ageing world."
> Professor Henry Brodaty

Professor Henry Brodaty joined more than 30 leading international experts to drive increased collaboration in research to defeat Alzheimer's disease and other dementias.

He co-authored a comprehensive report by the Lancet Neurology Commission published in April 2016, which identifies a range of issues that need to be addressed to reduce the burden of dementia and recommends that a concerted effort and long-term economic commitment is needed.

"This is the largest grouping of pre-eminent researchers and clinicians to collaborate in developing a blueprint for tackling the challenge that dementia presents to an ageing world," said Professor Henry Brodaty.

The report, led by Professor Bengt Winblad from the Center for Alzheimer Research in Sweden, also outlines recommendations about how patient care and basic and clinical research on Alzheimer's disease and other dementias should be organised in the future. The report was presented to the European Parliament Commissioners in Brussels on March 15.

The Commission advocates that public governmental agencies form large multinational partnerships with academic centres and pharmaceutical companies to deploy capital resources and share risk.

The Lancet Neurology Commission paper is a work by researchers from Sweden, France, UK, Australia, Denmark, Canada, Switzerland, Italy, Luxembourg, the United States, Germany and Netherlands.

PUBLICATION: Winblad et al., 'Defeating Alzheimer's disease and other dementias: a priority for European science and society', Lancet Neurology, 2016; 15: 455-532.

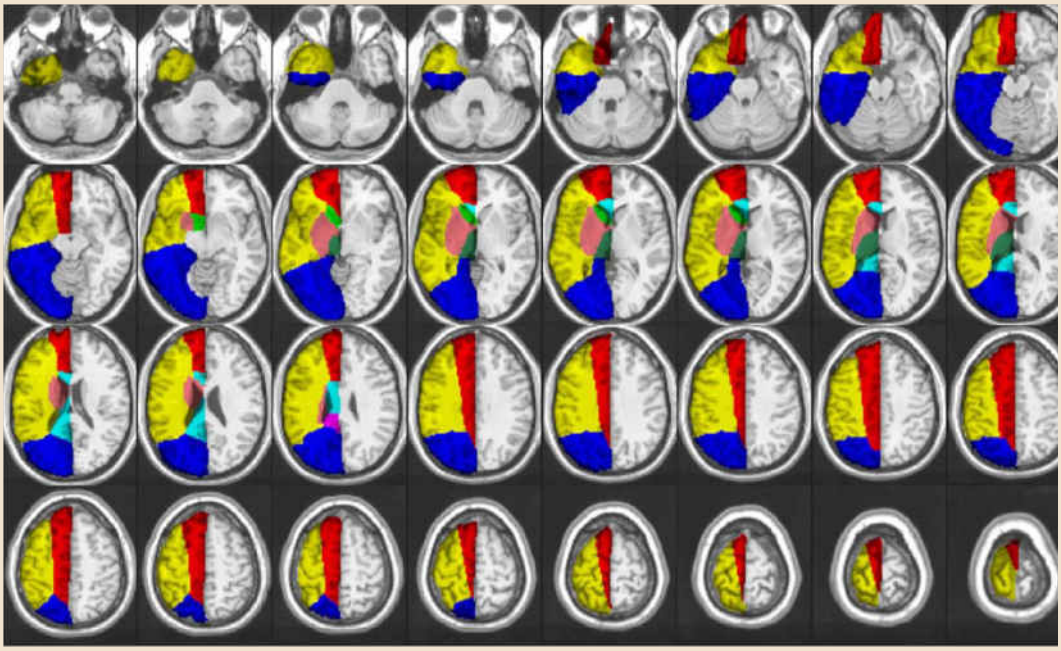
RESEARCH HIGHLIGHTS

"Our belief is dementia is at least partially preventable through strategies that will push back its onset."

Professor Henry Brodaty

GENETIC HERITABILITY OF WHITE MATTER HYPERINTENSITIES

CHeBA researchers identified genetic patterns associated with white matter hyperintensities (WMH), or signal changes in the brain's white matter, which are markers of small vessel disease in the brain.



"This is the first time WMH heritability was examined for specific cerebral regions and in both sexes."

Professor Perminder Sachdev

The study which analysed T2-weighted magnetic resonance imaging scans for 320 twin participants from CHeBA's Older Australian Twins Study was published in the June 2016 edition of the eminent journal, *Stroke*.

Lead author and CHeBA Co-Director Professor Perminder Sachdev said the findings were exciting and significant because it was the first time WMH heritability, or the degree to which traits are passed from parent to offspring, was examined for specific cerebral regions and in both sexes.

"We found a strong genetic influence for WMH, but the extent varied across different brain regions. Heritability was higher for deep regions of the brain, but lower for the cerebellum and brain stem," said Professor Sachdev.

Heritability of deep WMH decreased with age, especially after 75 years, which Professor Sachdev said was consistent with current knowledge.

The study also examined differences between men and women, finding higher WMH heritability for all brain regions in women.

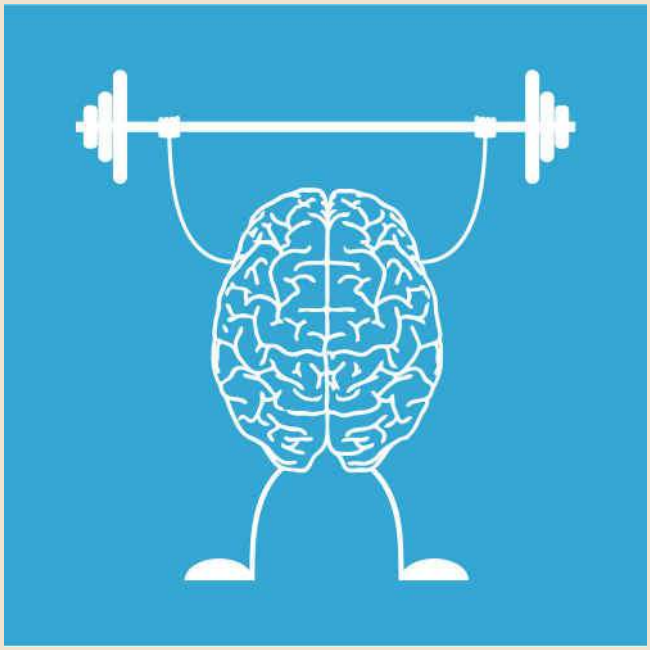
PUBLICATION: Sachdev et al., 'White matter hyperintensities are under strong genetic influence', Stroke, 2016; 47(6): 1422-1428.

SMART TRIAL: OVER 55? HIT THE GYM TO IMPROVE YOUR MUSCLE AND BRAIN STRENGTH

"This study goes some way in answering the question: what kind of exercise should I do to protect my brain?"
Professor Perminder Sachdev

A collaborative study published by CHeBA and the Universities of Sydney and Adelaide found over 55s with mild cognitive impairment can improve their brain function by building muscle strength.

The randomised, double-blind trial study was published in the October 2016 edition of the *Journal of American Geriatric Society.*



Findings from the Study of Mental and Resistance Training (SMART) trial show, for the first time, a positive causal link between muscle adaptations to progressive resistance training and the functioning of the brain among those aged over 55 years with mild cognitive impairment (MCI).

"The people I meet often ask me the question: what kind of exercise should I do to protect my brain? This study goes some way in answering this question, even though much further work remains," said co-author Professor Perminder Sachdev, Co-Director of CHeBA.

Participants doing resistance exercise were prescribed weight lifting sessions twice a week for six months, working to at least 80 per cent of their peak strength. As they got stronger, the amount of weight they lifted on each machine was increased to maintain the intensity at 80 per cent of their peak strength.

These new findings reinforce research from the SMART trial published earlier in 2016, whereby MRI scans showed an increase in the size of specific areas of the brain among those who took part in the weight training program. These brain changes were linked to the cognitive improvements after weight lifting.

PUBLICATION: Mavros et al., 'Mediation of cognitive function improvements by strength gains after resistance training in older adults with mild cognitive impairment: Outcomes of the Study of Mental and Resistance Training', Journal of the American Geriatric Society, 2017; 65(3): 550-559 (epub 2016, Oct 24).

A NEW TOOL TO ASSESS COMPLEX EVERYDAY ACTIVITIES IN PEOPLE WITH COGNITIVE IMPAIRMENT

A new instrument to assist in research and clinical assessments was developed by Dr Simone Reppermund and her colleagues at CHeBA and The Department of Developmental Disability Neuropsychiatry (3DN) at UNSW.

This tool is designed to assess instrumental activities of daily living (IADL), which are complex everyday functional skills necessary for independent living (such as managing medications, shopping, or handling finances). Preserved IADL is one of the defining features distinguishing mild cognitive impairment (MCI) from dementia.

Dr Reppermund said that the new performance-based instrument, called the STAM (Sydney Test of Activities of daily living in Memory disorders) will assess everyday activities in a time-efficient and reliable way. It has the advantage of objectively scoring individuals on their ability to perform everyday activities rather than relying on subjective self-ratings or second-party judgements.

“With an average administration time of 16 minutes, the STAM has the potential to be used widely in research as well as in clinical assessments,” said Dr Reppermund.

“It can be used to determine the level of functional impairment. This will be important in helping clinicians to diagnose dementia more reliably. It will assist with diagnostic classification for the detection of IADL impairment in the early stages of dementia.”

“A major advantage is STAM’s strong value to distinguish groups with normal cognition, MCI and dementia,” said Dr Reppermund. “In particular, we are able to distinguish between MCI and dementia with high sensitivity and specificity, whereas other performance-based instruments have been shown to have ceiling effects.”

PUBLICATION: Reppermund et al. ‘Performance-based assessment of instrumental activities of daily living: Validation of the Sydney Test of Activities of daily living in Memory disorders (STAM)’, Journal of the American Medical Directors Association, 2017; 18(2): 117-122.

POMEGRANATE DIET IMPROVES BRAIN FUNCTION IN MICE WITH ALZHEIMER'S DISEASE

A diet rich in pomegranates had significant positive impacts for the brain health of mice with Alzheimer's disease, an international research team led by CHeBA found.

The innovative study, published in the October 2016 edition of the journal *Oncotarget*, demonstrated that dietary supplementation of 4% pomegranate extract to a standard diet over a 15-month period resulted in a range of neuroprotective effects in transgenic mice.

Lead author of the study, CHeBA's Dr Nady Braidy, says the findings are an exciting advance into the role of diet in tackling dementia.

> "Our findings are an exciting advance into the role of diet in tackling dementia."
> Dr Nady Braidy

"Something as simple as the introduction of pomegranate into the diet of these mice resulted in a range of important health impacts. We observed decreased oxidative stress and neuroinflammation, a reduction in the production of amyloid-beta (Aβ) protein, and improved synaptic plasticity in the brains of the transgenic mice fed with pomegranate extract compared with the control group."

Pomegranates contain high concentrations of polyphenols compared to other fruits and vegetables. Naturally occurring in food, polyphenols are compounds with antioxidant properties, which current evidence suggests play an important role in preventing neurodegenerative disease.

"Therapeutic strategies for the treatment of AD are currently limited. Our findings support the growing body of research which suggests that the synergistic effect of polyphenols together with the compounds they naturally co-occur with may provide a more beneficial approach."

The researchers note that further testing will be needed to determine whether the results translate in the human population.

PUBLICATION: Braidy et al., 'Consumption of pomegranates improves synaptic function in a transgenic mice model of Alzheimer's disease', Oncotarget, 2016; 7: 64589-64604.

INVESTIGATING PLASMA LEVELS AS A BIOMARKER FOR ALZHEIMER'S DISEASE

CHeBA published the first detailed study of the relationship between plasma levels of two amyloid beta peptides (Aβ1-40 and Aβ1-42), brain volumetrics (measures studying brain size, which shrinks with Alzheimer's disease) and cognitive performance in an investigation of the usefulness of plasma levels as a biomarker for Alzheimer's disease (AD).

Lead author and head of CHeBA's Proteomics group, Dr Anne Poljak, said that since amyloid beta (Aβ) peptides are the main component of the amyloid plaques found in Alzheimer patients' brains, changes in levels of Aβ in blood plasma may provide a biomarker for detecting increased risk or early diagnosis of disease.

> "These findings certainly suggest that plasma Aβ measures may serve as biomarkers of Alzheimer's disease."
> Professor Perminder Sachdev

"While Aβ has traditionally been measured using cerebrospinal fluid, plasma presents a more accessible sample for routine collection and screening although results to date have been variable," Dr Poljak said.

Plasma levels of the two peptides and the Aβ1-42/1-40 ratio were lower in individuals with amnestic mild cognitive impairment and Alzheimer's disease than in cognitively normal controls, and lower levels of Aβ1-42 were associated with lower global cognition and hippocampal volume and higher levels of white matter hyperintensities (which are believed to contribute to Alzheimer's disease). A genetic component was also identified, with associations between Aβ1-40 and cognitive and brain volume measures predominantly observed in individuals carrying the ε4 allele, while the opposite was observed in non-carriers. Longitudinal analysis revealed greater decline in global cognition and memory for the highest quintiles of Aβ1-42 and the ratio measure.

PUBLICATION: Poljak et al., 'The relationship between plasma Aβ Levels, cognitive function and brain volumetrics: Sydney Memory and Ageing Study', Current Alzheimer Research, 2016; 13(3): 243-255.

REACTION TIME TEST PREDICTS DEMENTIA RISK

CHeBA researchers found that older adults' performance on reaction time tasks indicated their likelihood of developing dementia within the next four years.

The study tested 861 community living 70-90 year-olds from CHeBA's longitudinal Sydney Memory and Ageing Study (MAS) using computer-administered reaction time tasks and was published in the March 2016 edition of the *American Journal of Geriatric Psychiatry.*

Lead author and co-leader of CHeBA's Neuropsychology group, Dr Nicole Kochan said the findings highlight the potential of reaction time tasks to detect early cognitive changes associated with various types of dementia.

"We were surprised that these brief computerised tests that take only about four minutes to complete were comparable to a lengthy two hour traditional battery of neuropsychological tests in predicting a loss in everyday function over the four year period," explained Dr Kochan.

The simplest of the tasks - requiring participants to quickly touch the screen as soon as a coloured square appeared - was the best predictor of dementia. Individuals who had slower responses on this simple reaction time task compared to the typical performance of the group were two to three times more likely to receive a diagnosis of dementia within four years. Slower reaction time and more inconsistent or variable responses on the task represented an important risk for dementia, after accounting for other typical dementia risk factors such as age, depression, cerebrovascular risk and genetic susceptibility.

Computer-administered reaction measures have the potential to provide cost-effective, efficient and accessible screening of cognitive impairment and dementia and may be suitable for inclusion in an annual broad health check for aged persons," said Dr Kochan.

PUBLICATION: Kochan et al., 'Reaction time measures predict incident dementia in community-living older adults: The Sydney Memory and Ageing Study', American Journal of Geriatric Psychiatry, 2016; 24(3): 221-231.

CHeBA'S RESEARCH

"CHeBA's multi-disciplinary approach enables us to better understand the complexities of cognitive ageing."

Professor Perminder Sachdev

GROUP SNAPSHOT

EPIDEMIOLOGY

Professor Perminder Sachdev

The Epidemiology group is interested in studying the patterns, causes and effects of neurocognitive disorders, in particular dementia, in elderly populations in Australia and internationally. The group analyses longitudinal cohorts from CHeBA's own studies – the Sydney Memory and Ageing Study, the Older Australian Twins Study, the Sydney Centenarian Study and the Sydney Stroke Study – as well as from international studies grouped into consortia, including the CHeBA-led COSMIC, STROKOG and ICC-Dementia. Another important aspect of this work is genetic epidemiology, which uses various approaches including genome-wide association studies and Mendelian randomisation methods to examine risk factors for dementia and other neurocognitive disorders.

NEUROPSYCHIATRY

Professor Perminder Sachdev

CHeBA Neuropsychiatry is a collaborative group composed of staff from CHeBA and the Neuropsychiatric Institute (NPI) at the Prince of Wales Hospital, Sydney. The NPI is a tertiary referral unit that specialises in the diagnosis and treatment of cognitive and psychiatric disorders associated with medical and neurological illnesses. It is unique in Australia in bringing together expertise within Psychiatry, Neurology, Neuropsychology, Neurophysiology and Neurosurgery to bear upon complex diagnostic issues. The Neuropsychiatry group is at the forefront of diagnostic research into neuropsychiatric disorders, in particular dementia, stroke and Parkinson's disease, and the use of brain stimulation for treatment. The group also provides important education services for clinicians and trainees.

GENETICS & GENOMICS

Dr Karen Mather

The Genetics & Genomics group has grown out of our interest in the genetic and epigenetic factors involved in brain ageing and age-related disease. Heritability studies suggest that there is a genetic component to most age-related traits. To fully understand ageing and age-related disease, we need to better understand how both genetics and environment contribute to these processes. Successful grants have enabled us to collect genetic samples in addition to demographic, lifestyle, neuroimaging and health data that facilitates genetic studies investigating brain ageing and age-related disease.

MOLECULAR BIOLOGY & STEM CELLS

Dr Nady Braidy & Hon. Associate Professor Kuldip Sidhu

The Molecular Biology & Stem Cells group aims to investigate the molecular basis of ageing, with the objective of identifying potential molecular targets to slow the ageing process. It is developing animal models of ageing, including the South American rodent *Octodon degu* which is a possible natural model of Alzheimer's disease. Additionally, cellular models of neurodegenerative diseases are being developed using induced pluripotent stem cells (iPSCs).

Dr Nady Braidy

Hon. Associate Professor Kuldip Sidhu

NEUROIMAGING

Associate Professor Wei Wen

By studying neuroimaging modalities, the Neuroimaging group aims to improve understanding of brain ageing pathways, which in turn will lead to clinical advances in prediction, diagnosis and treatment. We are interested in computational neuroanatomy: the development of a comprehensive structural and functional model of the brain. Our neuroimaging studies address normal ageing, mild cognitive impairment (MCI) and dementia.

NEUROINFLAMMATION

Professor Julian Trollor

Metabolic and inflammatory factors have recently been proposed as key risk factors in cognitive ageing and age-related brain disorders, such as the dementias. The Neuroinflammation group is aiming to evaluate the influence of these factors on brain ageing and the modulating effects of genetic susceptibility, physical health, lifestyle and nutrition.

NEUROPSYCHOLOGY

Dr Teresa Lee & Dr Nicole Kochan

The Neuropsychology group aims to advance scientific knowledge in relation to the cognitive changes occurring in the brain in normal ageing, mild neurocognitive syndromes and dementia, using neuropsychological methods.

We have established strong collaborative links with other researchers in CHeBA, and are actively involved in research investigating the associations between memory and other areas of cognition with brain structure, genetics, bilingualism, medical comorbidities, inflammatory markers and falls in the older adult population.

We are also interested in establishing much needed normative data for older adults which will be extremely valuable in clinical and research settings by enhancing diagnostic accuracy of mild neurocognitive disorders and dementia.

PROTEOMICS

Dr Anne Poljak

The Proteomics group is a collaborative group composed of staff and students from CHeBA, the Neuropsychiatric Institute (NPI) and the MW Analytical Centre Bioanalytical Mass Spectrometry Facility (BMSF) at UNSW. The group was formed to apply state-of-the-art analytical techniques to the advancement of biomarker and pathophysiology research in the areas of normal ageing, mild cognitive impairment (MCI), Alzheimer's disease and other age-related neurodegenerative conditions. While proteomics is a major focus area, the group utilises a broad spectrum of technologies and scientific approaches, including NMR, electron microscopy, confocal and fluorescence microscopy, FTIR spectroscopic imaging, LA-ICPMS mass spectrometric imaging as well as lipidomics and metabolomics techniques.

HIGHLIGHTS FROM OUR GROUPS

Risk factors for developing MCI or dementia within a 6-year follow-up period included: increasing age, MCI at baseline, poorer smelling ability, being an APOE ε4 carrier and slower walking speed. There was a considerable overlap between the risk factors for mortality and those for dementia (Lipnicki et al., *Journal of the American Medical Directors Association*).

Recent alcohol consumption (including "low consumption" and "risky consumption") was not associated with incident dementia at 4-year follow-up. Carriers of the APOE ε4 allele were more likely to develop dementia, but there was no significant interaction with alcohol consumption (Heffernan et al., *Journal of Alzheimer's Disease*).

Poorer neuropsychological test performance and higher rates of cognitive impairment were observed in proficient English speakers from linguistic minorities and could not be explained by poorer health or psychological profile, and only partially accounted for by factors such as whether English was their preferred language and the number of years lived in Australia, urging caution when diagnosing Mild Cognitive Impairment and dementia in linguistic minorities (Kochan et al., *Alzheimer's Association International Conference, Toronto*).

Heritability of language functions was highest for letter fluency, moderate for picture naming, and lowest for semantic fluency. The genetic correlations between performances on these three tests ranged from .43 to .77, suggestive of a common genetic substrate for language expression. Understanding the genetic influence on these verbal tests can inform gene discovery for language-associated neurodegenerative disorders, such as frontotemporal dementia and Alzheimer's disease. Findings of environmental influence may suggest there are potentially modifiable factors that can reduce risk of age-related cognitive decline (Lee et al., *Behavior Genetics*).

Significant gray matter correlations with vascular cellular adhesion molecule–1 were located in the bilateral anterior cingulate cortices, and with plasminogen activator inhibitor–1 in the cerebellum and right hippocampus, in non-demented older adults. The neuroanatomical correlation patterns of two proinflammatory cytokines and two vascular inflammatory markers might be reflective of the effects of neurodegenerative and vascular pathological processes in the ageing brain (Zhang et al., *Neurobiology of Aging*).

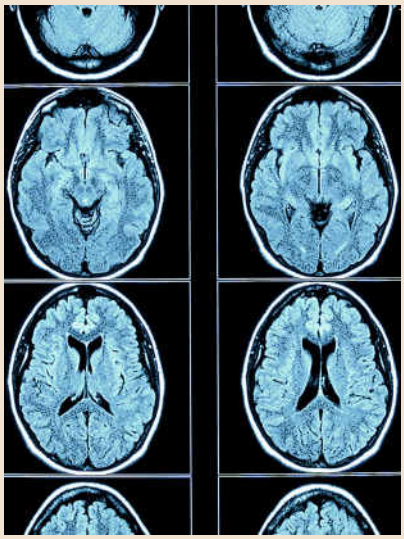
Macrophage inhibitory cytokine-1 (MIC-1/GDF15) could be considered as a marker of age-related cognitive decline and brain structural changes. Combining MIC-1/GDF15 with other biomarkers may provide clinical diagnostic and prognostic utility (Jiang et al., *Current Opinion in Psychiatry*).

57 replicated, differentially expressed genes in the brain and 21 in peripheral tissues of older people with depression were identified. Functional overlap between brain regions and the periphery strongly implicates shared pathways in a comorbid phenotype of depression and cardiovascular disease. The findings highlight dermal fibroblasts as a promising experimental model for depression biomarker research, provide partial support for all major theories of depression and suggest a novel candidate gene, PXMP2, which plays a critical role in lipid and reactive oxygen species metabolism (Ciobanu et al., *Neuroscience & Biobehavioral Reviews*).

Structural MRI distinguishes the brains of elderly individuals with 'amnestic MCI' from those classified as 'cognitively normal'. Amnestic MCI was associated with smaller volumes of overall cortex, medial temporal structures, anterior corpus callosum and select frontal and parietal regions compared with brains from cognitively normal individuals. (Yang et al., *Current Alzheimer Research*).

The brain structures that best distinguish amnestic mild cognitive impairment from normal controls differ in those aged <85 years from those ≥85 years, suggesting different neuropathological underpinnings of cognitive impairment in the very old. (Yang et al., *Current Alzheimer's Research*).

Corresponding cerebral cortical and subcortical structures in the two hemispheres of the human brain were influenced by the same genetic factors, showing moderate to high heritability. There were three genetically correlated clusters, comprising (i) the cortical lobes; (ii) the basal ganglia with weak correlations with cortical lobes; and (iii) the amygdala, hippocampus, thalamus and nucleus accumbens grouped together, which correlated with both basal ganglia and cortical lobes. A complex but patterned and clustered genetic architecture of the human brain, with divergent genetic determinants of cortical and subcortical structures, was demonstrated (Wen et al., *Scientific Reports*).


Topology of hub-regions in the healthy elderly brain was consistent with a young adult population and previously published adult connectomic data. The architectural features of hub connections reflected their ongoing vital role in network communication. Substantial sexual dimorphisms were observed, with females exhibiting stronger inter-hemispheric connections between cingulate and prefrontal cortices. Left-lateralized subnetworks consistent with the neural circuitry specialised for language and executive functions were observed (Perry et al., *NeuroImage*).

The pattern of genetic correlations for the surface of the hippocampus partially corresponded to neuroanatomical division of hippocampal subfields. The patterns of heritability and genetic correlations of the right and left hippocampi were similar, but not bilaterally symmetrical on the vertex level (Wen et al., *OHBM*).

Sex differences occurred in the asymmetry of the globus pallidus and putamen. Heritability estimates revealed that additive genetic factors influenced the asymmetry of these two structures and that of the hippocampus and thalamus. Handedness had no detectable effect on subcortical asymmetries, but the asymmetry of the putamen varied with age. Genetic drivers of asymmetry in the hippocampus, thalamus and basal ganglia may affect variability in human cognition, including susceptibility to psychiatric disorders (Guadalupe et al., *Brain Imaging and Behavior*).

A significant linear negative relationship between gray matter and age was observed using high-resolution MRI in non-demented individuals aged over 80 years. Significant quadratic age effects on total white matter and white matter hyperintensities were observed. Heterogeneous differences occurred across brain regions between the oldest old and young old, with an emphasis on hippocampus, temporoposterior cortex, and white matter hyperintensities (Yang et al., *Neurobiology of Aging*).

Five new genetic variants for intracranial volume (which reflects brain size and brain development until maturation) were discovered. High genetic correlation exists with child head circumference. Variants for intracranial volume were also related to childhood and adult cognitive function, and Parkinson's disease, and were enriched near genes involved in growth pathways, including PI3K-AKT signalling (Adams et al., *Nature Neuroscience*).

Common genetic risk factors for Alzheimer's disease (AD) were associated with reduced hippocampal volume in healthy older adults and those with mild cognitive impairment. This shows there is a neurodegenerative effect visible in the hippocampus before clinical manifestations of AD occur in older adults (Lupton et al., *Neurobiology of Aging*).

Specific genetic variants were linked to blood levels of Apolipoprotein H (ApoH), which transports fats and other molecules around the body and has been linked to cognitive ageing, and cardiovascular and autoimmune diseases (Mather et al., *Scientific Reports*).

Proteomic changes were more pronounced at the symptomatic vs asymptomatic stage of dominantly inherited Alzheimer's disease (Muenchhoff et al., *Scientific Reports*).

All seven mammalian sirtuins were successfully detected and quantified in the central nervous system using multiple reaction monitoring (MRM) for the first time, paving the way for more quantitative and functional studies (Jayasena et al., *Scientific Reports*).

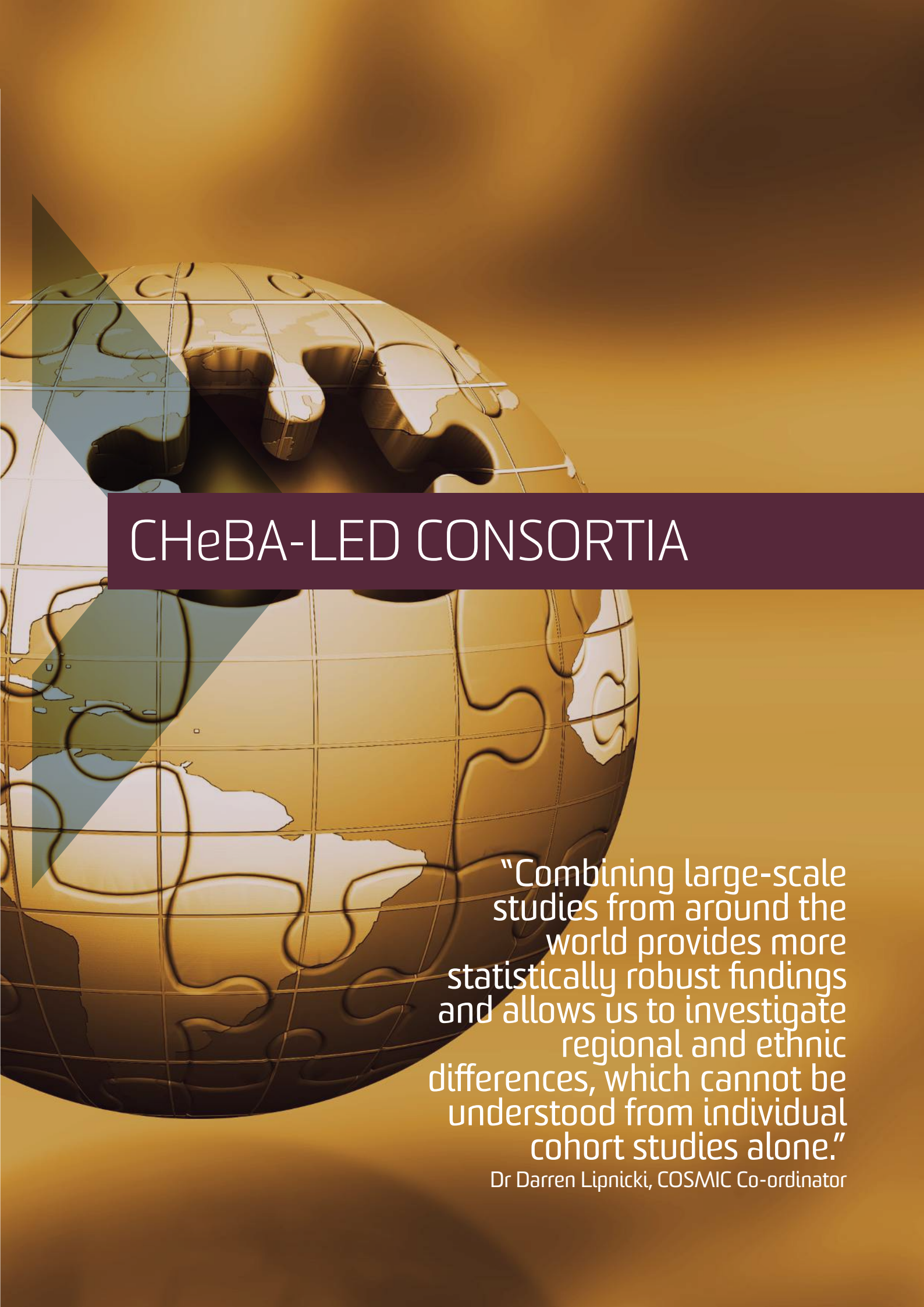
The progress of lipid biomarker research for Alzheimer's disease was reviewed and considerations for designing large-scale experiments to help standardise findings across laboratories were identified, as well as challenges for clinical application (Wong et al., *Alzheimer's & Dementia*; Wong et al., *Current Opinion in Psychiatry*).

Researchers combined resveratrol with antioxidants and chelating agents to mimic the synergistic effect of red wine without the negative effects of alcohol. Trialled on 50 people, the combination increased the activity of NAD+, which plays a key role in maintaining healthy cells. It is being researched as a potential therapeutic candidate for Alzheimer's disease (Braidy et al., *Current Topics in Medicinal Chemistry*; Ahmed et al., *Molecular Neurobiology*).

Apigenin was able to protect iPSC-derived Alzheimer's disease (AD) neurons via multiple means by reducing the frequency of spontaneous Ca2+ signals and significantly reducing caspase-3/7 mediated apoptosis. These data demonstrate the broad neuroprotective action of apigenin against AD pathogenesis in a human disease model (Balez et al., *Scientific Reports*).

Genetic factors accounted for a moderate amount of the variability in late-life depression in healthy elderly twins. Late-life depression was significantly genetically correlated with anxiety and hypertension, suggesting shared genetic factors likely contribute to the co-occurrence of these traits.





CHeBA-LED CONSORTIA

"Combining large-scale studies from around the world provides more statistically robust findings and allows us to investigate regional and ethnic differences, which cannot be understood from individual cohort studies alone."

Dr Darren Lipnicki, COSMIC Co-ordinator

CONSORTIA

COSMIC

About

Established in 2012, COSMIC (Cohort Studies of Memory in an International Consortium) aims to bring together cohort studies of cognitive ageing internationally in order to facilitate a better understanding of the determinants of cognitive ageing and neurocognitive disorders. The two main objectives are to:

1) Harmonise shared, non-identifiable data from cohort studies that longitudinally examine change in cognitive function and the development of dementia in older individuals (60+ years).

2) Perform joint or mega-analyses using combined, harmonised data sets that yield collated results with enhanced statistical power, in addition to comparisons across geographical regions.

The geographical regions and countries represented by the member studies include: Asia (China, Hong Kong, India, Indonesia, Japan, Korea, Singapore), Australia, Europe (France, Germany, Greece, Italy, Spain, The Netherlands, UK), North America (Canada, USA), and South America (Brazil).

Highlights

- Mini-Mental State Examination (MMSE) and memory, processing speed, language and executive functioning test scores all declined with age, and rates of decline accelerated with age, in a cognitive performance data analysis of 14 studies comprising 42,170 individuals across 12 countries (Australia, Brazil, France, Greece, Hong Kong, Italy, Japan, Singapore, Spain, South Korea, United Kingdom, USA). The 14 studies showed different rates of decline. Decline in MMSE scores was faster for Asians than whites, females than males, and APOE ε4 carriers than non-carriers. The findings suggest that international differences in rates of cognitive decline might contribute to the global variation in dementia prevalence. Further research is needed to determine whether cardiovascular, lifestyle and other risk factors for dementia have different associations with cognitive decline in different ethnocultural and geographic regions. Findings were presented at the Alzheimer's Association International Conference in Toronto, Canada 2016, and a manuscript is being revised for submission to *PLOS Medicine*.

We began the following research projects investigating:

- The impact of reproductive experiences on the risks of cognitive decline and dementia in older women, using data from Korea, Greece, France, India and Spain.
- How olfactory ability and other factors affect language function and MMSE scores in Australian and Indonesian cohorts.
- Whether visual-only memory impairments are sufficient to diagnose amnestic MCI in conjunction with studies from Australia, USA, Greece and Spain.

Funding was obtained for a new project to begin in 2017: "The effects of sedentary behaviour on cognitive function and cognitive decline in older persons without dementia", combining data from Australia, Greece, Ireland, Japan, Singapore and The Netherlands.

ICC-DEMENTIA

About

Combining 17 different centenarian and near-centenarian studies from Asia, Europe, the Americas, and Oceania, ICC-Dementia seeks to harmonise these studies internationally to describe the cognitive and functional profiles of exceptionally old individuals and systematically explore the factors involved in dementia and longevity. ICC-Dementia aims to spearhead an international effort to promote successful brain ageing by identifying risk and protective factors into the 11th decade of life that are robust across cohorts.

Highlights

- Four new studies joined the consortium (The Oporto Centenarian Study from Portugal, The Kurihara Project from Japan, The Fordham Centenarian Study from New York and the 2nd Heidelberg Centenarian Study from Germany).
- The first paper from ICC-Dementia was published in *BMC Neurology*. The protocol paper outlined the aims and structure of the consortium, selection criteria for participating studies, and a summary of planned harmonisation and statistical procedures.
- A brief summary of ICC-Dementia was published in the *Atlas of Science*.
- Preliminary findings on the cognitive and functional profiles of centenarians were presented at the International Consortia of Centenarians (ICC) Conference in Porto in June. These findings suggested that overall, out of almost 4000 centenarians and near centenarians, 51.4% were cognitively impaired, 62.9% were functionally dependent and 46.7% met criteria for dementia. These findings differed across age groups (with more impairment observed in older age groups) and study location.

"Examining rates of dementia in the oldest members of society will give us important insights into the disease process, particularly around risk and protective factors, since these individuals may provide real-life models of healthy brain ageing."

Professor Henry Brodaty

PROMOTE

About

Launched in 2013, PROMOTE (Psychosocial Research Consortium to Advance Mental Health of Older People in the Asia Pacific region) is a consortium of psychosocial researchers in the Asia-Pacific region aiming to advance psychosocial research. In attempting to ensure quality and person centred dementia care, members of PROMOTE are working on the first regional collaborative study "Testing feasibility and face validity of Quality Indicators (QIs) for psychosocial interventions". This collaboration is a replication of a European multinational consortium project which was initiated and led by Alzheimer Europe. This project includes data from Hong Kong, South Korea, Malaysia, Australia, China, Singapore and Thailand.

Highlights

- Findings were presented at the Alzheimer's Disease International Asia-Pacific Regional meeting, New Zealand, in November 2016. Six Asia-Pacific countries and one territory (Australia, China – Beijing and Hong Kong, South Korea, Singapore, Thailand, Malaysia) tested European quality indicators (QIs) for psychosocial interventions in nursing homes. European QIs were unsuitable and regional - specific QIs need to be developed.

STROKOG

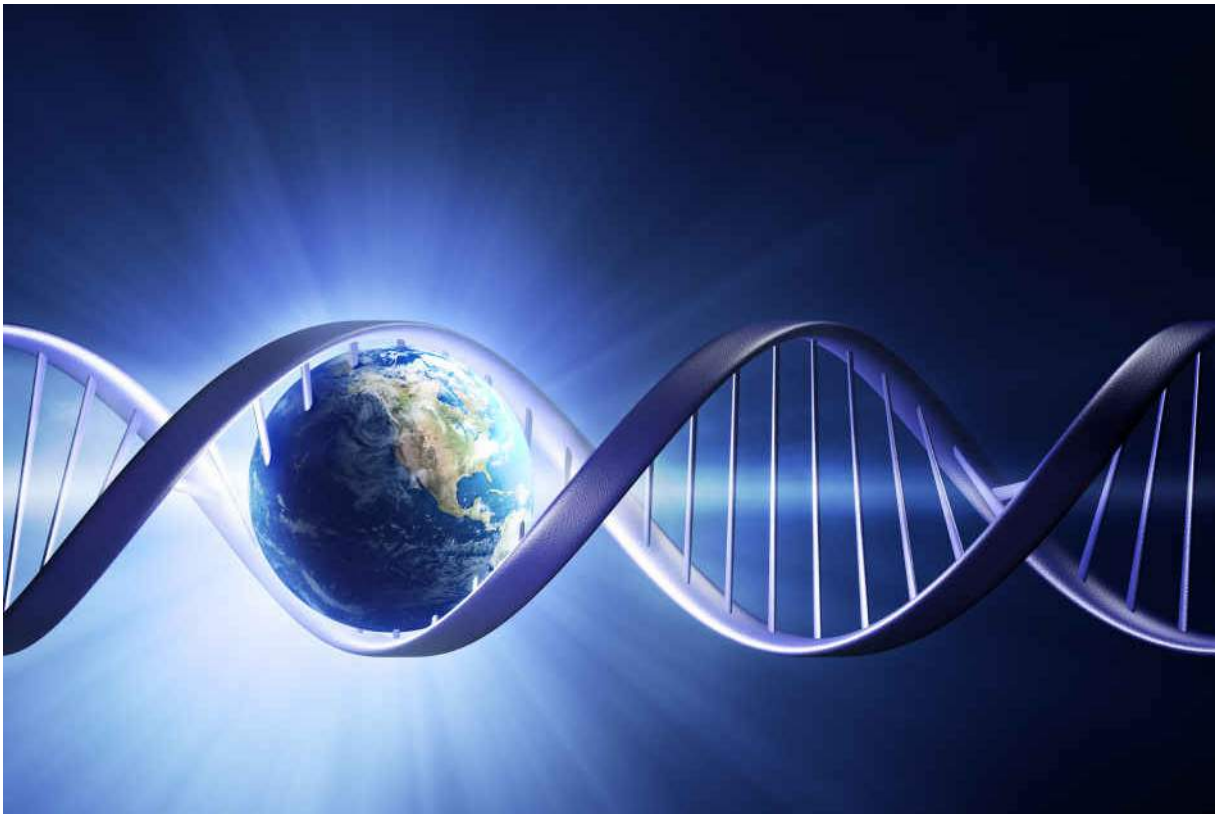
About

STROKOG is a consortium of longitudinal studies of cognitive disorders following stroke, TIA or small vessel disease. Developed under the auspices of VASCOG (Society for the Study of Vascular Cognitive and Behavioural Disorders), it is the first international effort to harmonise work on post-stroke dementia. The consortium brings together studies that have examined post-stroke or other high vascular risk cohorts longitudinally, with cognitive decline and dementia (including sub-types) as primary outcome variables. The included studies (N=25; total sample of more than 10,000 individuals, representing 17 countries) have rich neuropsychological and MRI data,

and some recent studies have included amyloid imaging in sub-samples. A number of studies have CSF and/or plasma available for biomarker studies, and participant enrolment in brain banks for neuropathology.

Highlights

- 1 new study joined from the UK.
- 1 methodology paper was published (Sachdev et al., *Alzheimer's & Dementia: DADM*).
- Members from STROKOG met at the VASCOG Conference in Amsterdam in October where they shared preliminary results from the first project and discussed new project ideas. Preliminary analysis examining the profile of post-stroke/TIA participants across diverse geographical regions and ethnic groups (14 studies, >3600 participants) showed that 46% of participants had impairment in 2 or more cognitive domains and 68% had impairment in 1 or more domains. Participants diagnosed with diabetes or had a prior stroke have poorer cognition.



CHeBA CONSORTIA COLLABORATIONS

In addition to the CHeBA-led consortia (COSMIC, ICC-Dementia, PROMOTE and STROKOG), CHeBA is a member of the following:

- BRIDGET (Brain imaging, cognition, Dementia and next generation Genomics: a Transdisciplinary approach to search for risk and protective factors of neuro-degenerative disease)
- CHARGE (Cohorts for Heart and Ageing Research in Genetic Edpidemiology)
- DIAN (Dominantly Inherited Alzheimer Network)
- EADB (European Alzheimer's Disease DNA BioBank)
- ENIGMA (Enhancing Neuro Imaging Genetics through Meta-Analysis)
- EuroDiscoTWIN (European Discordant Twin Study)
- PERADES (Defining Genetic, Polygenic and Environmental Risk for Alzheimer's disease).

COLLABORATIVE RESEARCH: GENOME-WIDE SIGNIFICANT RESULTS IDENTIFIED IN BLOOD PROTEIN LEVELS

CHeBA researchers have undertaken the largest study of its kind to better understand the contribution of genetics to blood apolipoprotein H levels.

The study, published in *Nature Scientific Reports* in March 2016 identified genetic variants that influence blood circulating apolipoprotein H levels. Apolipoprotein H has been linked to cognitive ageing, Alzheimer's disease, diabetes and cardiovascular and autoimmune diseases, such as antiphospholipid syndrome and lupus.

Lead author and leader of CHeBA's Genetics & Genomics group Dr Karen Mather said "To identify genes that influence the blood levels of apolipoprotein H we looked at data from over 2 million individual genetic variants from more than 900 older adults, using participants from CHeBA's Sydney Memory and Ageing Study and the Older Australian Twins Study."

Co-author and CHeBA Co-Director Professor Perminder Sachdev said "We identified specific genetic variants located in or near the APoH gene that influence ApoH levels and replicated the results in an independent cohort of middle-aged to older adults, the Hunter Community Study, which is an important validation step in genetic studies."

Dr Mather said she was extremely encouraged by the results of this study, which was carried out in collaboration with researchers at the University of Newcastle.

"ApoH has important physiological roles and is involved in negative health consequences. This study increases our knowledge regarding the determinants of ApoH levels and may lead to strategies that aim to reduce risk and prevent disease as well as to the development of novel treatments."

PUBLICATON: Mather et al., 'Genome-wide significant results identified for plasma apolipoprotein H levels in middle-aged and older adults', Scientific Reports, 2016; 6: 23675.

MONTEFIORE CONTINUES TO FUND RESEARCH AT CHeBA

Montefiore Home has been a major donor to CHeBA since 2012. Most of this contribution has been utilised to fund research led by **Professor Lynn Chenoweth**. Drawing on her extensive networks and extensive expertise, Professor Chenoweth has contributed to a wide range of research projects in her role with CHeBA including: developing evidence-based nursing competencies for care of older people; trialling facilitated case conferencing for improving end of life outcomes for people with advanced dementia living in residential aged care and their families; and evaluating the effectiveness of Dementia Care Mapping to enable person-centred care training in nursing homes. Professor Chenoweth was involved in 6 research projects and co-authored 17 papers accepted for publication in 2016.

"A strong, ongoing partnership with Montefiore Home offers an excellent opportunity for large scale research that can have a transformative effect on the care of the elderly."

Professor Perminder Sachdev

MONTEFIORE

CHeBA AND MONTEFIORE HOME LINKS

1. Our pilot project successfully demonstrated that nurses can be trained to devise and implement oral health plans for nursing home residents. This has formed the basis for an application for a larger randomised controlled trial for improving oral health care in nursing homes.

2. We commenced a study (Chenoweth, Brodaty) to improve collaboration between staff and families of residents in Montefiore Home Randwick.

3. Professors Chenoweth and Brodaty met with senior Montefiore Home staff to explore and decide on future research priorities for Montefiore Homes.

4. Professor Brodaty presented at the inaugural Montefiore Home Silver Tea Fundraising Lunch.

5. Professor Brodaty presented at the 10th anniversary celebration of Montefiore Home Randwick campus.

DR NADY BRAIDY'S DECRA SUCCESS

Dr Nady Braidy was awarded an Australian Research Council/ Discovery Early Career Researcher Award in November 2016.

Dr Nady Braidy is the co-leader of CHeBA's Molecular Biology & Stem Cells group. The award provides funding for Dr Braidy to continue his ground-breaking research in the field of sirtuins. Sirtuins, or "silent information regulators" of gene transcription, are enzymes found in all life. Accumulating evidence suggests that they are key regulators of stress resistance, cell division and repair, and cell death. Gene silencing by the sirtuin protein is directly correlated with longer lifespans in yeast and worms. While the first member of the sirtuin family, SIRT1, has been extensively studied, Dr Braidy's research will investigate another sirtuin, the under-researched SIRT2.

"My research was the first to show that intracellular levels of NAD+, which is the essential substrate or reactant allowing sirtuins like SIRT2 to work, decline with age in humans and physiologically aged rats," said Dr Braidy.

Exactly how SIRT2 functions under physiological and pathological conditions is currently unclear according to Dr Braidy, although it appears to be significant for brain health. Previous research showed that SIRT2 is indirectly associated with chronic oxidative stress and inflammation, both known factors in cognitive decline and Alzheimer's and dementia in particular.

Building on his existing work, including his well-established Wistar "aged rat" model, Dr Braidy plans to investigate how pharmacological strategies designed to elevate intracellular NAD+ levels will maintain optimal SIRT2 function to extend lifespan and improve age-related cognitive decline in vivo.

"The timeliness and relevance of sirtuins to a rapidly ageing population is indicated by our publications in this field having already received over 200 citations in the last 3 years," said Dr Braidy.

BRAIN DONATION PROGRAM

Dr Kristan Kang, Data Manager is the co-ordinator of Brain Donation Program

The CHeBA Brain Donation Program collaborates with a number of other brain bank networks, including the Sydney Brain Bank, the Victorian Brain Bank Network, the Queensland Brain Bank and the Australian Brain Bank Network. The CHeBA Brain Donation Program collects brain tissue from donors sourced from the Memory & Ageing Study (MAS), Older Australian Twins Study (OATS), and the Sydney Centenarian Study (SCS). As all our donors have participated in our longitudinal research, CHeBA possesses rich and extensive pre-mortem clinical, behavioural, and biomarker data on its donors. This allows a unique opportunity to analyse post-mortem brain tissue and neuropathology relative to pre-mortem health, and the possibility of studying the neural pathology and outcomes of normal ageing and dementia at the microscopic level. Our research participants range from healthy 'controls' to those with mild cognitive impairment and dementia, as well as including rare phenotypes such as the extreme-elderly (95+ years) and twins. This allows for the opportunity to do detailed research into multiple aspects of ageing including healthy ageing, dementia and cognitive decline, as well as the role of genetics in ageing.

In 2016, 2 new brains were donated to the CHeBA Brain Donation Program, while an additional 7 research participants signed up.

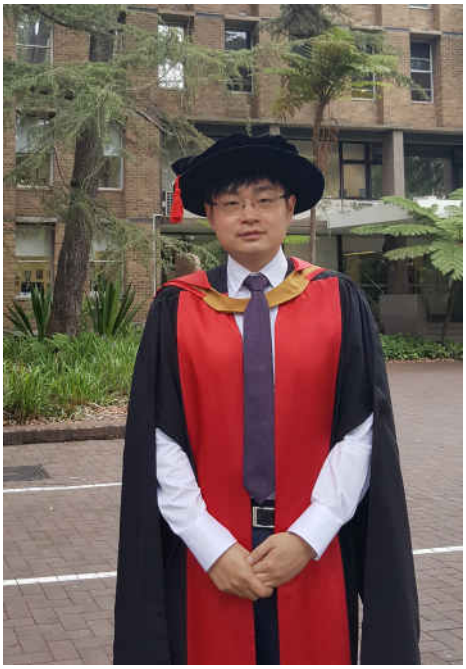
PhD COMPLETIONS

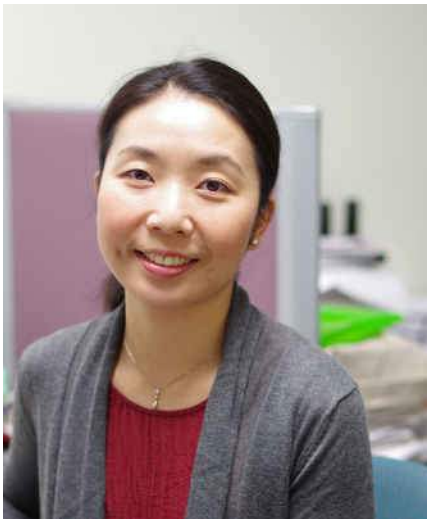
Dr Jiyang Jiang

Thesis: The relationships of inflammation with brain structures in older individuals as revealed by multimodal magnetic resonance imaging techniques

My research found ageing-related, low grade, chronic inflammation contributes to structural degeneration of the brain. In a related finding, levels of Macrophage Inhibitory Cytokine-1 (MIC-1) in blood samples provide a robust biomarker for brain atrophy in ageing individuals.

Working with CHeBA gave me access to novel and unique datasets, helpful supervisors and staff and opportunities to participate in international projects.





Dr Zixuan (Sophie) Yang

Thesis: Structural MRI in late life with a special focus on the oldest old

This is the first study of its kind to extend our understanding of brain ageing on structural magnetic resonance imaging (MRI) into the 10th and 11th decades of life. Identifying MRI markers of dementia and amnestic mild cognitive impairment at advanced age could potentially assist in early diagnosis of dementia, as well as improving understanding the mechanisms of brain resilience in the oldest old. We observed a linear, negative relationship between age and grey matter volume in non-demented participants, which continued into the 10th and 11th decades of life. The medial temporal lobe and parietal and occipital cortices experienced the greatest effects of age. Thinner cortex and a smaller hippocampus were strong indicators of dementia at all ages, as were deep white matter hyperintensities and brain infarcts (≥2) at 80 but not at 95 years old. Structural MRI markers could distinguish amnestic mild cognitive impairment (MCI), but not non-amnestic MCI, from normal individuals from 71 to 103 years. However, the MRI markers that were most indicative of amnestic MCI differed in the young old from the oldest old. Having studied in France and China, CHeBA has been my best experience in research to date.

OUR COMMUNITY

"Our goal is for members of the community to add life to their years, not just years to their life. Even small lifestyle changes can have an enormous impact on healthy brain ageing."

Professor Henry Brodaty

THE DEMENTIA MOMENTUM

SPOKESMAN'S REPORT

When we launched **The Dementia Momentum** initiative last year, we set ourselves a very ambitious goal of raising $10 million over 5 years to change the future of dementia in Australia and internationally. Although ambitious, the goal was necessary given the staggering current projections of the cost and impact of dementia on Australia. By 2050, dementia is expected to account for 2-3% of Australia's GDP. The aged care workforce in Australia will need to triple and 500 new nursing home beds for dementia-related care will be needed per month over the next 40 years to meet demand.

These statistics hold a personal resonance: the inspiration behind The Dementia Momentum is my wife, Suellen, who was diagnosed with young-onset Alzheimer's disease in 2011. Given that she is now in advanced decline, I am grateful for the opportunity to continue in my role as spokesman to generate greater public awareness about the disease and drive change to prevent future generations from experiencing the same impact as our family, and many others like us.

"We need to keep the information flow strong from our researchers to politicians so that this huge (and growing) problem gets the funding support needed."

Richard Grellman AM

The Dementia Momentum is a worthy initiative and, in 2016, we made great strides in our progress. We raised over $2 million towards our goal; substantially increased our corporate and philanthropic support base, including a $600,000 donation from the John Holden Family Foundation; and hosted a number of outreach campaigns and events. Events were generously hosted by KPMG, ARIA Restaurant Sydney and Genworth. We held the third and fourth **Wipeout Dementia** surfing competitions in May and November 2016, respectively. To date, the Wipeout campaign has raised $350,000, with approximately 100 corporate participants, support from key political figures and widespread media coverage. The campaign itself has expanded from its traditional base at Queenscliff Surf Life Saving Club, with the inaugural property industry event held at Bondi Beach for the first time in November. I would like to thank all of our supporters in 2016, particularly major sponsors Morgans and Kennards Hire, and fellow Wipeout Dementia Ambassador and good friend former World Surfing Champion Wayne 'Rabbit' Bartholomew AM.

We have made substantial inroads in 2016, but there is still much to be done in the coming years. In 2017, expect to see more Wipeout Dementia events and possibly some new initiatives, which will seek to raise awareness and funding by tapping into different community groups.

CHeBA is doing the hard yards in tackling a disease as complex and insidious as dementia. As a community we should be very grateful that folk like Henry, Perminder and their colleagues are so focussed on this elusive challenge. We need to keep the information flow strong from our researchers to politicians so that this huge (and growing) problem gets the funding support needed, and to ensure our tax dollars are invested well and proactively.

We thank our existing supporters for their continued enthusiasm and encouragement, and look forward to welcoming a new generation of supporters in 2017.

Richard Grellman AM
Chairman, IPH Ltd & AMP Foundation

THE DEMENTIA MOMENTUM ANNIVERSARY AT KPMG

The Dementia Momentum reached its first anniversary on 25 March 2016 and celebrated with KPMG Sydney hosting a second corporate cocktail event on 25 February to launch the Wipeout Dementia video. Partner John Teer delivered a heart-warming speech on behalf of KPMG and confirmed their ongoing support of the initiative.

"We are thrilled by the success The Dementia Momentum has achieved this far," said Co-Directors Professors Henry Brodaty and Perminder Sachdev. "With dementia posing an enormous burden on society, we are very encouraged by the corporate and community response we have received and look forward to building on this in the coming years to change the future of dementia incidence."

The Wipeout Dementia video was launched at the KPMG-hosted anniversary by Spokesman Richard Grellman as part of an awareness and outreach campaign to increase physical activity to reduce dementia risk and drive philanthropic funds into research.

"This funding is vital not only to understanding the worldwide risk and protective factors, but also for identifying and targeting at-risk groups. Starting from 2016, we will test intervention strategies for the modifiable lifestyle factors identified to reduce dementia risk," said Professor Brodaty.

The Wipeout Dementia video can be viewed at: https://www.youtube.com/watch?v=Hy1ICNGp-IE

"To achieve the end-goal of wide-scale societal change, continued support from the corporate, philanthropic and wider community is vital to the success of The Dementia Momentum and the future of dementia in Australia."

Professor Henry Brodaty

Professor Henry Brodaty, Professor Perminder Sachdev, Richard Grellman

> "We are pleased to be able to donate to The Dementia Momentum and support its innovative, large-scale approach to improving understanding and reducing incidence of the disease."
> Mr John Holden, Founder John Holden Family Foundation

JOHN HOLDEN FAMILY FOUNDATION GIVES $600,000

The John Holden Family Foundation became the first Diamond Member of The Dementia Momentum when it committed $600,000 to CHeBA's initiative, received in mid-2016.

The contribution will fund a project led by Associate Professor Wei Wen, leader of CHeBA's Neuroimaging group. The project will bring together a large number of studies from around the world to collectively examine the clinical implications and the genetic basis of white matter hyperintensities (WMHs) and lacunes (small silent strokes), and thereby cerebral small vessel disease. The research will also examine how closely WMHs and lacunes are associated with dementia and cognitive decline among other factors.

"We are pleased to be able to donate to The Dementia Momentum and support its innovative, large-scale approach to improving understanding of the disease and reducing incidence through evidence-based modifiable lifestyle strategies," said Mr Holden.

CHeBA Co-Director Professor Perminder Sachdev said large injections of funding allow researchers to achieve considerable outcomes in shorter timeframes.

Dr Jiyang Jiang with Mr John Holden

"Significant funding to fully support a project allows us to conduct research proactively," said Professor Sachdev. "We can establish and implement larger research studies from the outset."

"The generosity of the John Holden Family Foundation is humbling," he said.

Following an international recruitment round, Dr Jiyang Jiang was selected for the post-doctoral fellowship position funded by the John Holden Family Foundation. The first project involved creation of an automated WMH extraction pipeline to process the large volume of data available. The pipeline can process approximately 250 brain images in two to three days, with a publication of the process due in 2017.

WIPEOUT DEMENTIA

2016 saw the continued success of CHeBA's *Wipeout Dementia* campaign, with the third and fourth events held in May and November respectively. Sydney corporate surfers complete a gruelling four-week strength for surfing training course, culminating in a Surf Off competition. To date, the campaign has raised $350,000, involved over 100 participants and generated widespread media interest.

"We are delighted and encouraged by the growing awareness and support Wipeout Dementia is generating within the Australian corporate community," said Spokesman for The Dementia Momentum Mr Grellman, Chairman of IPH Limited and AMP Foundation and former Chairman of The Association of Surfing Professionals (International) Limited. "Long-term partnership between research and business is critical for us to face the social and economic challenges dementia incidence poses."

The third campaign held in May at Queenscliff Surf Life Saving Club exceeded its fundraising target, raising over $82,000. John Cunningham, team captain of Cunningham's Cruisers since the inception of Wipeout Dementia in 2015 and Managing Director of Cunninghams, personally raised over $16,000 while bringing the company on board as supporter sponsor. He was awarded the prestigious 'Gnarly Award' for the highest fundraiser, receiving a Mark Richards 1982 replica twin fin surfboard.

The fourth campaign in November, the inaugural property industry Wipeout Dementia held for the first time at Bondi Beach, built upon previous success and set the benchmark for other industries to get on board. Mr Grellman extended particular thanks to Director of Avenor, Peter Clemesha and Managing Director of Colliers International, Peter Chittenden, for promoting this event and leading a new wave of support for the campaign.

> "The appeal of the Wipeout Dementia campaign is that all funds raised go directly to researching the prevention, diagnosis and treatment of dementia. At the same time, we get to have a lot of fun doing something we love."
>
> Wayne 'Rabbit' Bartholomew AM, Wipeout Dementia Ambassador & 1978 World Surfing Champion

"Our dream has always been that the Wipeout Dementia concept will be so attractive that there will be contests between different sectors, at different beaches and perhaps even in different states."

"As the husband of a dear girl suffering very advanced young onset Alzheimer's disease my hope is that firstly, on the back of Wipeout Dementia, the broader community realises that this is a serious economic issue and secondly, that more people get involved to help with fundraising to support CHeBA's research," he said.

Peter Clemesha said he was really happy to be involved and that he intended for this to be an annual event across the property industry.

"I'm thrilled to see the property industry get behind Wipeout Dementia," said Mr Clemesha. "Many of us have witnessed the devastating impact of dementia and it's a privilege to support research while promoting the benefits of physical activity for brain health."

Surfers in the inaugural property industry event included CEO of State Property, Brett Newman; Group Director of Ray White, Dan White, Ray White Commercial Managing Director, Jeff Moxham and Director of Bates Smart, Philip Vivian.

Mark Gross, two time surfer in Wipeout Dementia and Executive Director at Morgans, won the 'Gnarly Award' in November after raising over $16,000 and bringing Morgans on board as major sponsor in both the May and November 2016 events. He said it was a privilege to be involved in the event. "The research and development work undertaken by CHeBA can help dramatically to reduce future suffering. Morgans is delighted to be able to sponsor this campaign, allowing all funds raised to go directly to research."

Wipeout Dementia Ambassador and 1978 World Surfing Champion **Wayne 'Rabbit' Bartholomew AM** congratulated all participants in 2016 for their enthusiasm and involvement.

"The appeal of the Wipeout Dementia campaign is that all funds raised go directly to researching the prevention, diagnosis and treatment of dementia," said Rabbit. "At the same time, we get to have a lot of fun doing something we love."

CHeBA Co-Directors, Professor Perminder Sachdev and Professor Henry Brodaty expressed their appreciation to all participants, major sponsors Morgans and Kennards Hire, Ambassadors Richard Grellman and Wayne 'Rabbit' Bartholomew, as well as event creator and coordinator Heidi Mitchell and Coach Craig Douglass.

"Participants in Wipeout Dementia are great exemplars of the modifiable lifestyle factors we know help prevent or reduce dementia incidence," said Professor Brodaty. "They are physically active, have great social connections and are engaging in complex mental activity by learning new skills throughout the course."

Research shows physically inactive individuals have an 80% increased risk of dementia. By contrast, physical exercise has positive and protective effects on brain function, not only reducing risk factors but increasing neuroplasticity.

Wipeout Dementia is held in honour of Richard's wife Suellen who has advanced young onset Alzheimer's disease and now requires full time high level care and attention at age 66.

"Participants in Wipeout Dementia are great exemplars of the modifiable lifestyle factors we know help prevent or reduce dementia incidence. They are physically active, have great social connections and are engaging in complex mental activity by learning new skills throughout the course."
Professor Henry Brodaty

Morgans and Kennards Hire were the major sponsors for Wipeout Dementia in May and November 2016.

Cunninghams, Watson Mangioni Lawyers, Sandler Shoes and Sparke Helmore Lawyers were supporter sponsors in May. Ray White Commercial and Colliers International were secondary sponsors in November.

Hurley, Dripping Wet, Queenscliff Surf Life Saving Club and The Bucket List provided in-kind support.

WIPEOUT DEMENTIA 2016 PARTICIPANTS

- Scott Anderson
- Jeff Atkinson
- Wayne 'Rabbit' Bartholomew (Ambassador)
- Darren Beasley
- Phil Butt
- Tony Camphin
- Ben Caunt
- Peter Chittenden
- Jon Chomley
- Chris Clarke (Most Valuable Player on Grellman's Evergreens, May)
- Peter Clemesha
- Andrew Cowan
- Andrew Coward
- Warwick Crane
- John Cunningham (Team Captain; Gnarly Award for highest fundraiser, May)
- Nick Ebrill (Wave of the Day Award, November)
- Julian Etter
- Ian Freestone (Most Valuable Player on Cunningham's Cruisers, May)
- Don Giles
- Robert Gillespie
- Ben Grellman
- Richard Grellman
- Mark Gross (Gnarly Award for highest fundraiser, November)
- Shawn Hobbs (Wipeout Award, May)
- Rob Johns
- Andy Kennard (Player's Player Award, May)
- Peter Kleijn
- Guy Lake
- Stephen Lennard
- Adrian McGregor
- David Michel
- John Morgan (Wipeout Award, November)
- Nikki Morley
- Jeff Moxham
- Peter Murphy (Most Valuable Player on Gillespie's Grommet's Forever, May)
- Brett Newman
- James Paver
- Simon Ranson
- James Regan
- Karl Riedel
- Craig Rodgers
- James Smith
- Philip Vivian
- Austin Ware (Wave of the Day Award, May)
- Steve Watson
- Stephen Westfield (Coach's Award, May)
- Dan White
- Phillip Wicks

CONTINUED SUPPORT FROM GENWORTH

Alceon became a Teal Member of The Dementia Momentum in May 2016 with a generous donation of $5,000. Alceon's donation follows the attendance of Founder and Managing Director, Trevor Loewensohn, at a corporate leader luncheon hosted by Genworth to support The Dementia Momentum on 29 March 2016.

Spokesman for The Dementia Momentum, Richard Grellman AM, addressed the attendees of this event and called on the corporate world to accept the challenge of increasing research funding into dementia and, specifically, Alzheimer's disease.

CHeBA Co-Director Professor Henry Brodaty also spoke at the event.

"Alceon is proud to respond to Richard Grellman's call for Australian corporates to fund CHeBA's research and drive a brighter future for all Australians," said Mr Loewensohn.

Richard Grellman said Alecon's response was encouraging.

"It is inspiring to see the incredible generosity from not just the big corporations, but also smaller corporate groups in Sydney like Alceon supporting The Dementia Momentum," said Mr Grellman.

ARIA RESTAURANT SYDNEY HOSTED CORPORATE LUNCH

ARIA Restaurant Sydney continued their partnership with CHeBA in 2016 by hosting the fourth annual senior executives' corporate lunch for the Centre. UNSW Dean of Medicine Professor Rodney Phillips was Master of Ceremonies at this year's luncheon with guest speakers Richard Grellman AM, Spokesman for The Dementia Momentum, and daughter Sarah Holmes, who gave a candid and touching daughter's perspective on her mother's journey with young onset Alzheimer's disease.

CHeBA's Co-Director Professor Henry Brodaty also delivered a talk on the developments of research under The Dementia Momentum initiative and the launch of the Maintain Your Brain study.

Sarah Holmes, Richard Grellman, Professor Rodney Phillips, Professor Henry Brodaty

VINCENT FAIRFAX FAMILY FOUNDATION FUNDS STROKOG CO-ORDINATOR

The Vincent Fairfax Family Foundation (VFFF) awarded CHeBA a $300,000 philanthropic grant over three years to investigate risk and protective factors for dementia. VFFF's contribution supports the salary of the STROKOG consortium study co-ordinator, a position filled by Ms Jessica Lo in 2016.

The role of The Dementia Momentum in raising awareness about the disease inspired Ms Lo to work for CHeBA.

"The Dementia Momentum is a great initiative which brings together researchers and the community," said Ms Lo. "It allows the community to invest in bringing about positive, significant social change. By bringing an increased investment in dementia research, this initiative is allowing researchers to continue to work on finding the risk and protective factors for the disease."

Starting the role in January 2016, Ms Lo said that while the workload has been significant, CHeBA's innovative push for creating international-scale, big data-sets is a key motivator.

"While academia can sometimes be competitive, at CHeBA we work collaboratively by setting up a number of international consortiums, including STROKOG, to address universal issues such as healthy ageing and age-related diseases. I think it's our collaborative and international effort that makes CHeBA unique."

Ms Jessica Lo

Launched in 2015, STROKOG (International Consortium of Studies of Post-stroke Cognitive Disorders) brings together prospective post-stroke studies from around the world in order to better understand the longitudinal course of cognitive impairment after stroke and ask questions in relation to risk and protective factors. The findings of STROKOG will help guide preventative strategies and health policy both in Australia and internationally. Currently studies from Australia, Hong Kong, Singapore, Korea, China, Poland, France, Finland, Ireland, the UK, Sweden, Germany, South Africa, Nigeria and the USA are represented.

"I look forward to being able to disseminate STROKOG's results to our collaborators and to the community. I'm excited about seeing our research being widely talked about and to see public interest in our consortia findings from The Dementia Momentum initiative," said Ms Lo.

"Probably one of the misconceptions is that there is nothing a person can do once they have dementia. It is important the public know there are ways to slow its progress and our research certainly aims to find ways to delay the onset of dementia."

"Ageing and dementia are universal concerns. If people care about their health then they should also care about ageing brain health. Brain disorders such as dementia take a devastating toll on not only those with the disease, but entire families as well as their friends."

Chief Executive Officer of Vincent Fairfax Family Foundation (VFFF), Jenny Wheatley, said they are pleased to support The Dementia Momentum which aligns with VFFF's funding principles of adopting an innovative approach.

"This initiative has the potential to achieve system change within dementia research," said Ms Wheatley.

Ms Lo holds a Master of Science in Medical Statistics from the London School of Hygiene and Tropical Medicine. She was a medical statistician at King's College London for four years, including working on clinical trials. She also has experience in museum studies, web marketing and graphic design. In her spare time, Ms Lo plays music, exercises four times a week and eats a healthy fish-based diet to protect her brain health.

CHeBA CHAMPIONS

In 2016, the CHeBA Champions continued to promote healthy brain ageing from a young age through a variety of fitness activities and engagement with the media. The CHeBA Champions are Fitness Ambassadors for CHeBA in their 20s, 30s and 40s; all striving for optimal brain health in late life by adopting risk-reducing lifestyle strategies early. PJ Lane is the Ambassador for this initiative.

Brain abnormalities that lead to dementia are known to start at least 20-30 years before the disease becomes manifest, suggesting that behaviours in young and mid adulthood will have a significant impact on brain health in old age.

HAILEY MAXWELL

A CHeBA Champion since the program's inception in 2012, Hailey has raised over $20,000 for CHeBA's research.

Following the death of her beloved grandmother in 2016 who suffered from Alzheimer's disease, Hailey attempted the 240km Coast to Kosciusko ultra-marathon on 9 December.

"It was pretty hard for me and my family [when my grandma died] so I thought I would do something just as hard. I've been raising funds for CHeBA for a couple of years now and this has certainly spurred me on a lot more."

Hailey Maxwell

A successful social media campaign - #RunforNan - accompanied her efforts which also made it to her local newspaper.

GENWORTH-SPONSORED BETTER BRAIN. BETTER LIFE CORPORATE FORUMS

In 2016, the **Better Brain. Better Life** series was extended from the public to the corporate sector to encourage the implementation of lifestyle changes to reduce risk of dementia in the workplace.

Platinum sponsor Genworth continued its generous support of the Better Brain. Better Life series in its corporate incarnation. The first two events were hosted by ansarada and Genworth, with further events planned for 2017.

Speakers included CHeBA's Dr Nicole Kochan, Dr Nicola Gates and Associate Professor Belinda Goodenough.

PUBLIC FORUMS

MAXIMISING BRAIN HEALTH

In a joint initiative of Hunters Hill Council, Lane Cove Council and Alzheimer's Australia, Professor Henry Brodaty delivered a public talk on maximising brain health.

With community education a priority focus for CHeBA, this talk discussed memory and ageing and the latest research on brain health and dementia risk reduction.

KICK START HEALTHY AGEING

Close to 500 seniors registered for the annual positive ageing forum at The Juniors in Kingsford on 9 November 2016. The forum, 'Kick Start Healthy Ageing', was a joint project of CHeBA and the Aged Care Psychiatry Service, Eastern Suburbs Mental Health Service (ACPS), which focused on how the aspects of maintaining health into late life, particularly in relation to brain health.

The 2016 event comprised a series of expert talks from some of Australia's pre-eminent researchers in the field of old age psychiatry, including recipient of the 2016 Ryman Prize Professor Henry Brodaty AO and Professor Maria Fiatarone Singh; geriatrician and expert in physical exercise and brain health at the University of Sydney and Professor Sharon Naismith, head of the Healthy Brain Ageing Program at the University of Sydney.

Chairman of South Eastern Sydney Local Health District (SESLHD), Michael Still, provided the opening address and acknowledged the efforts of the organisers of this highly successful annual event.

> "Our goal is for members of the community to add life to their years, not just years to their life. Even small lifestyle changes can have an enormous impact on healthy brain ageing."
> Professor Henry Brodaty

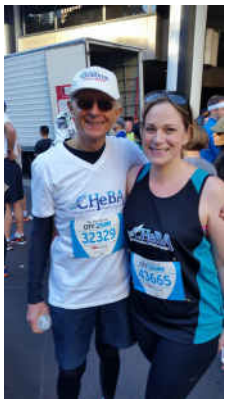
In its 15th year running, the free forum which is co-ordinated by Professor Brodaty, social worker Daniella Kanareck and their team at ACPS, has proven to be an extraordinary community success and a highlight on the Eastern Suburbs calendar.

The event was sponsored by CHeBA, The Juniors Kingsford, Waverley Council Small Grant Program, SESLHD Mental Health Services, Ministry of Healthy, Arts Health Institute, Dementia Collaborative Research Centres (DCRC) and Genworth.

CHeBA IN THE MEDIA

In 2016 there were a number of high profile media features on CHeBA's research. Significant highlights included coverage of Dr Adith Mohan's transcranial direct current stimulation research on *Channel 9* and Professor Henry Brodaty talking about memory and neuroplasticity on *Studio 10*. Our community endeavours also reached the media with the CHeBA Champions continuing to achieve local coverage from their events. Wipeout Dementia was also featured in *The Daily Telegraph* and local newspapers.

CITY2SURF



The challenging City2Surf fun run is a highlight of the year for CHeBA with many people keen to promote the healthy brain ageing message.

2016 was a significant year at the start-line for Team CHeBA, with new recruits Sarah and Rob Holmes and Tori and Brett Peacock joining those who have participated alongside Co-Directors Professor Perminder Sachdev and Professor Henry Brodaty to honour a family member with dementia. These four, who together raised $2,569 for The Dementia Momentum, ran and power walked for Sarah's mum, Suellen Grellman, who was diagnosed with young onset Alzheimer's disease at just 61 years of age and is now in full time high care. Spokesman for The Dementia Momentum and Sarah's father, Richard Grellman, said that Suellen would have been proud of their daughter's awareness-raising efforts.

CHeBA's positive ageing heroes are Graham Gates (who has now completed the course for the fourth time for CHeBA at age 86), Colin Blake (who has completed every City2Surf except two of them since the very first event in 1971). On behalf of all of Team CHeBA we thank these lads for the incredible inspiration and for their solid annual fundraising efforts. Both Graham and Colin have each raised more than $3,000 for CHeBA's research.

Special thanks also go to Susan Coorey who is a repeat supporter and who has heartbreakingly witnessed her grandmother, her aunt and her mother all endure Alzheimer's disease.

The City2Surf event is a great opportunity for CHeBA to promote the relationship between cardiovascular health and brain health, particularly its significance as a risk factor for dementia. There is incontrovertible evidence that physical inactivity increases the risk of heart disease, high blood pressure, stroke, obesity, Type 2 diabetes and depression as well as vascular and Alzheimer's dementia.

A heartfelt thanks to everyone for their strong support.

SUPPORTERS & DONORS

A MESSAGE FROM OUR CENTRE MANAGER

About a year ago, one of my very good friends' father lost his battle with dementia. He was a devoted family man, a Navy man, and a good man. Just two weeks ago another very good friend's father passed away from Lewy Body Dementia. He too was a devoted family man who led a simple, loving life and wanted nothing more than to see his children reach their full potential. He was a fantastic ballroom dancer and all the ladies wanted to dance with him. And just this week one of our colleagues sadly told us that his father passed away after a three year struggle with vascular Parkinsonism and dementia. Why am I telling you this? To highlight the fact that dementia touches us all in some way, either directly or indirectly, and to me that is why the research we undertake at CHeBA is vitally important in the quest to find answers to this debilitating and devastating disease, in all its forms. On behalf of all of us at CHeBA, I give thanks to each and every one of our donors for the generous contributions that help us to pursue our research into neurodegenerative diseases, particularly the dementias.

Angie Russell
Centre Manager

MAJOR SUPPORTERS

GOVERNMENT & PARTNERS

Australian Government
NHMRC National Institute for Dementia Research

Australian Government
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DCRC
Dementia Collaborative Research Centres

NHMRC

UNSW SYDNEY

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CHeBA COLLABORATORS

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- Anglicare P/L
- BaptistCare
- Lebanese Muslim Association, Australian Multicultural Aged care Nursing (AMAN)
- Montefiore Home

SOCIETIES/PROFESSIONAL ASSOCIATIONS

- Alzheimer's Australia
- Alzheimer's Disease International (ADI)
- Australasian Association of Gerontology (AAG)
- Australasian Society for Psychiatric Research (ASPR)
- International College of Geriatric Psychoneuropharmacology (ICGP)
- International Neuropsychiatric Association (INA)
- International Psychogeriatric Association (IPA)
- Royal Australian & New Zealand College of Psychiatrists (RANZCP)
- Faculty of Old Age Psychiatry, RANZCP
- International Society of Vascular Behavioural and Cognitive Disorders (VASCOG)

NATIONAL

COMMONWEALTH

- Australian Government Department of Social Services
- Australian Government Department of Health

WESTERN AUSTRALIA

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- Murdoch University, Perth

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- Academic Department for Old Age Psychiatry (ADFOAP), Prince of Wales Hospital
- Australasian Research Institute, Sydney Adventist Hospital
- Australian Catholic University
- Bankstown-Lidcombe Hospital
- Bioanalytical Mass Spectrometry Facility, Mark Wainwright Analytical Centre, UNSW
- Black Dog Institute, UNSW
- Brain Sciences UNSW
- Centre of Excellence in Population Ageing Research (CEPAR), UNSW
- Clinical Research Unit for Anxiety and Depression (CRUfAD), UNSW
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- Keio University, Japan
- Kyushu University, Japan
- National Center for Geriatrics and Gerontology, Japan
- Tohoku University, Japan
- University of Macau, Macau
- Universiti Putra Malaysia, Malaysia
- Department of Neuropsychiatry, Gyeonggi Provincial Hospital for the Elderly, Republic of Korea
- Hallym University, Republic of Korea
- Seoul National University, Republic of Korea
- Changi General Hospital, Singapore
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- National University Health System, Singapore
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- Neuroscience Network Düsseldorf, Heinrich Heine University, Germany
- University of Leipzig, Germany
- University of Marburg, Germany
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- Golgi-Cenci Foundation, Italy
- Institute of Biomembranes and Bioenergetics, National Council of Research, Bari, Italy
- Mario Negri Institute for Pharmacological Research, Italy
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- University of Groningen, The Netherlands
- VU University, The Netherlands

UK

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- University of Georgia, Georgia, USA
- Northwestern University, Illinois, USA
- Johns Hopkins Medicine, Maryland, USA
- Mayo Clinic, Minnesota, USA
- University of Minnesota, Minnesota, USA
- Boston University, Massachusetts, USA
- Harvard University, Massachusetts, USA
- Washington University, Missouri, USA
- Cleveland Clinic, Nevada, USA
- Columbia University, New York, USA
- Fordham University, New York, USA
- Gertrude H. Sergievsky Center, New York, USA
- Yeshiva University, New York, USA
- University of Pittsburgh, Pennsylvania, USA

SOUTH AMERICA

- Instituto Rene´ Rachou da Fundaçaõ Oswaldo Cruz, Brazil
- University of São Paulo, Brazil
- Pontificia Universidad Católica de Chile, Chile

CURRENT PROJECTS

A study of the effect of acute physical illness requiring hospitalisation on the long-term cognitive and functional trajectory of two elderly cohorts: The Sydney Memory and Aging Study (MAS) and the Older Australian Twins Study (OATS)

CHeBA staff: Lucia Chinnappa-Quinn (PhD student), Perminder Sachdev, Nicole Kochan, John Crawford.

Other investigators: Professor Michael Bennett (Prince of Wales Clinical School, UNSW).

Aims:

- Observe the effect of acute physical illness requiring hospitalisation on cognitive and functional trajectory over several years in longitudinal cohort studies of cognitive ageing.
- Examine whether variables describing the nature of the illness and hospitalisation influence the level of decline in cognition and function over time.
- Explore whether a number of risk-factor variables, such as APOε4 carrier status or MCI, act as moderator variables to increase the effect of acute physical illness requiring hospitalisation on cognitive and functional decline.

Findings: Ethics approved and data collected for analysis.

Funding: Australian Society of Anaesthetists, DCRC-ABC.

Abeta (Aβ) peptides in plasma

CHeBA staff: Anne Poljak (conjoint), John Crawford, Henry Brodaty, Melissa Slavin (conjoint), Nicole Kochan, Julian Trollor (conjoint), Wei Wen, Karen Mather, Perminder Sachdev, Amelia Assareh.

Other investigators: Ms PC Ng (formerly Brain & Ageing Research Program), Associate Professor George Smythe (SOMS, UNSW).

Aims:

- Determine if plasma Aβ peptides 1-40 and 1-42 may be potential peripheral markers to assist in diagnosis of MCI and/or Alzheimer's disease (AD).
- Explore the possibility that plasma Aβ peptide levels are correlated with brain volumetric and cognitive changes.

Findings:

- Plasma levels of Aβ peptides are lower in amnestic MCI and AD, and the Aβ1–42 peptide is positively associated with global cognition and hippocampal volume and negatively with white matter hyperintensities.
- The relationships of Aβ1-40 and Aβ1-42 peptides are predominantly observed in β4 allele carriers and non-carriers respectively.
- Longitudinal analysis reveals greater decline in global cognition and memory for the highest quintiles of Aβ1–42 and the ratio measure.
- Plasma Aβ levels and the Aβ1–42/1-40 ratio are related to cognition and hippocampal volumes, with differential associations of Aβ1-40 and Aβ1-42 in β4 carriers and non-carriers. These data support the Aβ sink model of AD pathology, and suggest that plasma Aβ measures may serve as biomarkers of AD.

Funding: NHMRC, ARC, Rebecca L. Cooper Medical Research Foundation, Alzheimer's Australia Rosemary Foundation.

Age-related cognitive decline and risk associations across ethno-cultural and geographic regions: A collaborative cohort study (COSMIC) (Formerly: Determine rates & patterns of cognitive decline in ageing populations from different geographical regions (using data from COSMIC))

CHeBA staff: Darren Lipnicki, John Crawford, Rajib Dutta, Anbupalam Thalamuthu, Nicole Kochan, Gavin Andrews (conjoint), Henry Brodaty, Perminder Sachdev.

Other investigators: Dr Simone Reppermund (UNSW Medicine) (CHeBA Hon. Research Fellow); 34 investigators from 12 different countries as part of COSMIC.

Aims:

- Explore how a range of genetic, epigenetic, cardiovascular and lifestyle related factors contribute to cognitive decline and neurocognitive disorders.
- Determine the extent to which associations vary internationally across ethno-cultural and geographic regions.

Findings: The first project exploring associations with sex, education and apolipoprotein E genotype is complete (see: Completed projects - Age-related cognitive decline and associations with sex, education and apolipoprotein E genotype across ethno-cultural and geographic regions: A collaborative cohort study). Recruitment of population studies from ethno-cultural groups and geographical regions which were absent in the first project has been achieved or is underway, including Africa, India and mainland China. A number of additional risk factors (including health, anxiety, depression, blood pressure and hypertension, cardiovascular disease, diabetes, cholesterol levels, stroke, smoking, alcohol use, and physical activity) have been harmonised for preliminary analysis.

Funding: Direct donations to The Dementia Momentum Fund.

Amyloid-beta blood levels as an early marker of neurodegenerative disease, using data from multiple studies, including Sydney MAS, DIAN, AIBL, ADNI and OATS

CHeBA staff: Anne Poljak (conjoint), John Crawford, Henry Brodaty, Perminder Sachdev.

Other investigators: Professor Randall J. Bateman (Washington University), Professor Anne Fagan (Washington University), Professor Ralph Martins (Edith Cowan University), Professor Colin Masters (University of Melbourne), Professor John Morris (Washington University).

Aims:

- Explore covariates for correlation with Aβ levels across all cohorts. Covariates to explore include: comorbidities, therapeutic drugs, blood biochemistry, as well as lifestyle choices.
- Compare corrected Aβ levels (all cohorts) across neurodegenerative diseases: Alzheimer's disease, Parkinson's disease and Mild Cognitive Impairment (MCI).
- Identify effects of soluble Aβ levels on brain volumetric parameters, across the neurodegenerative conditions tested.

Findings: Data access has been granted and this project is in progress.

Funding: NHMRC, ARC, Rebecca L. Cooper Medical Research Foundation.

Apolipoproteins in plasma (particularly ApoA1, ApoD, ApoJ and ApoH)

CHeBA staff: Julia Muenchhoff, Anne Poljak (conjoint), Nady Braidy, Nicole Kochan, Wei Wen, John Crawford, Julian Trollor (conjoint), Henry Brodaty, Perminder Sachdev.

Other investigators: Dr Fei Song (CHeBA Hon. Research Fellow), Professor John Attia (University of Newcastle), Professor Mark Duncan (University of Colorado), Professor Ralph Martins (Edith Cowan University), Associate Professor Mark McEvoy (University of Newcastle), Associate Professor Peter W. Schofield (University of Newcastle).

Aims:

- Determine if apolipoprotein changes observed in MCI and AD plasma, relative to normal controls, would be reproducible across independent cohorts of similar design.
- Identify which of the apolipoproteins change with age and/or are dysregulated in MCI and AD.
- Correlate plasma apolipoprotein changes with cognitive domain scores and brain volumetrics.
- Study the mechanisms of action, expression changes with age, and dysregulation in neurodegenerative diseases of ageing, including animal models for apolipoproteins ApoA1, ApoD, ApoJ and ApoH.

Findings: The literature has long recognised the ApoE ε4 allele variant as the most significant genetic risk factor for AD. Our work has shown that the impact of the apolipoprotein family extends well beyond, to many of the members of this protein family, showing that:

- Lower levels of many apolipoprotein family members are associated with mild cognitive impairment.

- Altered expression of apolipoprotein family members is observed in a number of cohorts, including MAS, HCS and DIAN.
- The mechanism by which ApoE allele variants alter AD risk may involve lower in vivo protein half-life. In support of this possibility we have shown that ApoE ε4 and ε2 carriers have lower and higher plasma apolipoprotein levels respectively (particularly ApoE, but also ApoJ and ApoH).
- Genetic variation in ApoA1 and ApoH (such as methylation and SNPs) are associated with memory and cognitive performance, as shown by our affiliated Genetics group members using GWAS data.

Funding: NHMRC, Rebecca L. Cooper Medical Research Foundation, Alzheimer's Australia Rosemary Foundation, Sachdev

Are visual-only memory impairments sufficient to diagnose amnestic MCI?

CHeBA staff: Darren Lipnicki, Perminder Sachdev.

Other investigators: Javier Oltra-Cucarella (PhD student), Professor Rosario Ferrer-Cascales, Miriam Sánchez-San Segundo (University of Alicante, Spain); and others from studies that contribute data.

Aim: Determine if the risk of developing dementia is lower for individuals with visual-only amnestic mild cognitive impairment (aMCI) than those with verbal aMCI.

Findings: Data are yet to be compiled and analysed.

Funding: Direct donations to The Dementia Momentum Fund.

Brain proteomics: Differential expression of the proteome in AD brain

CHeBA staff: Anne Poljak (conjoint), Nady Braidy, Tharusha Jayasena, Perminder Sachdev.

Other investigators: Professor Glenda Halliday (NeuRA, UNSW), Professor Catriona MacLean (Monash University), Associate Professor Mark Raftery (BMSF, UNSW), Dr Claire Shepherd (NeuRA, UNSW), Associate Professor George Smythe (SOMS, UNSW).

Aims:

- Determine if there are brain regional differences in the proteome profile comparing normal and AD brain sections.
- Determine if proteomic expression correlates with level of brain pathology (Braak stage).
- Identify age-related changes in the brain proteome profile.

Findings: One of the main enigmas of Alzheimer's disease (AD) is the question of why there are regional differences in the onset and severity of pathology in the various cortical regions. For instance, why does pathology first begin in the entorhinal cortex, hippocampus and temporal lobe regions, why is the pathology load much heavier here and why are regions such as the occipital lobe relatively spared? We are addressing this question by exploring mechanisms and cellular or biochemical pathways in the brain which may offer protection from AD pathology and mediate brain defense. Proteomics is an ideal approach to compare protein expression variation across the brain cortex. We have identified differences in the expression of a number of functional protein groups, including metabolism/mitochondrial as well as proteins which might be involved in cellular regeneration.

Funding: NHMRC, Rebecca L. Cooper Medical Research Foundation.

BRIDGET Consortium: Brain imaging, cognition, dementia and next generation genomics: A transdisciplinary approach to search for risk and protective factors of neuro-degenerative disease

CHeBA staff: Perminder Sachdev, Karen Mather, Wei Wen, Anbupalam Thalamuthu.

Other investigators: Dr Nicola Armstrong (Murdoch University) (CHeBA Hon. Research Fellow), members of BRIDGET Consortium.

Aims:

- Identify rare and common genetic variants influencing brain structure in older adults.
- Explore the determinants of brain ageing from a life-course perspective, including genomic, epigenomic and environmental factors.

- Examine whether identified genes predict decline in memory performance and an increased risk of Alzheimer's disease.

Findings: First BRIDGET consortium annual meeting held in Bordeaux, France in May 2016. Dr Mather presented a summary of the cohorts, samples and data available from the Sydney Memory and Ageing Study (MAS) and the Older Australian Twins Study (OATS). At this meeting and subsequent teleconferences, discussions were held regarding the first phenotypes to investigate and the samples available for genetic and epigenetic assays. In 2017, the first genetic and epigenetic assays and analyses will be undertaken.

Funding: NHMRC National Institute for Dementia Research (NNIDR) (administered by CHeBA), European Union Joint Programme for Neurodegenerative Disease (not administered by CHeBA).

Collaboration between family members and direct care staff in quality improvement of residential care services

CHeBA staff: Lynn Chenoweth, Henry Brodaty.

Other investigators: Tracey Clarke, Megan Mills and Jeanine Lew (Sir Moses Montefiore Homes), Janet Cook (DCRC, UNSW).

Aim: Develop and pilot test a protocol which promotes collaboration and positive relationships between family and direct care staff for the purpose of improving the quality of residential care services.

Findings: 48 nurses, direct care staff and allied health staff, 37 family carers of aged care residents, 10 Montefiore staff trainers and 6 Montefiore family liaison staff personnel have joined the study and completed baseline questionnaires on expectations and experiences of family/staff relationships and aged care service quality. A face to face and online train-the-trainer approach to staff and family carer education and support is being used, guided by a Study Management Committee and an Advisory Group of volunteer family and resident representatives, nurses, care staff and allied health staff and aged care advocates. The 7 session education program commenced in February 2017 and uses evidence-based multimedia education materials, including resources developed by La Trobe University for the Australian Institute for Primary Care and Ageing. Trained Family Liaison personnel and Staff Trainers are, respectively, educating and supporting family carers and direct care staff in adopting the family/staff relationship model. Sessions emphasise: reflection and self, relationship development, interpersonal and communication skills and conflict resolution. Executive and managerial support has been critical to the successful implementation of interventions designed to increase collaboration between staff and family in pursuing service quality for aged care residents. Post-test participant and knowledge translation data will be collected in May 2017, with follow-up data to be collected in October 2017. Evaluation of knowledge and skills application is occurring regularly over the study period.

Funding: Montefiore Home.

Defining the role of inflammation in depression during ageing

CHeBA staff: Perminder Sachdev, Julian Trollor (conjoint).

Other investigators: Professor Bernhard Baune (University of Adelaide).

Aims:

- Understand the prospective relationship between inflammation and depression during ageing, through the investigation of the bidirectional relationship between inflammatory biomarkers in the Sydney Memory and Ageing Study (MAS).
- Investigate the molecular underpinnings of inflammation during aging by using genetic, gene expression, and proteomic data.
- Develop an inflammation based prediction model of depression (consisting of genetic, gene expression and proteomic data in the context of inflammation) during aging in MAS (discovery sample) and to replicate in a second ageing sample, the Older Australian Twins Study (OATS).

Findings: By examining 16 brain regions and 5 cell types from the periphery, we identified 57 replicated differentially expressed genes in the brain and 21 in peripheral tissues of older people with depression. Functional overlap between brain and periphery strongly implicates shared pathways in a comorbid phenotype of depression and cardiovascular disease. The findings highlight dermal fibroblasts as a promising experimental model for depression biomarker research, provide partial support for all major theories of depression and suggest a novel candidate gene, PXMP2, which plays a critical role in lipid and reactive oxygen species metabolism (Ciobanu et al, Neurosci Biobehav Rev).

Funding: NHMRC (administered by University of Adelaide).

Deprescribing guidelines for people with dementia: Cholinesterase inhibitors and memantine

CHeBA staff: Lynn Chenoweth.

Other members: Professor Sarah Hilmer (University of Sydney), Professor Ken Rockwood (Dalhousie University), Professor Parker Magin (University of Sydney), Tara Quirke (consumer), Barbara Farrell, Mary Gorman, Nathan Herrmann, Dr Graeme Bethune, Wade Thompson, Professor Ingrid Sketris (Dalhousie University), Ms Christina McNamara (Dalhousie University), Dr Emily Reeve (NHMRC/ARC Dementia Research Fellow, University of Sydney).

Aims:

- Provide recommendations regarding in what situations it might be suitable to withdraw the dementia medications, cholinesterase inhibitors and memantine.
- Provide guidance on how to conduct withdrawal, and develop additional materials to provide information to people with dementia and their family members.

Findings: A lack of evidence-based deprescribing guidelines has been identified by health care professionals as a significant barrier to optimisation of medication use in older people. Acetylcholinesterase inhibitors have been identified as a medication class where an evidence-based deprescribing guideline would be of significant benefit to clinicians. A systematic review of the literature on the outcomes of withdrawal of acetylcholinesterase inhibitors and memantine coupled with a review on the potential harm, cost considerations and patient and carer attitudes towards these medications is in process, due for completion April 2017. Details on the guideline are available at: https://www.clinicalguidelines.gov.au/register/evidence-based-clinical-practice-guideline-deprescribing-cholinesterase-inhibitors-and. My role is to review and comment on published studies included in the review, including methodology, resource implications and other tools used to conduct systematic reviews, as well as to mentor NHMRC/ARC Dementia Research Fellow Emily Reeve in undertaking the review and report of findings.

Funding: NHMRC and ARC (administered by University of Sydney).

Dysregulation of lipids in the ageing brain and Alzheimer's disease: A novel biomarker approach

CHeBA staff: Anne Poljak (conjoint), Nady Braidy, Perminder Sachdev, Matthew Wong (PhD student).

Other investigators: Dr Russ Pickford (BMSF, UNSW).

Aims:

- Identify lipid biomarkers in plasma to assist in diagnosis of MCI and/or Alzheimer's disease (AD).
- Explore the possibility that plasma lipids are correlated with brain volumetric and cognitive changes.

Findings: We have carefully reviewed the literature, identified several lipid extraction protocols and compared these using a lipidomics discovery approach using LCMSMS. Most of these are effective in extraction of a broad range of lipids, and compare well with each other. However the method of Alshehry et al. provides somewhat better yields for specific lipid families, is technically the simplest to implement and is the most conservative of valuable plasma. We are currently applying this method to study how lipidomic profiles vary with age, sex, BMI and ApoE allele variation.

Funding: Australian Postgraduate Award PhD Scholarship.

EADB Consortium: A European DNA bank for deciphering the missing heritability of Alzheimer's disease

CHeBA staff: Perminder Sachdev, Karen Mather, Wei Wen, Anbupalam Thalamuthu, Henry Brodaty.

Other investigators: Dr Nicola Armstrong (Murdoch University) (CHeBA Hon. Research Fellow), members of EADB Consortium.

Aim: Identify common and rare novel genetic variants for Alzheimer's disease by collecting a very large data set of individuals who are cognitively normal, have mild cognitive impairment or Alzheimer's disease and have genetic data available.

Findings: Data collection from studies around the world is progressing. Analyses will begin in 2017.

Funding: NHMRC National Institute for Dementia Research (NNIDR) (administered by CHeBA), European Union Joint Programme for Neurodegenerative Disease (not administered by CHeBA).

Epigenetic and genetic factors and AD development

CHeBA staff: Karen Mather, Helen Wu (PhD student), Perminder Sachdev, Henry Brodaty, Anbupalam Thalamuthu.

Other key investigators: Dr Nicola Armstrong (Murdoch University) (CHeBA Hon. Research Fellow), Professor Bernhard Baune (University of Adelaide), Associate Professor John Kwok (NeuRA, UNSW), Professor Peter Schofield (NeuRA, UNSW).

Aim: Understand the relationships between DNA methylation, micro RNAS, genome and gene expression in early Alzheimer's disease (AD).

Findings: Micro RNA assays have been completed in a pilot study of Sydney Memory & Ageing Study (MAS) participants, comprised of cognitively normal controls, those with mild cognitive impairment (MCI) and Alzheimer's disease. A number of significant results were observed. These results will be validated using an alternate technique and replication in other independent cohorts. DNA methylation assays have also been undertaken in the same sample, but no significant differences in methylation were observed.

Funding: The Mason Foundation, The Roth Charitable Foundation, NHMRC, Thomas Foundation.

Evaluating the effectiveness and cost-effectiveness of DCM to enable person centred care training: A cluster randomised trial

CHeBA staff: Lynn Chenoweth.

Other investigators: Professor Claire Surr (Leeds Beckett University, UK), Professor Clive Ballard (King's College London, UK), Professor Murna Downs (University of Bradford, UK), Dr Anne Corbett (King's College London,UK), Sue Fortescue (Alzheimer's Society Research Network), Kirsty Nash (Oxford Health NHS Foundation Trust), Professor Louise Robinson (University of Newcastle, UK), Professor Graham Stokes (Bupa Care Services, Leeds, UK), Professor Amanda Farrin (University of Leeds, UK), Alison Ferguson (University of Leeds, UK), Dr Jane Fossey (University of Oxford, UK), Lucy Garrod (Oxford Health NHS Foundation Trust), Ms Liz Graham (University of Leeds, UK), Dr Alys Griffiths (University of Bradford, UK), Madeline Harms (University of Leeds, UK), Ivana Holloway (University of Leeds, UK), Steph Jones (University of Bradford, UK), Amanda Lilley-Kelly (University of Leeds, UK), Dr Najma Siddiqi (University of Leeds, UK), Dr Daphne Wallace (University of Bradford, UK).

Aims:

- Evaluate the clinical and cost-effectiveness of Dementia Care Mapping (DCM) in supporting the implementation of person-centred care training (PCCT).
- Evaluate its effectiveness as a process for improving care quality and quality outcomes for people with dementia, compared with usual dementia care.

Findings: 62 homes in three regions of the UK were enrolled in the trial (31 interventions, 31 controls) from 250 aged care homes screened for eligibility. Once baseline data were obtained from participating staff and aged care residents with dementia, all 31 intervention home staff were educated and trained in two cycles of the PCCT intervention by skilled dementia nurses. All 31 of the control home staff have received education and training in 2 cycles DCM by trained DCM staff. Since these interventions occur at the unit level, in at least half of all homes the data collectors have become un-blinded as to which intervention is occurring in subsequent periods of data collection. Overall, 47% of residents were lost to follow-up by 16 months after baseline data collection, mainly because of death. A decision was made by the study team to recruit a second wave of residents and to educate and train a second wave of newly employed staff, in order to obtain sufficient participant numbers to determine treatment effect. From a statistical point of view, recruiting additional residents and staff has been useful, but the team will need to consider the implications of variation in cluster size on analysis. Study results are pending. The study protocol paper was published, with protocol update planned and three conference papers have been delivered.

Funding: National Institute for Health Research, UK (administered by Leeds Beckett University; contract between CHeBA, UNSW and Leeds Beckett University, UK. for L. Chenoweth's contribution).

Genetic and epigenetic markers of late-life depression

CHeBA staff: Ruby Tsang (PhD student), Perminder Sachdev, Karen Mather, Anbupalam Thalamuthu.

Other key investigators: Dr Simone Reppermund (UNSW Medicine) (CHeBA Hon. Research Fellow), Professor David Ames (National Ageing Research Institute, Royal Melbourne Hospital), Dr Nicola Armstrong (Murdoch University) (CHeBA Hon. Research Fellow), Associate Professor John Kwok (NeuRA, UNSW), Professor Peter Schofield (NeuRA, UNSW), Professor Naomi Wray (Queensland Brain Institute, University of Queensland), Associate Professor Margaret J. Wright (QIMR Berghofer Institute, Brisbane, Australia).

Aims:

- Estimate heritability for late-life depression and depressive symptoms.
- Calculate bivariate genetic correlations between measures for depression and related phenotypes, such as anxiety.

Findings: Using the OATS cohort, moderate heritability was observed for late-life depression. Significant genetic correlations with late-life depression, anxiety and hypertension were observed suggesting common genetic factors may contribute to these measures. The results are being written up for publication.

Funding: NHMRC, Thomas Foundation, Viertel PhD Scholarship (Alzheimer's Australia Dementia Research Foundation).

Genetic influence on human hippocampal atrophy

CHeBA staff: Wei Wen, Anbupalam Thalamuthu, Perminder Sachdev, Karen Mather.

Other investigators: Professor David Ames (National Ageing Research Institute; Royal Melbourne Hospital), Associate Professor Pierre Lafaye de Micheaux (Université de Montréal, Canada), Dr Margaret J. Wright (QIMR Berghofer Institute, Brisbane, Australia), Dr Wanlin Zhu (Beijing Normal University) (CHeBA Hon. Research Fellow).

Aim: Examine whether and how genetics influence ageing-related hippocampal atrophy.

Findings: The pattern of genetic correlations for the surface of the hippocampus partially corresponded to neuroanatomical division of hippocampal subfields. The patterns of heritability and genetic correlations of the right and left hippocampi were similar, but not bilaterally symmetrical on the vertex level.

Funding: NHMRC.

Genetic influence on white matter fibre tracts between brain regions – is genetic correlation and fibre tract connectivity associated?

CHeBA staff: Wei Wen, Anbupalam Thalamuthu, Alistair Perry (PhD student), Perminder Sachdev.

Other investigators: Professor David Ames (National Ageing Research Institute; Royal Melbourne Hospital), Associate Professor Pierre Lafaye de Micheaux (Université de Montréal, Canada), Dr Margaret J. Wright (QIMR Berghofer Institute, Brisbane, Australia), Dr Wanlin Zhu (Beijing Normal University).

Aims:

- Test the hypotheses that:
  - White matter fibre connection between two brain regions that are genetically similar will be stronger than those which are genetically less similar.
  - This pattern will be symmetric in both hemispheres.
- Investigate whether the connections between network hub regions are genetically stronger than those of non-hub regions, including feeders and non-feeders.

Findings: We have performed computations on diffusion scans and arrived at connectivity matrices. In 2017, we will compute the properties of these connectivity matrices.

Funding: NHMRC, Alzheimer's Australia Dementia Research Foundation Postdoctoral Fellowship.

Genetics and epigenetics of longevity

CHeBA staff: Perminder Sachdev, Karen Mather, Anbupalam Thalamuthu, Mary Revelas (PhD student), Jessica Lazarus (PhD student), Julian Trollor (conjoint).

Other key investigators: Dr Nicola Armstrong (Murdoch University) (CHeBA Hon. Research Fellow), Professor John Attia (University of Newcastle), Associate Professor John Kwok (NeuRA, UNSW), Dr Chris Oldmeadow (University of Newcastle), Professor Peter Schofield (NeuRA, UNSW); Professor David Ames (National Ageing Research Institute; Royal Melbourne Hospital), Associate Professor Margaret J. Wright (QIMR Berghofer Institute, Brisbane, Australia).

Aim: Identify genetic and epigenetic variation associated with longevity and longevity-related phenotypes, such as markers of healthy longevity (e.g. intact cognitive functioning).

Findings: Meta-analysis of longevity associated genes has been completed and a manuscript is being written. Two popular epigenetics clocks for a subset of SCS and OATS participants have been computed and compared. The manuscript is under revision.

Funding: Sachdev Foundation, NHMRC, Thomas Foundation.

Genetics of growth differentiation factor 15 (GDF-15/MIC-1)

CHeBA staff: Jiyang Jiang, Anbupalam Thalamuthu, Karen Mather, Perminder Sachdev, Wei Wen, Julian Trollor (conjoint).

Other key investigators: Dr Nicola Armstrong (Murdoch University) (CHeBA Hon. Research Fellow), Associate Professor John Kwok (NeuRA, UNSW), Professor Peter Schofield (NeuRA, UNSW), Professor D Brown (St Vincents Hospital, UNSW), Professor SN Breit, (St Vincents Hospital, UNSW), Dr Jennifer E. Ho (Massachusetts General Hospital, Harvard Medical School, USA), Professor Andrew Morris (University of Liverpool, UK), Dr Weronica Ek (Uppsala University, Sweden).

Aim: Identify genetic variants associated with GDF-15 in mid to late life using community-based cohorts.

Findings: Meta-analysis of GWAS results on GDF-15 levels based on four cohorts including MAS has been completed. Genes associated with GDF-15 have been replicated although no novel genes were identified. The manuscript is being written.

Funding: NHMRC, Thomas Foundation.

Genetics of white matter hyperintensities

CHeBA staff: Karen Mather, Wei Wen, Anbupalam Thalamuthu, Perminder Sachdev, Amelia Assareh.

Other key investigators: Dr Paul Nqyuist (NIH, USA), Dr Nicola Armstrong (Murdoch University) (CHeBA Hon. Research Fellow), Professor David Ames (National Ageing Research Institute, Royal Melbourne Hospital), Associate Professor John Kwok (NeuRA, UNSW), Professor Peter Schofield (NeuRA, UNSW), Associate Professor Margaret J. Wright (QIMR Berghofer Institute, Brisbane, Australia), and other external collaborators.

Aim: Identify genetic variants associated with deep and periventricular white matter hyperintensities (WMHs).

Findings: Genome-wide association studies (GWAS) of WMHs in multiple participating cohorts have been completed. Meta-analysis of GWAS results is being undertaken.

Funding: NHMRC, Thomas Foundation.

Genome-wide Association Studies (GWAS) of brain measures in collaboration with the ENIGMA consortium (Enhancing Neuroimaging Genetics through Meta-Analyses)

CHeBA staff: Wei Wen, Karen Mather, Anbupalam Thalamuthu, Perminder Sachdev.

Other key investigators: Dr Nicola Armstrong (Murdoch University) (CHeBA Hon. Research Fellow), Professor David Ames (National Ageing Research Institute, Royal Melbourne Hospital), Associate Professor John Kwok (NeuRA, UNSW), Professor Peter Schofield (NeuRA, UNSW), Associate Professor Margaret J. Wright (QIMR Berghofer Institute, Brisbane, Australia).

Aim: Identify single nucleotide polymorphisms (SNPs) for various brain measures, such as subcortical volume.

Findings: Novel genes for hippocampal volume have been identified and a manuscript has been accepted (Hibar et al., *Nat Commun*). A GWAS study on subcortical volumes is underway.

Funding: NHMRC, Thomas Foundation.

Genome-wide Association Studies (GWAS) of various measures, including cognitive performance, in collaboration with the CHARGE consortium (Cohorts for Heart and Aging Research in Genomic Epidemiology)

CHeBA staff: Perminder Sachdev, Karen Mather, Anbupalam Thalamuthu, Wei Wen, Nicole Kochan, Teresa Lee, Amelia Assareh.

Other key investigators: Dr Nicola Armstrong (Murdoch University) (CHeBA Hon. Research Fellow), Professor David Ames (National Ageing Research Institute, Royal Melbourne Hospital), Associate Professor John Kwok (NeuRA, UNSW), Professor Peter Schofield (NeuRA, UNSW), Associate Professor Margaret J. Wright (QIMR Berghofer Institute, Brisbane, Australia).

Aim: Identify single nucleotide polymorphisms (SNPs) associated with cognitive performance and other measures, such as brain imaging traits.

Findings:

- A novel genetic variant for information processing speed in the cell adhesion molecule 2 (CADM2) gene was identified (Ibrahim-Verbaas et al., *Mol Psychiatry*).
- In a combined study with the ENIGMA consortium of over 30,000 adults, new genetic loci for intracranial volume were identified (Adams et al., *Nat Neurosci*).

Funding: NHMRC, Thomas Foundation.

ICC-Dementia (International Centenarian Consortium - Dementia): An international consortium to determine the prevalence, incidence and trajectories of decline for dementia in centenarians

CHeBA staff: Perminder Sachdev, Henry Brodaty, Catriona (Keenie) Daly, John Crawford, Nicole Kochan.

Other investigators: Study leaders and other researchers from among 18 ICC-Dementia member cohorts.

Aims:

- Describe the cognitive, functional and psychological profiles of centenarians across diverse ethnoracial and sociocultural groups.
- Determine risk factors for dementia and cognitive decline in centenarians.
- Assess protective factors for exceptional brain ageing in centenarians, through investigating the reasons some individuals achieve extreme old age without showing cognitive decline.
- Evaluate international prevalence rates of cognitive impairment, functional dependence and dementia status in the oldest old.
- Develop, apply and test a uniform algorithm for assessing dementia status across study sites.

Findings:

- Protocol paper outlining the aims and structure of the consortium, selection criteria for participating studies, and a summary of planned harmonisation and statistical procedures was published (Brodaty et al., *BMC Neurol*).
- Preliminary findings on the cognitive and functional profiles of centenarians and near centenarians around the world were presented at the ICC conference in Portugal in June, 2016. These findings suggested that overall, out of almost 4000 centenarians and near centenarians, 51.4% were cognitively impaired, 62.9% were functionally dependent and 46.7% met criteria for dementia. These findings differed across age groups (with more impairment observed in older age groups) and study location.
- The above findings are currently being extended to test the utility of different algorithms for assessing dementia status across study sites. A number of algorithms have been created based on existing research and the current dataset.
- Data on risk and protective factors are currently being collected from studies.

Funding: Thomas Foundation, Vincent Fairfax Family Foundation

Identifying expression quantitative trait loci (eQTLS) in older adults

CHeBA staff: Anbupalam Thalamuthu, Karen Mather, Perminder Sachdev.

Other key investigators: Professor Bernhard Baune (University of Adelaide), Liliana Ciobanu (University of Adelaide), Dr Nicola Armstrong (Murdoch University) (CHeBA Hon. Research Fellow), Associate Professor

John Kwok (NeuRA, UNSW), Professor Peter Schofield (NeuRA, UNSW).

Aim: Identify genetic variants associated with gene expression

Findings: The expression quantitative trait locus (eQTL) analysis in MAS is completed. The replication analysis in OATS is underway.

Funding: NHMRC, Thomas Foundation.

Improved accessibility and long-term storage of biospecimens from the Centre for Healthy Brain Ageing's (CHeBA) longitudinal studies

CHeBA staff: Julia Muenchhoff, Niki He, Kristan Kang, Anne Poljak (conjoint), Henry Brodaty, Perminder Sachdev.

Aims:

- Inventory and aliquot samples for ready distribution to researchers.
- Improve the safety of sample storage by transferring samples into vapour phase liquid nitrogen tanks for long-term storage.

Findings: Most of the MAS longitudinal cohort has been aliquoted, with OATS and centenarians scheduled for 2017.

Funding: UNSW MREII 2015.

IMPROVING CLINICAL DIAGNOSIS OF MILD NEUROCOGNITIVE DISORDERS USING NEUROPSYCHOLOGICAL ASSESSMENT

CHeBA staff: Nicole Kochan, Perminder Sachdev, Henry Brodaty, Melissa Slavin (conjoint), John Crawford.

Other investigators: Professor Kaarin Anstey (Australian National University), Professor David Bunce (University of Leeds, UK), Professor John R Crawford (University of Aberdeen, Scotland), Dr Amanda Miller-Amberber (University of Sydney).

Aims:

- Establish Australian normative data for neuropsychological measures which are used in the assessment of cognition in older adults and which form part of diagnostic evaluations of dementia and other age-related cognitive disorders.
- Facilitate interpretation of neuropsychological test performance in persons from CALD backgrounds by investigating the influence of cultural, linguistic and educational factors.
- Evaluate the clinical utility of computerised neuropsychological testing for the early detection of neurocognitive disorders in older adults and to investigate the additional value over traditional neuropsychological measures for predicting future cases of mild cognitive impairment (MCI) and dementia.
- Evaluate the potential of a computerised neuropsychological test battery as a more culture-fair measure of cognition compared to traditional neuropsychological measures in older adults from CALD backgrounds.

Findings:

- We found that proficient English speakers from culturally and linguistically diverse (CALD) backgrounds perform more poorly than native English speakers on neuropsychological tests such as language tasks than expected, but also tasks of memory and processing speed.
- We found CALD individuals had poorer health and more depressive symptoms, but this did not significantly explain the poorer test scores.
- Acculturation and linguistic factors did partially explain worse scores on verbal tests but not on memory and processing speed tasks.
- Performance differences were also apparent on computerised neuropsychological measures which are thought to be more culture-fair.
- There may be other cultural characteristics such as test-taking approach (e.g. a speed/accuracy trade-off) that may underlie performance differences. Therefore caution should be applied when interpreting test performance in CALD individuals since poor cognitive performance may not indicate underlying neuropathology.
- In English-speakers, performance on a brief battery of computerised tests was comparable to a lengthier traditional neuropsychological test battery.

Funding: DCRC – Assessment and Better Care, UNSW, NHMRC Early Career Fellowship

Inflammatory markers and brain structure

CHeBA staff: Jiyang Jiang, Wei Wen, Julian Trollor (conjoint), Perminder Sachdev.

Other investigators: Professor Bernhard Baune (University of Adelaide), Associate Professor David Brown (St Vincent's Centre for Applied Medical Research), Dr Haobo Zhang (CHeBA Hon. Research Fellow).

Aims:

- Explore the relationships of brain structural indices with the circulating levels of a spectrum of inflammatory markers available in the Sydney Memory and Ageing Study (MAS), including interleukin (IL)-1β, IL-6, IL-8, IL-10, IL12p70, serum vascular cell adhesion molecule-1 (sVCAM-1), plasminogen activator inhibitor-1 (PAI-1), serum amyloid A (SAA), tumour necrosis factor α (TNFα), C-reactive protein (CRP), and macrophage inhibitory cytokine-1 (MIC-1/GDF15). The aim is to find a robust circulating biomarker of brain structural measures in non-demented older individuals.
- Examine the relationship of MIC-1/GDF15 serum levels with human brain structural measures using multimodal MRI data, in a community-dwelling sample aged 70-90 years over two years.
- Conduct a genome-wide meta-analysis to identify genetic variants of MIC-1/GDF15 serum levels in population-based cohorts, and to test whether these variants influence brain structures and cognitive performance in MAS.
- Examine the role of inflammation in cerebral small vessel disease.

Findings:

- Inflammation contributes to brain structural degeneration during ageing. Two proinflammatory cytokines (tumor necrosis factor-α [TNF-α] and interleukin-1β) and two vascular inflammatory markers (vascular cellular adhesion molecule-1 and plasminogen activator inhibitor-1) were negatively correlated with regional GM volumes. TNF-α and interleukin-1β were both significantly correlated with GM volumes in the left occipitotemporal area, left superior occipital gyrus, and left inferior parietal lobule. TNF-α was also significantly correlated with the bilateral medial prefrontal cortices and approached significance for the correlations with the bilateral hippocampi. Significant GM correlations with vascular cellular adhesion molecule-1 were located in the bilateral anterior cingulate cortices, and with plasminogen activator inhibitor-1 in the cerebellum and right hippocampus. The neuroanatomical correlation patterns of these two proinflammatory cytokines and two vascular inflammatory markers might be reflective of the effects of neurodegenerative and vascular pathological processes in the ageing brain.
- MIC-1/GDF15 is a novel and robust biomarker for age-related brain GM and WM atrophy.
- A locus in chromosome 19 is associated with blood MIC-1/GDF15 levels. No polygenic effects or secondary signals were observed in the GWAS of MIC-1/GDF15 levels.

Funding: NHMRC, John Holden Family Foundation.

Isoform-dependent ApoE processing by human induced pluripotent stem cells: A novel pathway linking ApoE genotype and Alzheimer's disease risk

CHeBA staff: Kuldip Sidhu (Visiting Honorary Associate Professor).

Other investigators: Professor Brett Garner (University of Wollongong), Dr Henry Li (University of Wollongong), Dr Lezanne Ooi (University of Wollongong).

Aims:

- Test the hypotheses that ApoE25 may play a neuroprotective role in the brain and that this contributes to the association of ApoE genotype with AD risk.
- Characterise ApoE25 generated by iPSCs and assess its potential neuroprotective properties.

Findings: We used a human induced pluripotent stem cell (iPSC) model of familial and sporadic AD, in addition to healthy controls, to assess the neuroprotective activity of apigenin, a plant polyphenol. The iPSC-derived AD neurons demonstrated a hyper-excitable calcium signalling phenotype, elevated levels of nitrite, increased cytotoxicity and apoptosis, reduced neurite length and increased susceptibility to inflammatory stress challenge from activated murine microglia, in comparison to control neurons. We identified that apigenin has potent anti-inflammatory properties with the ability to protect neuritis and cell viability by promoting a global down-regulation of cytokine

and nitric oxide (NO) release in inflammatory cells. In addition, we showed that apigenin is able to protect iPSC-derived AD neurons via multiple means by reducing the frequency of spontaneous Ca2+ signals and significantly reducing caspase-3/7 mediated apoptosis. These data demonstrate the broad neuroprotective action of apigenin against AD pathogenesis in a human disease model.

Funding: NHMRC grant (administered by University of Wollongong).

Longevity, ageing and transcriptomics

CHeBA staff: Karen Mather, Anbupalam Thalamuthu, Perminder Sachdev, Adith Mohan (PhD student).

Other key investigators: Dr Nicola Armstrong (Murdoch University) (CHeBA Hon. Research Fellow), Dr Michael Janitz (School of Biotechnology and Biomolecular Sciences, UNSW), Associate Professor John Kwok (NeuRA, UNSW), Professor Peter Schofield (NeuRA, UNSW).

Aims:

- Identify RNAs, including long non-coding RNAs associated with longevity.
- Identify transcriptomic changes in the ageing brain.

Findings: In preliminary findings, a number of differentially expressed genes were identified in exceptionally long-lived individuals from the Sydney Centenarian Study compared to younger controls from Sydney MAS, including genes from pathways previously linked to longevity. These findings are being written up for publication.

Funding: NHMRC, Thomas Foundation.

Maintain Your Brain

CHeBA staff: Henry Brodaty, Perminder Sachdev, Gavin Andrews.

Other investigators: Professor Kaarin Anstey (Australian National University), Professor Nicola Lautenschlager (Melbourne University), Professor Louisa Jorm (UNSW), Professor John McNeill (Monash University), Professor Anthony Maeder (Western Sydney University), Professor Maria Fiatarone Singh (University of Sydney), Professor Michael Valenzuela (University of Sydney).

Aims:

- Determine the efficacy of a multi-modal targeted intervention delivered 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.
- Examine the cost-effectiveness of the program with a view to making this a national and potentially a globally suitable program.

Findings:

- The IT platform was built and intervention modules designed.
- Validation studies of modules and of outcome measures plus full pilot will commence in 2017.
- Recruitment for the full trial is planned for mid-2017.

Funding: NHMRC Dementia Research Team Grant.

Meaningful relationships for people with dementia in long term care

CHeBA staff: Janet Mitchell (PhD student), Henry Brodaty, Lynn Chenoweth.

Other investigators: Professor Jeffrey Braithwaite (Australian Institute of Health Innovation and Centre for Healthcare Resilience and Implementation Science, Macquarie University), Dr Janet Long (Australian Institute of Health Innovation, Macquarie University).

Aim: Identify the occurrence and factors associated with meaningful relationships for people with dementia in long-term care.

Findings:

- 5 care homes have been recruited, with data collection completed in 2.
- Systematic review of social-professional networks in long-term care settings with people with dementia published (Mitchell et al., J Am Med Dir Assoc).
- Evidence to date indicates there will be benefits for organisational culture, systems and processes, physical layout and design as well as relationship structures that occur within residential aged care homes.

Funding: Thomas Foundation.

Metabolomic screening for discovery of low molecular weight blood-based biomarkers

CHeBA staff: Julia Muenchhoff, Anne Poljak (conjoint), Perminder Sachdev.

Other investigators: Dr Sonia Bustamante (BMSF, Mark Wainwright Analytical Centre, UNSW), Dr Donald Thomas (NMR Facility, Mark Wainwright Analytical Centre, UNSW).

Aims:

- Develop gas chromatography (GC-MS) and nuclear magnetic resonance (NMR) methods for detection and quantitation of metabolites in blood samples.
- Identify blood metabolites that differ in health individuals and patients with MCI or AD.

Findings: Our preliminary work on plasma from MCI, AD and cognitively normal (CN) subjects showed significant differences between AD and CN subjects in the NMR spectra (15 AD, 10 CN), and highlights the discovery potential of this approach. Although the sample number is small, these data clearly show that NMR metabolomics is able to distinguish between AD and CN plasma. Once discriminant analysis is used to identify the features in the spectrum that distinguish sample groups, the compounds corresponding to those spectral regions can also be identified either directly via database searching or, if required, in follow up experiments. By database searching, we are able to identify a minimum of 48 compounds in plasma.

Funding: Thomas Foundation.

MicroRNAs as biomarkers for Alzheimer's disease (AD): Comparison between Australian & Chinese populations

CHeBA staff: Helen Wu (PhD student), Karen Mather, Henry Brodaty, Perminder Sachdev.

Other investigators: Professor Shifu Xiao (Shanghai Mental Health Centre, School of Medicine), Dr Tao Wang (Shanghai Mental Health Centre, School of Medicine).

Aim: Examine the differences in microRNA expression among Chinese and Australian patients with mild cognitive impairment (MCI) and Alzheimer's disease (AD) compared to cognitively normal controls.

Findings:

- MicroRNA profiling of peripheral blood have been performed for Australian and Chinese patients with MCI, AD, and normal cognition.
- A number of miRNAs have been found to have differential expression among both Australian and Chinese patients with AD compared to Australian and Chinese patients with normal cognition. These candidate miRNAs will be further validated and then replicated in an independent cohort.

Funding: Shanghai Jiao Tong University SJTU-UNSW Collaborative Research Fund.

Nursing competencies in care of the older person

CHeBA staff: Lynn Chenoweth.

Other investigators: Kristine Rice and Tracey Osmond (Anglican Retirement Villages), Mary McConochie (Anglicare), Carolyn Moir and Donna Lennon (BaptistCare), E. Roy and D. Donaghy (Uniting Care), Elaine Griffin and Fiona Kendall (Scalabrini Villages), Jolan Stokes and C. Carter (Hammond Care), Dr Victoria Traynor (University of Wollongong).

Aim: Develop an evidence-based set of nurse competencies in care of the older person.

Findings: A comprehensive literature review was conducted and face-to-face consultation activities occurred during a workshop with senior registered nurses (n=50) to develop the first drafts of the Geriatric Nurse Competencies. Next, an expert panel of managers (n=7) reviewed and amended the draft versions of the GNCs. An on-line Delphi panel of 419 Australian nurses from six Australian states and one territory, and 19 participants from 9 other countries completed round 1 consultancy. They comprised 192 registered nurses involved with the care of older people and their family carers (44%), 145 aged care managers (33%), 83 aged care academics/ researchers (19%) and 18 policy makers (4%). Five rounds were conducted, with141 participants remaining in round 5. E-Delphi participants worked in residential aged care (n=250, 57%), 57 (13%) in community settings, 53 (12%) in multi-care settings, 47 (11%) in educational or research institutes and 22 (5%) in acute care. The online Delphi activity involved participants ranking the content of draft versions of the GNCs, achieving a minimum level of agreement (65%) for each core competency and domain of practice. 11 core competencies and 40 domains of

practice were agreed by consensus. The next stage of the study will test a pilot implementation of the GNCs in practice with the five industry partners who are undertaking this study. Three conference papers have been prepared and a manuscript describing the e-Delphi process and findings is in process.

Funding: Montefiore Home (administered by CHeBA); Anglican Retirement Villages, Uniting Care, BaptistCare, Scalabrini Villages, Hammond Care, University of Wollongong (none administered by CHeBA).

Olfactory ability and language test performance in Indonesian and Australian cohorts

CHeBA staff: Darren Lipnicki.

Other investigators: Dr Yuda Turana (Atma Jaya Catholic University, Indonesia).

Aim: Investigate how olfactory ability and other factors affect language function and Mini-Mental State Examination scores in both an Indonesian and an Australian cohort.

Findings: Older age, lower education and olfactory deficits were significantly associated with lower language test scores in both the Indonesian and Australian cohorts. Lower scores were also found for Indonesian participants who were female, and for Australian participants with either depression or diabetes.

Funding: Direct donations to The Dementia Momentum Fund.

OXIDATIVE STRESS IN AD

CHeBA staff: Anne Poljak (conjoint), Nady Braidy, Nicole Kochan, Wei Wen, John Crawford, Julian Trollor (conjoint), Henry Brodaty, Perminder Sachdev.

Other investigators: Professor John Attia (University of Newcastle), Professor Mark Duncan (University of Colorado, USA), Professor Ralph Martins (Edith Cowan University), Dr Mark McEvoy (University of Newcastle), Associate Professor Peter W. Schofield (University of Newcastle).

Aims:

- Determine if protein oxidation and/or glycation changes in MCI and AD plasma, and to check for reproducibility across independent cohorts of similar design.
- Identify which of the markers change with age and/or are dysregulated in MCI and AD.
- Correlate protein oxidation levels with cognitive domain scores and brain volumetrics.

Findings: We have identified significantly elevated levels of protein oxidation markers, *o*- and *m*-tyrosine in AD relative to control plasma. This work will be extended to early and preclinical stages of AD (cross-sectionally), and our longitudinal MAS study, where we can track whether oxidation levels change with disease progression.

Funding: NHMRC, ARC, Rebecca L. Cooper Medical Research Foundation, Alzheimer's Australia Rosemary Foundation, Sachdev Foundation, UNSW Faculty of Medicine FRG and Early Career Researcher Grants.

Personality and Total Health (PATH) Through Life project

CHeBA staff: : Perminder Sachdev, Wei Wen, Karen Mather, Anne Poljak (conjoint), Julia Muenchhoff.

Other key investigators: Professor Kaarin Anstey (Australian National University), Associate Professor Peter Butterworth (Australian National University), Dr Nicholas Cherbuin (Australian National University), Professor Helen Christensen (UNSW) Professor Simon Easteal (Australian National University), Professor Andrew MacKinnon (University of Melbourne), Dr Moyra Mortby (Australian National University).

Aims: The original aims were to investigate the causes of three classes of common mental health problems: (1) anxiety and depression (2) alcohol and other substance abuse (3) cognitive functioning and dementia. The project investigates a wide range of risk and protective factors from biological and psychosocial domains, as well as the impacts of cognitive impairment and common mental disorders. Data on health service use are also collected.

Findings:

1. We published longitudinal estimates of cortical thinning observed over 12 years in a large group (n = 396) of healthy individuals, aged 60-66 years at baseline scan, who were scanned with magnetic resonance imaging (1.5T) on 4 occasions. Longitudinal age-related thinning was observed across most of the cortices, with a mean change of -0.3% per year. We measured significant thinning in heteromodal association cortex, with less thinning in regions expected to atrophy later in life (e.g. primary

sensory cortex). Men showed more extensive thinning than women (Shaw et al., *Neurobiol Aging*).

2. We also published longitudinal estimates of age-related cortical thinning observed over 8 years, in a large (n = 404) group of healthy individuals aged 44-49 years at baseline, who were scanned with MRI (1.5T) on up to three occasions. Age-related cortical thinning was assessed across the whole cortex. We measured a mean annual decrease in cortical thickness of 0.26% on the left and 0.17% on the right hemisphere, and largely affecting frontal and cingulate cortices. Medial and lateral temporal regions were generally spared (Shaw et al., *Brain Topogr*).

3. We investigated the relationship between plasma glucose levels and striatal and hippocampal morphology using vertex-based shape analysis in 287 cognitively normal individuals. Higher plasma glucose was associated with shape differences indicating inward deformation, particularly at the caudate and putamen, among participants with normal fasting glucose (NFG) after controlling for age, sex, body mass index (BMI), hypertension, smoking and depressive symptoms. Those with type 2 diabetes showed shape differences indicating inward deformation at the right hippocampus and bilateral striatum, but outward deformation at the left hippocampus, compared with participants with NFG (Zhang et al., *BMJ Open Diab Res Care*).

4. We investigated in a large population-based sample of 280 adults (150 males, 130 females) in their late sixties and early seventies whether ADHD symptoms correlated with callosal thickness. In addition, we tested for significant sex interactions, which were followed by correlation analyses stratified by sex. Within males, there were significant negative correlations with respect to inattention and hyperactivity in various callosal regions, including the anterior third, anterior and posterior midbody, isthmus, and splenium. A thinner corpus callosum may be associated with fewer fibres or less myelination of fibres. Thus, the observed negative correlations suggest impaired inter-hemispheric communication channels necessary to sustain motor control and attention, which may contribute to symptoms of hyperactivity, impulsivity and/or inattention. Interestingly, within females, callosal thickness was positively related to hyperactivity in a small area within the rostral body, suggesting a sexually dimorphic neurobiology of ADHD symptoms. Altogether, the present results may reflect a lasting relationship between callosal morphology and ADHD symptoms throughout life (Luders et al., *Psychiatry Res*).

Funding: NHMRC (administered by ANU)..

Plasma proteomics biomarkers

CHeBA staff: Julia Muenchhoff, Anne Poljak (conjoint), Tharusha Jayasena (PhD student), Nicole Kochan, Julian Trollor (conjoint), Henry Brodaty, Perminder Sachdev.

Other investigators: Dr Fei Song (CHeBA Hon. Research Fellow), Professor John Attia (University of Newcastle), Professor Mark Duncan (University of Colorado, USA), Professor Ralph Martins (Edith Cowan University), Dr Mark McEvoy (University of Newcastle), Associate Professor Mark Raftery (BMSF, UNSW), Associate Professor Peter W. Schofield (University of Newcastle), Associate Professor George A. Smythe (SOMS, UNSW).

Aims:

- Determine if proteomic changes observed in MCI and AD plasma, relative to normal controls, would be reproducible across independent cohorts of similar design.
- Identify specific plasma proteins and protein families that are dysregulated in MCI and AD and validate these using ELISA assays and/or western blotting.
- Correlate the effects of plasma proteome changes with cognitive domain scores and brain volumetrics.

Findings: Our initial proteomics work using the MAS cohort has been replicated across two independent cohorts: the Hunter Community Study (HCS) and the Dominantly Inherited Alzheimer's disease Network (DIAN). While considerable variation can be observed for specific proteins across cohorts, the most consistent observations include altered expression of proteins involved in inflammation, lipid metabolism and vascular health. Apolipoprotein family members are generally downregulated, whereas upregulation of inflammation-associated and acute phase proteins, such as complement, is observed. Proteins representative of biological processes relevant to AD pathology such as the complement system, the coagulation cascade, lipid metabolism, and metal and vitamin D and E transport were found to differ in abundance in MCI in the MAS and HCS cohorts. In the DIAN cohort, fewer changes were observed at the asymptomatic than the symptomatic stage with seven and 16 proteins altered significantly in aMC and sMC, respectively. This included complement components C3, C5, C6, apolipoproteins A-I, A-IV, C-I and M, histidine-rich glycoprotein, and heparin cofactor II. Due to increasing evidence supporting the usefulness

of ADAD as a model for LOAD, these proteins will be further investigated in the full DIAN cohort.

Funding: NHMRC, ARC, Rebecca L. Cooper Medical Research Foundation, Alzheimer's Australia Rosemary Foundation, Sachdev Foundation, UNSW Faculty of Medicine FRG and Early Career Researcher Grants.

Profile of cognitive impairment at 3 to 6 months post-stroke or TIA in diverse geographical and ethno-cultural settings as represented by the STROKOG member cohorts (formerly called: Factors that determine the rate of cognitive decline in stroke patients and the interventions that prevent such decline in diverse geographical and ethno-cultural settings (using data from STROKOG))

CHeBA staff: Perminder Sachdev, Jessica Lo, Darren Lipnicki, John Crawford, Nicole Kochan.

Other investigators: STROKOG collaborators

Aims:

- Harmonise shared data from STROKOG studies.
- Perform joint analyses using combined, harmonised data to estimate prevalence of post-stroke cognitive impairment with greater statistical power.
- Compare prevalence estimates and profile of post-stroke cognitive impairment across geographical regions and ethnic groups.

Findings:

- We are combining and harmonising individual participant data from 14 studies (>3600 participants) to examine the profile of post-stroke/TIA cognitive impairment across geographical regions and ethnic groups. We have harmonised neuropsychological test data by deriving from them standardised cognitive domain scores. Through implementing a uniform method, we derived impairment rates and are able to compare them across different studies, as well as regions and ethnic groups. Preliminary analysis shows that 46% of participants in the combined sample of post-stroke/TIA participants had impairment in 2 or more cognitive domains and 68% had impairment in 1 or more domains.
- Additionally we are looking at the relationship between cognition and potential risk factors. Preliminary analysis shows that those diagnosed with diabetes or had a prior stroke have poorer cognition.
- After an extensive period of data request, cleaning, harmonising and analysis, we began drafting a paper for planned submission in 2017.

Funding: Vincent Fairfax Family Foundation.

Proteomics of natural and non-natural animal models for AD

CHeBA staff: Anne Poljak (conjoint), Nady Braidy, Tharusha Jayasena, Perminder Sachdev.

Other investigators: Professor Nibaldo Inestrosa (Pontificia Universidad Católica de Chile) (conjoint).

Aims:

- Determine if there are brain regional differences in the proteome profile comparing brain sections from APPSwe, 3xTG mice and *O. degus*.
- Determine if proteomic expression correlates with level of brain pathology (Braak stage).
- Identify age-related changes in the brain proteome profile.

Findings: We demonstrated a significant age-dependent increase in the levels of D-serine, L-serine and glycine in the hippocampus of *O. degus*, parallel to an increase in the expression of serine racemase and TUNEL expression. By contrast, we observed a significant age-dependent decline in the levels of L-alanine, and L-threonine. The expression of phosphorylated c-Jun N-terminal kinase increased with age, although no increase in total c-Jun N-terminal kinase was detected. Discovery based proteomics of *O. degus* brain is on-going.

Funding: NHMRC, Rebecca L. Cooper Medical Research Foundation.

The expression and distribution of sirtuins in the brain and CNS and their role in AD

CHeBA staff: Tharusha Jayasena (PhD student), Anne Poljak (conjoint), Nady Braidy, Perminder Sachdev.

Other investigators: Associate Professor Ross Grant (SOMS, UNSW; Australasian Research Institute; Sydney Adventist Hospital), Associate Professor Matthias Klugmann (SOMS, UNSW; NeuRA, UNSW; Prince of Wales Hospital), Associate Professor Mark Raftery (SOMS, UNSW; BMSF, UNSW), Associate

Professor George Smythe (SOMS, UNSW), Dr Ling Zhong (BMSF, UNSW).

Aims:

- Develop a stable isotope based MRM mass spectrometric quantitative assay for human sirtuins.
- Explore the distribution and expression level of sirtuins in the mammalian brain.
- Explore expression of sirtuins in plasma and cerebrospinal fluid (CSF) and variation with age and in AD and MCI.

Findings: Sirtuin proteins have a variety of intracellular targets, thereby regulating multiple biological pathways including neurodegeneration. However, relatively little is currently known about the role or expression of the 7 mammalian sirtuins in the central nervous system. Western blotting, PCR and ELISA are the main techniques currently used to measure sirtuin levels. To achieve sufficient sensitivity and selectivity in a multiplex-format, a targeted mass spectrometric assay was developed and validated for the quantification of all seven mammalian sirtuins (SIRT1-7). Quantification of all peptides was by multiple reaction monitoring (MRM) using three mass transitions per protein-specific peptide, two specific peptides for each sirtuin and a stable isotope labelled internal standard. The assay was applied to a variety of samples including cultured brain cells, mammalian brain tissue, CSF and plasma. All sirtuin peptides were detected in the human brain, with SIRT2 being the most abundant. Sirtuins were also detected in human CSF and plasma, and guinea pig and mouse tissues. In conclusion, we have successfully applied MRM mass spectrometry for the detection and quantification of sirtuin proteins in the central nervous system, paving the way for more quantitative and functional studies.

Funding: NHMRC, Rebecca L. Cooper Medical Research Foundation, UPRA PhD Scholarship.

The Older Australian Twins Study (OATS)

CHeBA staff:

Investigators: Perminder Sachdev, Henry Brodaty, Julian Trollor (conjoint), Wei Wen, Teresa Lee, Karen Mather, John Crawford, Anbupalam Thalamuthu

Study Coordinator: Amelia Assareh

NSW Research Assistant: Tanya Duckworth

NSW Admin Assistant: Suzy Forrester

Data Manager: Kristan Kang

Other Researchers: Anne Poljak (conjoint), Jiyang Jiang, Jessica Lazarus (PhD student), Ruby Tsang (PhD student), Helen Wu (PhD student).

Other investigators and staff:

Investigators: Professor David Ames (National Ageing Research Institute), Professor Nick Martin (QIMR Berghofer Medical Research Institute, Qld), Dr Margaret J. Wright (QIMR Berghofer Medical Research Institute/ University of Queensland), Professor Bernhard Baune (University of Adelaide), Professor Peter Schofield (NeuRA, UNSW), Professor Katherine Samaras (Garvan Institute, NSW), Professor Christopher Rowe (Austin Hospital, Victoria), Dr Eva Wegner (Prince of Wales Hospital, NSW); Research Assistants: Christel Lemmon (National Ageing Research Institute)

Other Researchers: Dr Michelle Lupton (QIMR Berghofer Medical Research Institute)

Fellows: Dr Rebecca Koncz (Prince of Wales Hospital/ UNSW).

Aims:

- Maintain a well-characterised cohort of identical (MZ) and non-identical (DZ) twin pairs for longitudinal study.
- Follow-up the OATS cohort for the relative genetic and environmental contributions to mild cognitive impairment and dementia.
- Characterise endophenotypes of dementia, including amyloid plaque build-up.
- Explore the genetic basis of cognitive decline and brain changes in old age, as part of international consortia.
- Determine the heritability of amyloid deposition in the brain as an endophenotype of Alzheimer's disease (AD).
- Determine the shared genetic and environmental variance between amyloid build-up and i) cognition, ii) cardiovascular disease, and iii) cerebral atrophy.
- Investigate the genetic and environmental risk (and protective) factors associated with amyloid build-up in older individuals.
- Investigate the relationship between amyloid build-up and memory function.

Findings:

- The OATS brain donor program had a significant increase in the number of recruits through Wave 3 with nearly 70 recruits over NSW, VIC and QLD in 2016.
- We had a new round of recruitment through the Australian Twin Registry for the Amyloid Imaging project (New Wave 1), investigating the deposition of amyloid plaques in the brain using positron emission tomography (PET) scans. We aim to recruit 100 twin pairs for the PET scans by the end of 2017.
- The OATS online project aims to give OATS access to more participants, particularly those in non-metropolitan areas. The online questionnaires have been conducted for some Wave 4 and all of our new Wave 1 participants. Negotiations were finalised and an agreement reached with Cogstate in late 2016 for computerised neuropsychiatric tests and we hope to be able to conduct the online cognitive testing in the first quarter of 2017.
- Four PhD projects used OATS samples/data.
- PhD student, Ruby Tsang has investigated the genetic and epigenetic factors associated with late-life depression. The heritability of late-life depression was estimated using OATS data, which show that genetic factors account for a moderate amount of the variability in late-life depression. In addition, significant genetic correlations of late-life depression with anxiety and with hypertension were observed, suggesting shared genetic factors likely contribute to the co-occurrence of these traits.
- Researchers looked at data from ~700,000 individual genetic variants from more than 1,000 people (including OATS participants) to identify genes that influence the blood levels of Apolipoprotein H (ApoH). ApoH transports fats and other molecules around the body. It has been linked to cognitive ageing, and cardiovascular and autoimmune diseases. The researchers identified specific genetic variants, which were linked to ApoH levels and the results have been replicated.
- White matter hyperintensities (WMHs) are signal changes in the brain's white matter, which are commonly seen on MRI scans in healthy elderly individuals as well as a number of neurological disorders. Using a twin design based on 320 participants (92 monozygotic and 68 dizygotic pairs) from OATS, researchers reported a high heritability of WMHs. High heritability implies genetic determination and this study showed that the genetic influence was higher in women.
- The heritability of brain grey matter structures was examined in a subsample of OATS participants (93 monozygotic and 68 dizygotic twin pairs). Corresponding structures in the two hemispheres were influenced by the same genetic factors and high genetic correlations were observed between the two hemispheric regions. This study was the first attempt to examine the genetic correlations between human cortex and subcortical structures, using the twin design. The data showed that cortical and subcortical structures had moderate to high heritability.
- Although brain size is highly heritable, the underlying genes remain largely unknown. In an international collaborative effort, researchers examined data on 32,438 subjects (including genetics and MRI data from OATS participants) and discovered five new genetic variants for intracranial volume (which reflects brain size and brain development until maturation). These genetic variants were also related to childhood and adult cognitive function, as well as Parkinson's disease.
- The two hemispheres of the human brain differ functionally and structurally. This so-called brain asymmetry is under the influence of several factors including genetics. In the largest ever analysis of brain asymmetries on 15,847 MRI scans (including those from OATS participants), heritability analyses revealed that genetic drivers of asymmetry in the hippocampus, thalamus and basal ganglia may affect variability in human cognition, including susceptibility to brain disorders.
- Common genetic risk factors for Alzheimer's disease (AD) were associated with reduced hippocampal volume in healthy older adults and those with mild cognitive impairment. This shows there is a neurodegenerative effect visible in the hippocampus before clinical manifestations of AD occur in older adults.
- Heritability of verbal ability on 42 monozygotic and 111 dizygotic twin pairs was investigated. The heritability of language functions showed to be highest for letter fluency, moderate for picture naming, and lowest for semantic fluency. The genetic correlations between performances on these three tests ranged from .43 to .77,

suggestive of a common genetic substrate for language expression. Understanding the genetic influence on these verbal tests can inform gene discovery for language-associated neurodegenerative disorders, such as frontotemporal dementia and Alzheimer's disease. Findings of environmental influence may suggest there are potentially modifiable factors that can reduce risk of age-related cognitive decline.

Funding: NHMRC.

The organisation of the elderly connectome

CHeBA staff: Alistair Perry (PhD student), Wei Wen, Anbupalam Thalamuthu, Perminder Sachdev.

Other investigators: Professor Michael Breakspear (QIMR Berghofer Medical Research Institute).

Aims:

- Examine the core features of structural networks in the elderly brain and how this compares to a young adult population and previously published data.
- Examine whether changes in both structural and functional connectivity is predictive of cognitive performance in the elderly.
- Examine whether age-related changes in cognition can be predicted by changes in structural and functional connectivity.

Findings:

- The topology of hub-regions in the elderly is consistent with adult connectomic data.
- Hub-regions still plausibly provide a vital role to network communication.
- Lateralizations and sexual dimorphisms in connectivity still exist in the elderly.
- The connectomic data of each elderly subject analysed is made available online.

Funding: NHMRC.

The role of polyphenolic compounds in modulating AD pathology

CHeBA staff: Tharusha Jayasena (PhD student), Anne Poljak (conjoint), Nady Braidy, Perminder Sachdev.

Other investigators: Professor Gerald Münch (University of Western Sydney), Associate Professor George A Smythe (SOMS, UNSW).

Aims:

- Determine whether polyphenolic compounds such as curcumin, resveratrol and others will affect in *vitro* Aβ oligomer and aggregate formation.
- Determine whether cells exposed to Aβ oligomers and aggregates suffer adverse metabolic effects, compromised cell permeability and early apoptosis.
- Explore whether polyphenolic compounds will ameliorate some of these effects.

Findings: Treatment of astroglial cultures with aggregated amyloid caused a significant drop in cell proliferation. This effect was prevented by co-incubation with the polyphenolic compound epigallocatechin gallate (EGCG). Curcumin and resveratrol did not significantly prevent the toxicity caused by amyloid alone but were shown to significantly prevent the toxic effects of metal addition to amyloid in the same astroglial model. Furthermore mitochondrial function was impaired in astrocytes following incubation with aggregated Aβ42, while co-treatment with selected polyphenols attenuated mitochondrial function to control levels.

Funding: NHMRC, Rebecca L. Cooper Medical Research Foundation, UPRA PhD Scholarship.

The Sydney Centenarian Study (SCS)

CHeBA staff: Perminder Sachdev, Henry Brodaty, John Crawford, Nicole Kochan, Karen Mather, Adam Theobald, Keenie Daly, Zixuan Yang (PhD student), Gavin Andrews (conjoint), Kristan Kang, Charlene Levitan (conjoint).

Aims:

- Determine the prevalence of major medical and neuropsychiatric disorders in individuals aged ≥95.
- Establish tools for the valid assessment of cognitive function in centenarians.

- Examine brain structure and function in centenarians and relate it to neuropathology.
- Determine the major genetic and environmental factors that influence longevity and normal cognitive function.
- Explore the determinants of "successful ageing".

Findings:

- The brain structures that best distinguish amnestic mild cognitive impairment from normal controls differ in those <85 from those ≥85, suggesting different neuropathological underpinnings of cognitive impairment in the very old (Yang et al., *Curr Alzh Res*).
- We examined cross-sectional brain morphological differences from the 8th to the 11th decades of life in non-demented individuals by high-resolution magnetic resonance imaging. Significant linear negative relationship of gray matter with age was found, with the greatest age effects in the medial temporal lobe and parietal and occipital cortices. This pattern was further confirmed by comparing directly the ≥90 years to the 71-89 years groups. Significant quadratic age effects on total white matter and white matter hyperintensities were observed. Our study demonstrated differences across brain regions between the oldest old and young old, with an emphasis on hippocampus, temporoposterior cortex, and white matter hyperintensities (Yang et al., *Neurobiol Aging*).

Funding: NHMRC.

The Sydney Memory and Ageing Study (Sydney MAS)

CHeBA staff: Henry Brodaty, Perminder Sachdev, Julian Trollor (conjoint), Brian Draper (conjoint), Nicole Kochan, Kristan Kang, John Crawford, Karen Mather, Wei Wen, Nicole Dargue, Paul Strutt, Kate Maston (Study Co-ordinator).

Aims:

- Examine the clinical characteristics and prevalence of Mild Cognitive Impairment (MCI) and related syndromes, including Alzheimer's disease, vascular dementia and frontotemporal dementia.
- Determine the rate of change in cognitive function over time.
- Investigate risk factors for and protective factors against cognitive decline and dementia.
- Develop and refine measures for early diagnosis, prognosis and biomarkers.

Findings:

- Development and validation of a new assessment tool, the Sydney Test of Activities of Daily Living (STAM). The STAM is designed to objectively assess an older person's level of independence in 'Instrumental Activities of Daily Living' such as managing medications, shopping and handling finances. The STAM can be used to differentiate between normal cognition, MCI, and dementia and can be a helpful tool for diagnostic classification both in clinical practice and research.
- Risk factors for developing MCI or dementia within a 6-year follow-up period included: increasing age, MCI at baseline, poorer smelling ability, being an *APOE* ε4 carrier and slower walking speed. There was a considerable overlap between the risk factors for mortality and those for dementia.
- Recent alcohol consumption (including "low consumption" and "risky consumption") was not associated with incident dementia at 4-year follow-up. Carriers of the *APOE* ε4 allele were more likely to develop dementia, but there was no significant interaction with alcohol consumption.
- Older adults' performance on a test of reaction time indicated their likelihood of developing dementia. Individuals who had slower responses on a simple reaction time task were 2-3 times more likely to receive a diagnosis of dementia within four years.
- Structural MRI distinguishes the brains of elderly individuals with 'amnestic MCI' from those classified as 'cognitively normal'. Amnestic MCI was associated with smaller volumes of overall cortex, medial temporal structures, anterior corpus callosum and select frontal and parietal regions compared with brains from cognitively normal individuals.

Funding: NHMRC.

Towards understanding the role of gene expression in ageing-related phenotypes

CHeBA staff: Karen Mather, Anbupalam Thalamuthu, Perminder Sachdev.

Other key investigators: Professor Bernhard Baune (University of Adelaide), Liliana Ciobanu (University of Adelaide), Dr Nicola Armstrong (Murdoch University) (CHeBA Hon. Research Fellow), Associate Professor John Kwok (NeuRA, UNSW), Professor Peter Schofield (NeuRA, UNSW).

Aim: Identify differentially expressed genes associated with ageing-related phenotypes, including memory performance.

Findings: Gene expression associated with memory and global cognition has been completed. Multivariate association analysis of genes within clusters and pathways are currently being investigated.

Funding: Yulgilbar Foundation Alzheimer's Research Program Grant, NHMRC, Thomas Foundation.

Transcranial direct current stimulation (tDCS) combined with cognitive training to enhance memory in patients with amnestic mild cognitive impairment (aMCI)

CHeBA staff: Adith Mohan, Henry Brodaty, Perminder Sachdev.

Other investigators: Professor Colleen Loo (Black Dog Institute), Dr Donel Martin (Black Dog Institute).

Aims: Investigate an exciting novel approach for improving memory in people diagnosed with amnestic mild cognitive impairment (aMCI): cognitive training (CT) combined with mild non-invasive brain stimulation (transcranial direct current stimulation (tDCS)).

Findings: The study is in the final stage of recruitment with 1 participant left to recruit. Follow up will be completed in 2017 when a complete analysis of the data is planned. Preliminary results indicate large-sized memory improvement at 3 month follow-up with active or sham tDCS combined with CT and support the utility of computerized CT for improving memory in aMCI.

Funding: Thomas Foundation, DCRC-ABC.

Using the discordant identical twin model to discover epigenetic and environmental factors contributing to ageing-related phenotypes

CHeBA staff: Karen Mather, Anbupalam Thalamuthu, Perminder Sachdev.

Other key investigators: Dr Nicola Armstrong (Murdoch University) (CHeBA Hon. Research Fellow), Professor David Ames (National Ageing Research Institute, Royal Melbourne Hospital), Associate Professor John Kwok (NeuRA, UNSW), Professor Peter Schofield (NeuRA, UNSW), Associate Professor Margaret J. Wright (QIMR Berghofer Institute, Brisbane, Australia), Professor Naomi Wray (Queensland Brain Institute, University of Queensland), EuroDiscoTWIN Consortium.

Aim: Identify differentially methylated regions of the genome and/or environmental factors associated with various traits, such as arthritis and hypertension.

Findings: DNA methylation assays of 113 OATS identical twin pairs have been completed. Identical twin pairs discordant for a number of different traits such as cognitive performance and hypertension will be selected for analyses seeking to identify differentially methylated regions. This work will then be replicated in other independent cohorts such as MAS.

Funding: NHMRC, Thomas Foundation, methylation work was supported by NHMRC Grants 613608 and 61302 (held by Professor Naomi Wray, administered by Queensland Brain Institute, University of Queensland).

Validating the VASCOG criteria for Vascular Cognitive Disorders: a comparison with four other sets of criteria for Vascular Dementia

CHeBA staff: Perminder Sachdev, Darren Lipnicki, John Crawford, Henry Brodaty

Aim: To validate VASCOG criteria by comparing them with other criteria in diagnosing dementia and mild vascular cognitive disorder in a post-stroke cohort, and their ability to predict mortality within 10 years.

Findings: VASCOG criteria compare well with DSM-5 criteria but have lower agreement with other criteria for vascular dementia. VASCOG criteria have an improved predictive validity over the previously used criteria.

Funding: Direct donations to The Dementia Momentum Fund.

Vitamin binding proteins in plasma (afamin and vitamin D binding protein VDBP)

CHeBA staff: Anne Poljak (conjoint), Nicole Kochan, Wei Wen, John Crawford, Julian Trollor (conjoint), Henry Brodaty, Perminder Sachdev.

Other investigators: Dr Fei Song (CHeBA Hon. Research Fellow), Professor Hans Dieplinger (Innsbruck Medical University, Austria), Professor John Attia (University of Newcastle), Associate Professor Peter W. Schofield (University of Newcastle), Dr Mark McEvoy (University of Newcastle), Professor Ralph Martins (Edith Cowan University).

Aims:

- Determine if vitamin binding protein levels are different in MCI and AD plasma relative to normal controls, and whether observations would be reproducible across independent cohorts of similar design.
- Identify which of the vitamin binding proteins change with age and/or are dysregulated in MCI and AD.
- Correlate plasma vitamin binding protein levels with cognitive domain scores and brain volumetrics.
- Afamin (vitamin E binding) and VDBP are of specific interest, based on our preliminary discovery proteomics data. We plan to assay plasma levels using ELISA quantification.

Findings: In our first iTRAQ study, two plasma vitamin binding proteins were downregulated in AD and MCI relative to controls: afamin (binds vitamin E) and vitamin D-binding protein precursor (VDBP). Western blotting confirmed the decreased afamin levels, and further work was initiated by a group in Austria headed by Professor Hans Dieplinger. Professor Dieplinger's group assayed the full MAS W1 cohort and some AD samples confirming lower levels of afamin and ELISA of VDBP in our own lab confirmed lower levels in MCI and AD plasma samples. Additional studies on both vitamin binding proteins are in progress.

Funding: NHMRC, ARC, Rebecca L. Cooper Medical Research Foundation, Alzheimer's Australia Rosemary Foundation, Sachdev Foundation, UNSW Faculty of Medicine FRG and Early Career Researcher Grants.

White matter hyperintensity extraction pipeline development

CHeBA staff: Wei Wen, Jiyang Jiang, Perminder Sachdev.

Other investigators: Dr Wanlin Zhu (Beijing Normal University) (CHeBA Hon. Research Fellow), Associate Professor Tao Liu (Beihang University, China) (CHeBA Hon. Research Fellow).

Aim: Build an automated white matter hyperintensity (WMH) extraction pipeline for the cerebral small vessel disease consortium, and other WMH processing tasks with large sample sizes.

Findings:

- We coded using Python to integrate different processing modules, and applied a machine learning algorithm (i.e. k-Nearest Neighbours, or kNN) to determine WMH regions.
- The pipeline can process ~250 brains in 2-3 days currently.
- We are in the process to improve the pipeline by a). reducing the processing time, b). adding quality control modules, and c). adding a user-friendly graphic interface.

Funding: NHMRC, John Holden Family Foundation.

COMPLETED PROJECTS

Age-related cognitive decline and associations with sex, education and apolipoprotein E genotype across ethno-cultural and geographic regions: A collaborative cohort study (Formerly: Examine the risk and protective factors for dementia that are consistent across the world and those that differ (using data from COSMIC))

CHeBA staff: Darren Lipnicki, John Crawford, Rajib Dutta, Anbupalam Thalamuthu, Nicole Kochan, Gavin Andrews (conjoint), Henry Brodaty, Perminder Sachdev.

Other investigators: Dr Simone Reppermund (UNSW Medicine) (CHeBA Hon. Research Fellow); 34 investigators from 12 different countries as part of COSMIC.

Aims:

- Investigate how rates of age-related decline in performance on different types of cognitive tests varied among 14 international cohort studies of cognitive aging.
- Determine the extent to which sex, educational attainment and apolipoprotein E ε4 allele *(APOE*4)* carrier status were associated with decline.

Findings: The 14 different studies showed different rates of decline, and decline in Mini-Mental State Examination scores was faster for Asians than whites, females than males, and *APOE*4* carriers than non-carriers. *APOE*4* carriers also declined faster than non-carriers on tests of memory, processing speed and language. Findings have been submitted for publication in *PLOS Medicine*.

Funding: NHMRC, Vincent Fairfax Family Foundation, direct donations to The Dementia Momentum Fund.

Assessment and management of the cognitively impaired older persons presenting to the Emergency Department with a musculoskeletal condition or injury

CHeBA staff: Lynn Chenoweth.

Other investigators: Professor Margaret Fry (University of Technology Sydney), Associate Professor Glenn Arendts (University of Western Australia).

Aim: Determine if the PAINAD screening tool assists emergency nurses to improve pain assessment and to facilitate timely analgesic responses for people age >64 years, including people with a cognitive impairment, presenting to the emergency department with a long bone fracture and with pain.

Findings: We enrolled 602 patients >64 years of whom 323 (54%) were at intervention sites (n=4). There was a clinical improvement of 17 minutes in pain assessment for intervention site patients compared with non-intervention site patient (127 vs 144 minutes). Univariate analysis, however, revealed no significant improvement (*P* 0.74) in time to analgesia between the groups, after adjusting for age, fracture type, arrival mode and triage category 28% of intervention and 32% of non-intervention patients (*P*=0.24) received analgesia within 60 minutes. While the clinical trend suggests that PAINAD can improve time to analgesia for older patients with a cognitive impairment, changing clinician behaviour and improving practice demands a more multidisciplinary leadership approach, family engagement and intensive staff education.

Funding: Montefiore Home (administered by CHeBA); Emergency Care Institute of NSW (not administered by CHeBA).

Cluster randomised controlled trial of facilitated case conferencing vs usual care for improving end of life outcomes for people with advanced dementia living in residential aged care and their families

CHeBA staff: Lynn Chenoweth.

Other investigators: Professor Meera Agar (South West Sydney Clinical School, UNSW), Professor Geoffrey Mitchell (University of Queensland), Dr Georgina Luscombe (University of Sydney), Professor Marion Haas (University of Technology Sydney), Professor Elizabeth Beattie (DCRC, Queensland University of Technology), Professor David Currow (Flinders University), Dr Amy Abernethy (Flinders University), Dr Tim Luckett (University of Technology Sydney).

Aim: Improve the quality of palliative care and wellbeing for people with advanced dementia living in residential aged care through a facilitated case conference (FCC) intervention.

Findings: Of 286 people with advanced dementia who participated in the trial, 131 died (64 in the non-intervention group and 67 in the intervention group). This less than expected number of deaths caused the study to be under-powered when assessing the main study outcomes (end-of-life quality of care (EOLD) scales). Significant differences were found in pharmacological ($P < 0.01$) and non-pharmacological ($P < 0.05$) palliative management during the last month of life. Intercurrent illness was associated with lower family-rated EOLD Satisfaction with Care ($P < 0.05$) and lower staff-rated EOLD Comfort Assessment with Dying ($P < 0.01$). There were positive relationships between EOLD scale results and staff hours to bed ratios, proportion of residents with dementia and staff attitudes about end of life care for people with dementia. FCC may facilitate a palliative approach to care, which future trials of case conferencing should evaluate.

Funding: Montefiore Home (administered by CHeBA); Department of Health and Ageing (not administered by CHeBA).

Determine the prevalence and incidence of mild cognitive impairment in diverse ethnoracial and sociocultural groups (using data from COSMIC)

CHeBA staff: Perminder Sachdev, Darren Lipnicki, John Crawford, Nicole Kochan, Anbupalam Thalamuthu.

Other investigators: Study leaders and other researchers from among 26 COSMIC member cohorts.

Aim: Establish more reliable comparisons of the prevalence of MCI and its amnestic and non-amnestic subtypes among the COSMIC cohorts, in addition to calculating an overall prevalence rate.

Findings: The published range of MCI prevalence estimates was 5.0%-36.7%. This was reduced with all cognitive impairment definitions: performance in the bottom 6.681% (3.2%-10.8%); Clinical Dementia Rating of 0.5 (1.8%-14.9%); Mini-Mental State Examination score of 24-27 (2.1%-20.7%). Prevalence using the first definition were 5.9% overall, and increased with age ($P < .001$), but were unaffected by sex or the main races/ethnicities investigated (whites and Chinese). Not completing high school increased the likelihood of MCI ($P \leq .01$). Applying uniform criteria to harmonised data greatly reduced the variation in MCI prevalence internationally (Sachdev et al., 2015, *PLOS ONE*).

Funding: NHMRC, Vincent Fairfax Family Foundation (from October 2015).

Domain-specific cognitive function in the post-acute phase of stroke predicts long-term mortality: Results from the Sydney Stroke Study

CHeBA staff: Darren Lipnicki, Henry Brodaty, Perminder Sachdev.

Other investigators: Syenna Schievink, Dr Sebastian Köhler, Professor Frans Verhey, Professor Robert van Oostenbrugge (Maastricht University, The Netherlands).

Aims:

- Test the value of domain-specific cognitive functioning after stroke for predicting five- and ten-year outcomes of dementia and mortality respectively.

- Determine which cognitive domain contributes most to predicting outcomes.

Findings: Lower cognitive functioning 3-6 months after stroke (particularly in executive functioning, information processing speed and verbal fluency) predicts mortality up to 10 years later, but cognitive functioning does not predict dementia up to 5 years after stroke. Findings have been submitted to the *Journal of the International Neuropsychological Society.*

Funding: Direct donations to The Dementia Momentum Fund.

Evaluating the benefits of smart technology in in-home care practice

CHeBA staff: Lynn Chenoweth.

Other investigators: University of Technology Sydney: Professor Gamini Dissanayanke, Dr Ravi Ranasinghe, Professor Dikai Lui, Stefan Lie.

Aim: Realise practical improvements to in-home aged care services and residential aged care services through assistive technologies.

Findings: We successfully demonstrated the utility of the 'Smart Hoist' in reducing lower back injuries in carers and improving the safety of carers and patients during transfer in an aged care setting by: assisting with manoeuvring and navigation, calculating patient Body Mass Index (BMI), monitoring the environment under furniture and behind the operator, detecting obstacles and avoiding collisions. This ultimately had a positive impact on the quality of transfers for dependent aged care residents. The outcomes of two trials of the 'Smart Hoist' with 100 carers and 50 aged care residents produced the following results: no significant improvements in swinging, seat comfort, assistance required and familiarity of use; significant ($P<0.05$) improvements in jolting and carer back strain, requiring a force less than 30N per handle (compared to 40N) to perform lifting, turning and pushing functions; significantly safer and more comfortable sling attachment; and smoother speed handling. Based on the promising project results, UTS Research and Innovation office and IRT have engaged in exploiting business opportunities to further develop the Smart Hoist as a product.

Funding: Montefiore Home (administered by CHeBA); Australian Research Council and the Illawarra Retirement Trust (not administered by CHeBA).

Genetics of apolipoproteins

CHeBA staff: Karen Mather, Anbupalam Thalamuthu, Anne Poljak (conjoint), Perminder Sachdev.

Other key investigators: Dr Fei Song (CHeBA Hon. Research Fellow), Professor John Attia (University of Newcastle), Professor David Ames (National Ageing Research Institute; Royal Melbourne Hospital), Dr Nicola Armstrong (Murdoch University), Associate Professor John Kwok (NeuRA, UNSW), Dr Chris Oldmeadow (University of Newcastle), Professor Peter Schofield (NeuRA, UNSW), Associate Professor Margaret J. Wright (QIMR Berghofer Institute, Brisbane, Australia).

Aim: Identify genetic variants associated with plasma apolipoproteins in mid to late life.

Findings: The major finding of this work was the identification of genetic variants for plasma levels of apolipoprotein H (ApoH). We undertook a genome-wide association study using data from the Sydney MAS and OATS cohorts and replicated the genome-wide significant results in the Hunter Community Study. This work has now been published (Mather et al., *Sci Rep*).

Funding: NHMRC, Thomas Foundation.

Heritability and genetic influence on brain structures

CHeBA staff: Wei Wen, Anbupalam Thalamuthu, Jiyang Jiang, Perminder Sachdev, Karen Mather.

Other investigators: Professor David Ames (National Ageing Research Institute; Royal Melbourne Hospital), Associate Professor Pierre Lafaye de Micheaux (Université de Montréal, Canada), Dr Margaret J. Wright (QIMR Berghofer Institute, Brisbane, Australia), Dr Wanlin Zhu (Beijing Normal University) (CHeBA Hon. Research Fellow).

Aim: Estimate heritability and genetic correlations of cortical and sub-cortical structures of the human brain.

Findings: The heritability estimates of subcortical regions ranged from 0.41 (amygdala) to 0.73 (hippocampus), and of cortical regions from 0.55 (parietal lobe) to 0.78 (frontal lobe). Corresponding structures in the two hemispheres were influenced by the same genetic factors and high genetic correlations were observed between the two hemispheric regions. There were three genetically correlated clusters, comprising (i) the cortical lobes (frontal, temporal,

parietal and occipital lobes); (ii) the basal ganglia (caudate, putamen and pallidum) with weak genetic correlations with cortical lobes; and (iii) the amygdala, hippocampus, thalamus and nucleus accumbens grouped together, which genetically correlated with both basal ganglia and cortical lobes, albeit relatively weakly. Our study demonstrates a complex but patterned and clustered genetic architecture of the human brain, with divergent genetic determinants of cortical and subcortical structures, in particular the basal ganglia (Wen et al., *Sci Rep*).

Funding: NHMRC, Alzheimer's Australia Dementia Research Foundation Postdoctoral Fellowship.

PROMOTE Consortium: Testing feasibility and face validity of quality indicators (QIs) for psychosocial interventions

CHeBA staff: Henry Brodaty.

Other investigators and affiliations: Professor Yun-Hee Jeon (University of Sydney), Professor Huali Wang (Beijing) Dr Rahimah Binti Ibrahim (Malaysia), Dr Daochompu Nakawiro (Thailand), Professor Wai Tong Chien (Hong Kong), Dr Jong-Chul Youn and Associate Professor JuYoung Ha, (South Korea), Associate Professor Tan Lay Ling (Singapore).

Aims:

Test the feasibility and face validity of the European QIs for psychosocial care in dementia in the context of residential aged care in Asia-Pacific countries.

Establish a set of QIs that are appropriate and valid to assess and improve quality of psychosocial care for people with dementia in the residential aged care setting in this region.

Findings: Six Asia-Pacific countries and one territory (Australia, China – Beijing and Hong Kong, South Korea, Singapore, Thailand, Malaysia) tested European QIs in nursing homes. They found that the European QIs were unsuitable. Regional specific QIs need to be developed. Findings were presented at the Alzheimer's Disease International Asia-Pacific Regional Meeting, New Zealand in November 2016. A paper has been submitted for publication.

Funding: SSEAC Cluster Research Grant (administered by University of Sydney).

Risk factors for mild cognitive impairment, dementia and mortality: the Sydney Memory and Ageing Study

CHeBA staff: Darren Lipnicki, John Crawford, Nicole Kochan, Julian Trollor (conjoint), Brian Draper (conjoint), Kate Maston, Karen Mather, Henry Brodaty, Perminder Sachdev.

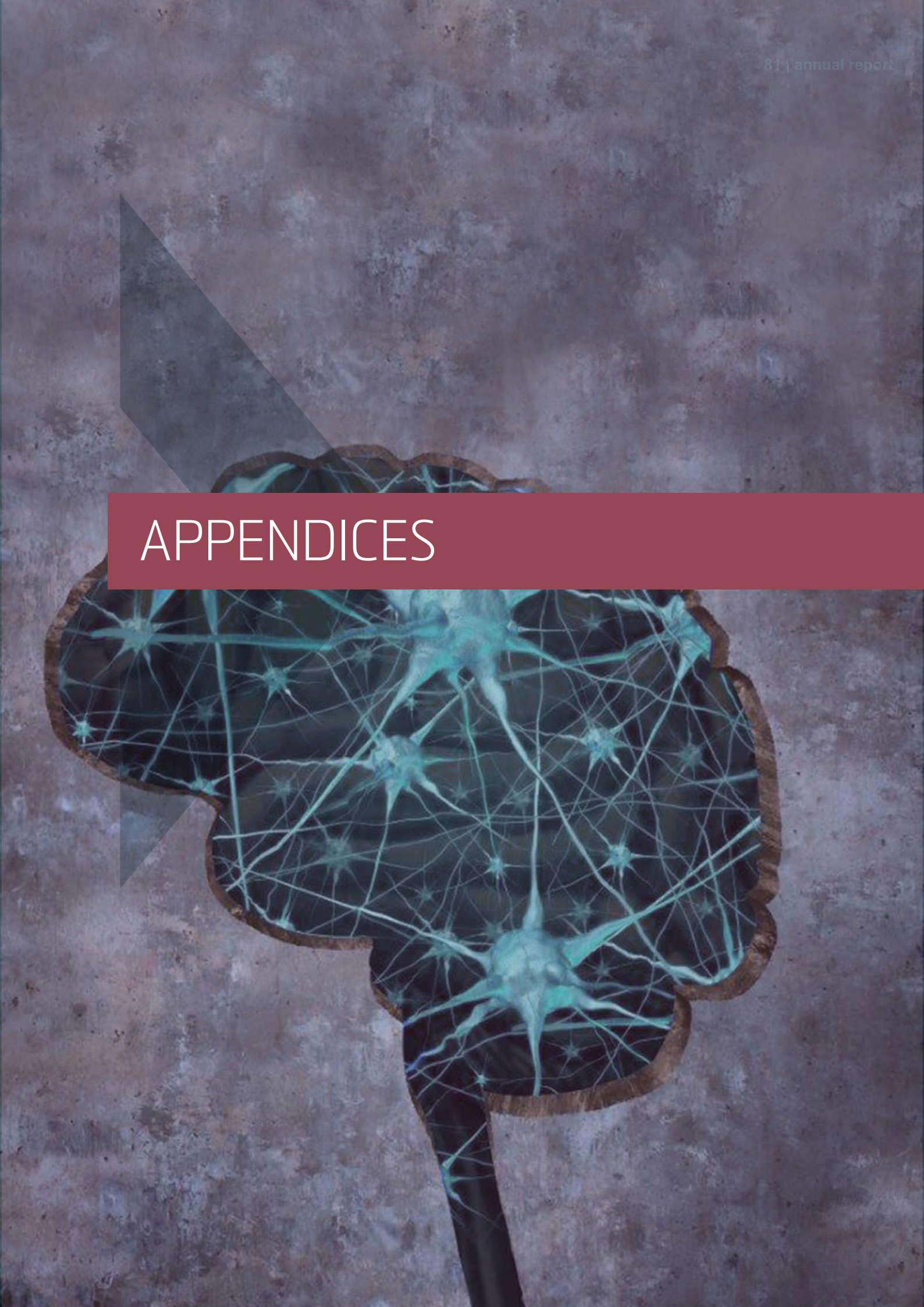
Other investigators: Dr Simone Reppermund (UNSW Medicine) (CHeBA Hon. Research Fellow).

Aim: Investigate potential risk factors simultaneously in a single cohort including many individuals initially with normal cognition and followed for six years.

Findings: A core group of late-life risk factors indicative of physical and mental frailty are associated with each of dementia, MCI, and mortality after six years. Tests for slower walking speed and poorer smelling ability may help screen for cognitive decline. Individuals with normal cognition are at greater risk of future cognitive impairment if they have a history of MCI (Lipnicki et al., *J Am Med Dir Assoc*).

Funding: NHMRC, direct donations to The Dementia Momentum Fund.

APPENDICES



APPENDIX A: STAFF LIST

Leadership

Henry Brodaty
Professor, Co-Director CHeBA, Montefiore Chair of Healthy Brain Ageing

Perminder Sachdev
Professor, Co-Director CHeBA, Leader Epidemiology Group, Leader Neuropsychiatry Group

Angela (Angie) Russell
Centre Manager

Academic Staff

Nady Braidy
Research Fellow, *Co-Leader Molecular Biology & Stem Cell Group*

Lynn Chenoweth
Professor of Nursing

Megan Heffernan
Postdoctoral Fellow, *Maintain Your Brain Project Coordinator*

Jiyang Jiang
Postdoctoral Fellow

Nicole Kochan
Research Fellow, *Co-Leader Neuropsychology Group*

Jessica Lo
Postdoctoral Fellow

Karen Mather
Lecturer, *Leader Genetics & Genomics Group*

Adith Mohan
Research Fellow

Julia Müenchhoff
Research Fellow
(until June 2016)

Matt Paradise
Postdoctoral Fellow

Anbupalam Thalamuthu
Postdoctoral Fellow

Wei Wen
Associate Professor, *Leader Neuroimaging Group, Director Neuroimaging Laboratory (NiL)*

Professional & Technical Staff - Research

Eshwar Anbupalam
Student Assistant (Casual)

Amelia Assareh
Research Study Coordinator, *Older Australian Twins Study (OATS)*

Jocelyn Bowden
Research Officer, *Older Australian Twins Study (OATS) Coordinator*
(until July 2016)

Tiffany Chau
Research Assistant

John Crawford
Senior Statistician

Catriona (Keenie) Daly
Research Assistant, *ICC-Dementia Consortium Co-ordinator*

Nicole Dargue
Research Assistant

Tanya Duckworth
Research Assistant

Rajib Dutta
Research Officer/Statistician

Ying (Niki) He
Technical Officer
(until April 2016)

Mahboobeh (Mabi) Hosseini
Research Assistant (BioBanking)

Sri Chandana Kanchibotla
Research Assistant (Casual)

Kristan Kang
Data Manager

Geraldine Koo
Student Assistant (Casual)

Manish Kumar
Research Data Management Officer, *Maintain Your Brain*

Darren Lipnicki
Research Officer, *COSMIC Consortium Co-ordinator*

Kate Maston
Research Officer

Sandra Ng
Student Assistant (Casual)

Tamara Paulin
Research Assistant

Debarun Sengupta
Student Assistant (Casual)

Paul Strutt
Research Assistant

Adam Theobald
Research Officer

Adam Vujic
Research Assistant (Casual)

Oscar Wen
Student Assistant (Casual)

Professional & Technical Staff - Support

Melissa Chungue
Administrative Assistant

Kate Crosbie
Administrative Assistant (Casual)

Sophia Dean
Administrative Officer

Craig Douglass
Administrative Assistant (Casual)

Suzanne Forrester
Administrative Assistant

Alejandra Grillo
Web Coordinator (Casual)
(until December 2016)

Esther Lefas
Administrative Assistant
(until June 2016)

Heidi Mitchell
Marketing & Communications Officer

Hsu Hnin (Brenda) Wai
Administrative Assistant (Casual)

Conjoint Staff

Gavin Andrews
Professor of Psychiatry, Chief Investigator, *NHMRC Program Grant ID1093083*

Brian Draper
Professor, Associate Investigator, *Sydney Memory & Ageing Study (ongoing)*

Nicola Gates
Lecturer
(2014-2018)

Rebecca Koncz
Conjoint Associate Lecturer
(2015-2018)

Teresa Lee
Senior Lecturer, *Co-Leader Neuropsychology Group (ongoing)*

Charlene Levitan
Adjunct Associate Lecturer
(2015-2019)

Ora Lux
Senior Lecturer
(2014-2018)

Anne Poljak
Lecturer, Protein Chemist, *Leader Proteomics Group*

Melissa Slavin
Senior Lecturer
(2014-2018)

Julian Trollor
Professor, *Leader Neuroinflammation Group*

Visiting Fellows

Bernhard Baune
Visiting Professorial Fellow
(January 2013-present)

David Bunce
Visiting Professorial Fellow, Epidemiological Studies of Cognition and Dementia
(February 2014-December 2017)

Nibaldo Inestrosa
Honorary Professor, *Molecular Biology & Stem Cell Group*

Lee-Fay Low
Senior Visiting Fellow
(January 2015-December 2016)

Kuldip Sidhu
Visiting Honorary Associate Professor, Co-Leader Molecular Biology & Stem Cells Group
(December 2015-December 2018)

Evelyn Smith
Visiting Fellow
(January 2015-December 2016)

Dr Wanlin Zhu
Visiting Fellow
(1 September 2016-31 December 2018)

CHeBA Honorary Research Fellows

Dr Nicola Armstrong

Dr Tao Liu

Dr Simone Reppermund

Dr Fei Song

Dr Haobo Zhang

APPENDIX B: EXTERNAL APPOINTMENTS

Dr Nady Braidy

- Honorary Fellow, Australian School of Advanced Medicine, Macquarie University
- Adjunct Lecturer, School of Biotechnology and Biomolecular Sciences, UNSW
- Health Services Advisor, Department of Aged Care and Rehabilitation, Bankstown-Lidcombe Hospital, Sydney, Australia
- Editor: *Current Alzheimer Research; CNS and Neurological Disorders; Analytical Cellular Pathology*
- Reviewer for ARC, NHMRC.

Professor Henry Brodaty

- Scientia Professor, Ageing and Mental Health, (previously Professor of Psychogeriatrics, 1990-2010), School of Psychiatry, UNSW (2011-2016)
- Montefiore Chair of Healthy Brain Ageing (2012-present)
- Director, Primary Dementia Collaborative Research Centre, UNSW (2006-present)
- Head (and Founder), Memory Disorders Clinic, Prince of Wales Hospital (1985 -present)
- Senior Clinician, Aged Care Psychiatry, Prince of Wales Hospital (1990-present)
- President International Psychogeriatric Association (2013-2015); Immediate Past-President (2015-2017)
- Member, International Advisory Committee of the National Institute of Dementia, South Korea (2013-2017)
- Honorary Professor, Kiang Wu Nursing College, Macau (2014-present)
- Theme Leader for psychosocial and public health, Scientific Program Committee, Alzheimer's Association International Conference (2014-2016)
- Honorary Lifetime Vice-President, Alzheimer's Disease International (ADI) (2005-present)
- Chair, Scientific Program Committee, Alzheimer's Disease International Annual Congress (2015)
- Honorary Medical Advisor, Alzheimer's Australia NSW (1992-present)
- Chairman, Dementia Research Foundation Ltd, Alzheimer's Australia (2002-2016)
- Member, Australian Advisory Board for Nutricia, (2012-present)
- Member, WHO Consultation Group on the Classification of Behavioural and Psychological Symptoms in Neurocognitive disorders for ICD-11 (2012-present)
- Ambassador, Montefiore Homes (2006-present)
- Chair, Clinical Advisory Committee, Montefiore Homes (2012-present)
- Editorial board for *Aging and Mental Health* (1996-present), *Alzheimer Disease and Associated Disorders : an International Journal* (1995-present), *Alzheimers and Dementia: Journal of the Alzheimers Association* (2005-present), *Australian and New Zealand Journal of Psychiatry* (1981-present), *CNS Drugs* (1999-present), *Dementia and Geriatric Cognitive Disorders* (2010-present), *International Psychogeriatrics* (1996-present), *Neurodegenerative Disease Management* (2010-present), *The Australian Journal of Dementia Care* (2012-present)

Professor Lynn Chenoweth

- Member, Research Advisory Group, Parkinson's Australia
- Member, Conference Advisory Committee, Alzheimer's Disease International
- Honorary Research Associate, Macau College of Nursing
- Member, UTS Centre for Mechatronic and Intelligent Systems, University of Technology Sydney
- Member, UTS Centre for the Study of Choice (CenSoc), University of Technology Sydney

- Approved Supervisor, Faculty of Health, University of Technology Sydney
- Adjunct Professor, School of Nursing, Notre Dame University
- Member, Nursing Curriculum Advisory Committee, Notre Dame University
- Member, Primary Health Care Curriculum Advisory Committee, Notre Dame University
- Member, Executive Board Advisory Committee, Australian Multicultural Aged care Nursing (AMAN), Lebanese Muslim Association
- Member, Expert Advisory Research Group, University of Bradford
- Editorial board for *International Journal of Older People Nursing, Nursing Older Person Journal, Austin Journal of Nursing and Health Care*.

Dr Nicole Kochan

- Clinical Neuropsychologist, Neuropsychiatric Institute, Prince of Wales Hospital
- Honorary Associate, Department of Psychology, Macquarie University
- Member, College of Clinical Neuropsychologists, Australian Psychological Society
- Approved Supervisor, College of Clinical Neuropsychologists, Australian Psychological Society

Dr Karen Mather

- Visiting Research Fellow, Neuroscience Research Australia (NeuRA)

Dr Adith Mohan

- Consultant Neuropsychiatrist, Neuropsychiatric Institute, Prince of Wales Hospital
- Fellow, the Royal Australian and New Zealand College of Psychiatrists (RANZCP)
- NSW jurisdictional representative, Section of Neuropsychiatry, RANZCP

Dr Anne Poljak

- Senior Research Scientist, Bioanalytical Mass Spectrometry Facility, Mark Wainwright Analytical Centre, UNSW
- Conjoint Lecturer, School of Medical Sciences, UNSW
- Member, Scientific Review Committee, NSW Brain Bank Network (NSWBBN)
- Member, Scientific Advisory Committee, Rebecca L. Cooper Medical Research Foundation
- Member, NHMRC National Institute for Dementia Research, Working Group: Standardisation Protocol for Blood Collection and Storage
- Reviewer, Alzheimer's Association International Conference (biomarkers, non-neuroimaging).

Professor Perminder Sachdev

- Scientia Professor, Neuropsychiatry (previously Professor of Neuropsychiatry, 1999-2009), School of Psychiatry, UNSW (2009-present)
- Clinical Director, Neuropsychiatric Institute, Prince of Wales Hospital, Sydney (1987-present)
- Chief Medical Adviser to Alzheimer's Australia (2014-present)
- Visiting Fellow, Australian National University (2009-present)
- Visiting Professor, National University of Korea, Seoul (2014-2018)
- Member of the International Advisory Group for the Revision of ICD-10 Mental and Behavioural Disorders and the International Advisory Group for the Revision of ICD-10 Diseases of the Nervous System, WHO ICD-11 Expert Working Group on Neurocognitive Disorders, Mental Health and Substance Abuse Department (2011-present)
- Committee Member of the WHO's Expert Advisory Committee for the Global Dementia Observatory (GDO)
- Executive Member of the International Society of Vascular Behavioural and Cognitive Disorders (VASCOG) (2012-present)
- Founding Executive Committee Member of the Tourette Syndrome Association of Australia (1989-present)
- Scientific Advisory Committee Member of the Alzheimer's Association of Australia (1995-present)
- Committee Member on Psychotropic Drugs and Other Physical Treatments, Royal Australian and New Zealand College of Psychiatrists (1996-present)

- Chair, Medical Advisory Committee of the Tourette Syndrome Association of Australia (1996-present)
- Fellow of the Australian Academy of Health & Medical Sciences (2015-present)
- Fellow of the NHMRC Academy 2011 (2011-present)
- Member of the NHMRC Assigner's Academy (2012-present)
- Invited Member, Task Force of the International League Against Epilepsy (ILAE) Neuropsychobiology Commission (2011-present)
- Editorial board for *Neuropsychiatric Disorders and Treatment, Acta Neuropsychiatrica, Current Opinion in Psychiatry, Middle Eastern Journal of Ageing, Middle Eastern Journal of Psychiatry & Alzheimer's, Brain and Mind Matters, The Open Neuroimaging Journal, American Journal of Geriatric Psychiatry.*

Hon. Associate Professor Kuldip Sidhu

- Visiting Professor, Department of Neurology, Tianjin Huanhhu Hospital, China
- Founding Director & CEO Cell Therapeutics Pty Ltd
- Director, CK Cell Technologies Pty Ltd
- Co-Chair, G20 Initiative SBMT
- President & Chief Operating Officer, World Brain Mapping Foundation, Australia
- Member, Board of Directors, Society for Brain Mapping & Therapeutics, USA
- Member, Executive Committee, Australasian Society of Stem Cells & Research, Australia
- Member, Expert Research Panel, European Union (2011-present)
- Expert Research Review Panel, A*Star, Singapore (2011-present)
- Editorial board for *International Journal of Stem Cells, International Journal of Biological Chemistry, Recent Patents on Stem Cells, Journal of Neurological Disorders, The Open Stem Cell Journal, Journal of Neurology & Neuroscience, The Journal of Stem Cells & Therapeutics, Austin Alzheimer's and Parkinson's Disease.*

Professor Julian Trollor

- Chair, Intellectual Disability Mental Health, School of Psychiatry, UNSW
- Senior Medical Practitioner (Academic), Professor in Neuropsychiatry and Intellectual Disability, South Eastern Sydney Local Health District, Sydney
- Visiting Senior Research Fellow, Neuroscience Research Australia (NeuRA)
- Member, NSW Institute of Psychiatry Board
- Convenor of RANZCP 2017 Congress, Member of the Scientific Program Committee
- Fellow, the Royal Australian and New Zealand College of Psychiatrists (RANZCP)
- Member, Faculty of Psychiatry of Old Age, RANZCP
- Founder, Neuropsychiatry Section, RANZCP
- Co-Founder & Executive Member, Intellectual and Developmental Disability Special Interest Group, RANZCP
- Executive Committee Member, NSW Health Agency for Clinical Innovation, Intellectual Disability Health Network
- Executive Member, NSW Ministry of Health; Department of Family and Community Services, Joint Committee Intellectual Disability Mental Health
- Member, Panel of Expert Advisers, NSW Ombudsman
- Executive Member & Immediate Past Secretary & Treasurer, International Neuropsychiatric Association
- International Member, Neuroleptic Malignant Syndrome Information Service
- Member, Australasian Society for the Study of Intellectual Disability
- Member, National Association for the Dually Diagnosed
- Member, Joint Committee, NSW Health and Ageing Disability and Home Care, NSW Government Family and Community Services
- Member, Intellectual Disability Advisory Committee 2016
- Member, NSW Council for Intellectual Disability
- Member, Research Advisory Committee, NSW Mental Health Commission
- Member, Society for the Study of Behavioural Phenotypes

- Vice President & Member, Australian Association of Developmental Disability Medicine
- Member, Neurocognitive Disorder Working Group, Diagnostic Manual for Intellectual Disability
- Unconditional Registration, the New South Wales Medical Board, currently Australian Health Practitioner Regulation Agency
- Member, Research and Development Committee, NSW Health Agency for Clinical Innovation, Intellectual Disability Health Network
- Member, UNSW/FACS Joint Working Group
- Member, The Australasian Society for Psychiatric Research
- Member, The Australian Medical Association
- Member, The Australian Salaried Medical Officers Federation
- Member, The International Association for the Scientific Study of Intellectual Disability
- Member, Australasian Society for the Study of Intellectual Disability
- Member, International Neuropsychiatric Association
- Member, Health Education and Training Institute Higher Education Governing Council HETI.

APPENDIX C: POSTGRADUATE STUDENTS

CURRENT

Andrew Affleck

- Effects of anti-hypertensive medications on Alzheimer and cerebrovascular disease neuropathology
- PhD student
- School of Psychiatry, Faculty of Medicine, UNSW
- Supervisors: Professor Perminder Sachdev, Professor Glenda Halliday

Anne-Nicole Casey

- Two degrees to social isolation: Friendship schema & resident peer networks within a high-care residential aged care facility
- PhD student
- School of Psychiatry, Faculty of Medicine, UNSW
- Supervisors: Associate Professor Lee-Fay Low, Professor Yun-Hee Jeon, Professor Henry Brodaty

Sophie Chen

- The relationship of diet to neurocognitive health
- Masters by Research student
- School of Psychiatry, Faculty of Medicine, UNSW
- Supervisors: Professor Henry Brodaty, Dr Fiona O'Leary

Lucia Premilla Chinnappa-Quinn

- A study of the effect of acute physical illness requiring hospitalisation on the long-term cognitive and functional trajectory of two elderly cohorts: The Sydney Memory and Aging Study (MAS) and the Older Australian Twins Study (OATS)
- PhD student
- School of Psychiatry, Faculty of Medicine, UNSW
- Supervisors: Professor Michael Bennett, Professor Perminder Sachdev, Dr Nicole Kochan, Dr John Crawford

Fleur Harrison

- Apathy in older community-dwelling persons: Improving assessment, investigating its association with immune markers, differentiating from depression and fatigue and modelling its longitudinal course
- PhD student
- School of Psychiatry, Faculty of Medicine, UNSW
- Supervisors: Professor Henry Brodaty, Dr Liesbeth Aerts, Dr Katrin Seeher, Professor Adam Guastella, Professor Julian Trollor, Professor Andrew Lloyd

Jessica Lazarus

- Epigenetics and longevity
- PhD student
- Department of Anatomy, School of Medical Sciences, Faculty of Medicine, UNSW
- Supervisors: Dr Karen Mather, Associate Professor John Kwok

Janet Mitchell

- Service networks and their influence on the care of those with dementia in residential care
- PhD student
- School of Psychiatry, Faculty of Medicine, UNSW
- Supervisor: Professor Henry Brodaty, Professor Jeoffrey Braithwaite

Adith Mohan

- Influence of ageing on the human brain transcriptome
- PhD student
- School of Psychiatry, Faculty of Medicine, UNSW
- Supervisors: Dr Karen Mather, Professor Perminder Sachdev, Dr Anbupalam Thalamuthu

Claire O'Connor

- Understanding behaviour and function in frontotemporal dementia: Developing better assessments and intervention approaches
- PhD Student
- University of Sydney
- Supervisors: Professor Lindy Clemson, Professor Henry Brodaty

Alistair Perry

- Combined investigation of structural and functional connectivity in normal ageing and Alzheimer's disease
- PhD student
- School of Psychiatry, Faculty of Medicine, UNSW
- Supervisors: Associate Professor Wei Wen, Professor Perminder Sachdev, Professor Michael Breakspear

Mary Revelas

- The genetics of exceptional longevity and successful ageing
- PhD student
- School of Psychiatry, Faculty of Medicine, UNSW
- Supervisors: Dr Karen Mather, Dr Anbupalam Thalamuthu, Professor Perminder Sachdev

Upul Senanayake

- Computer aided early identification system for Individuals at risk of dementia
- PhD student
- School of Computer Science and Engineering, Faculty of Engineering, UNSW
- Supervisors: Professor Arcot Sowmya, Dr Laughlin Dawes, Professor Perminder Sachdev, Associate Professor Wei Wen

Gillian Stockwell-Smith

- A randomised controlled trial of a community based intervention for caregivers of people with dementia
- PhD student
- Centre for Health Practice Innovation, Griffith University
- Supervisors: Dr Ursula Kellett, Professor Wendy Moyle, Professor Henry Brodaty

Ruby Tsang

- Biomarkers of late-life depression
- PhD student
- School of Psychiatry, Faculty of Medicine, UNSW
- Supervisors: Dr Simone Reppermund, Professor Perminder Sachdev, Associate Professor Wei Wen, Dr Karen Mather

Jacqueline Wesson

- Evaluating functional cognition and performance of everyday tasks in older people with dementia – the validity, reliability and usefulness of the Allen's model of cognitive disability
- PhD student
- Faculty of Health Sciences, University of Sydney
- Supervisors: Professor Lindy Clemson, Professor Henry Brodaty, Dr Simone Reppermund

Matthew Wong

- Biomarkers of oxidative stress in healthy human brain ageing and Alzheimer's disease
- PhD student
- School of Psychiatry, Faculty of Medicine, UNSW
- Supervisors: Dr Nady Braidy, Professor Perminder Sachdev, Dr Anne Poljak

Helen Wu

- The role of peripheral blood microRNAs as biomarkers of early Alzheimer's disease
- PhD student
- School of Psychiatry, Faculty of Medicine, UNSW
- Supervisors: Dr Karen Mather, Professor Perminder Sachdev, Professor Henry Brodaty

SUBMITTED

Tharusha Jayasena

- The role of polyphenolic compounds in modulating sirtuins and other pathways involved in Alzheimer's disease
- PhD student
- School of Psychiatry, Faculty of Medicine, UNSW
- Supervisors: Professor Perminder Sachdev, Dr Anne Poljak
- Thesis submitted September 2016

COMPLETED

Jiyang Jiang

- The association of macrophage inhibitory cytokine-1 with ageing brains
- PhD student
- School of Psychiatry, Faculty of Medicine, UNSW
- Supervisors: Associate Professor Wei Wen, Professor Perminder Sachdev
- PhD conferred June 2016

Zixuan Yang

- Age-associated structural brain changes on MRI from the eighth to eleventh decade of life
- PhD student
- School of Psychiatry, Faculty of Medicine, UNSW
- Supervisors: Professor Perminder Sachdev, Associate Professor Wei Wen
- PhD conferred June 2016

APPENDIX D: AWARDS & PROMOTIONS

Dr Nady Braidy

- ARC DECRA Early Career Research Fellowship (commences in 2017) for a project titled *"Promotion of NAD+ anabolism to promote lifespan"*.
- Promoted to Lecturer in the School of Psychiatry.

Professor Henry Brodaty

- Ryman Prize.

Professor Perminder Sachdev

- Mahatma Gandhi Pravasi Samman Award for outstanding services, achievements and contributions. Presented at the Global Indian Summit at the House of Lords, London, UK, 30 September 2016.

APPENDIX E: RESEARCH GRANTS & FUNDING

GRANTS

Risk factors, early diagnosis and effective interventions for neurocognitive disorders

Funding Source: National Healthy & Medical Research Council (NHMRC)
Project ID: RG141685
Investigator/s: Prof Perminder Sachdev, Prof Henry Brodaty, Prof Gavin Andrews
Duration: 5 years: 2016-2020
Total Funds: $6,782,730

BRIDGET: Brain imaging, cognition, Dementia and next generation GEnomics: A Transdisciplinary approach to search for risk and protective factors of neurodegenerative disease

Funding Source: NHMRC NIDR-EU JPND Co-funded Project Grant
Project ID: RG152067
Investigators: Prof Perminder Sachdev, Dr Karen Mather, Dr Anbupalam Thalamuthu, A/Prof Wei Wen, Dr Nicola Armstrong
Duration: 3 years: 2016-2018
Total Funds: $1,081,489

A European DNA bank for deciphering the missing heritability of Alzheimer's disease (EADB)

Funding Source: NHMRC NIDR-EU JPND Co-funded Project Grant
Project ID: RG152100
Investigators: Prof Perminder Sachdev, Dr Karen Mather, Dr Anbupalam Thalamuthu, Dr Nicola Armstrong, Prof Henry Brodaty
Duration: 3 years: 2016-2018
Total Funds: $1,556,995

Apathy in older community-dwelling persons: Assessment, investigation, differentiation

Funding Source: Alzheimer's Australia Dementia Research Fund (AADRF)/DCRC Early Diagnosis and Prevention Shared Grant – PhD Scholarship for Ms Fleur Harrison
Project ID: RG161424
Investigator/s: Prof Henry Brodaty (Supervisor), Ms Fleur Harrison
Duration: 4 years: 2016-2019
Total Funds: $60,000

A novel MRI-based cerebrovascular pathology index: Development and validation

Funding Source: ANU NNIDR DCRC Early Diagnosis and Prevention Shared Grant
Project ID: RG161864
Investigator/s: Dr Matthew (Matt) Paradise
Duration: 1 year: July 2016- July 2017
Total Funds: $56,717

MicroRNAs as biomarkers for Alzheimer's disease – comparison between Australian and Chinese populations

Funding Source: SJTU-UNSW Collaborative Research Fund – Seed Grant
Project ID: RG152795
Investigator/s: Prof Henry Brodaty, Dr Helen Wu
Duration: 1 year: 2016*
Total Funds: $10,000

***Extended to 30 June 2017*

Structure and function of two apolipoproteins with roles in brain ageing

Funding Source: UNSW Sydney - Goldstar Award
Project ID: RG153025
Investigator/s: Prof Perminder Sachdev, Dr Anne Poljak, Prof Mark Duncan
Duration: 1 year: 2016
Total Funds: $40,000

Maintain Your Brain

Funding Source: NHMRC
Project ID: RG142234
Investigator/s: Prof Henry Brodaty, A/Prof Michael Valenzuela, Prof Perminder Sachdev, Prof John McNeil, Prof Anthony Maeder, Prof Nicola Lautenschlarger, Prof Louisa Jorm, Prof Maria Fiatarone Singh, Prof Kaarin Anstey, Prof Gavin Andrews
Duration: 5 years: 2015-2019
Total Funds: $6,467,015

The genetic and environmental determinants of amyloid deposition in older individuals: An amyloid imaging study using the twin design

Funding Source: NHMRC
Project ID: RG140593
Investigators: Prof Perminder Sachdev, Professor Christopher Rowe, A/Prof Wei Wen, Dr Melissa Slavin
Duration: 3 years: 2015-2017
Total Funds: $625,404

Apolipoprotein levels and post-translational modifications as blood biomarkers for early stages of Alzheimer's disease

Funding Source: Rebecca L Cooper Medical Research Foundation
Project ID: RG142199
Investigator/s: Dr Julia Muenchhoff, Dr Anne Poljak, Prof Perminder Sachdev
Duration: 1 year: April 2015-April 2016
Total Funds: $21,398

Improved accessibility and long-term storage of biospecimens from the Centre for Healthy Brain Ageing's (CHeBA) longitudinal studies

Funding Source: UNSW Australia MREII Grant
Project ID: RG142871
Investigator/s: Prof Perminder Sachdev, Prof Henry Brodaty, Dr Julia Muenchhoff, Dr Anne Poljak, Dr Nady Braidy, et. al
Duration: 1 year: 2015*
Total Funds: $173,871

**Extended to November 2016*

Biomarkers of late-life depression and associated cognitive impairment

Funding Source: Alzheimer's Australia Dementia Research Foundation – Postgraduate Scholarship
Project ID: RG134526
Investigator/s: Ms Ruby Tsang, Prof Perminder Sachdev
Duration: 3 years: 2014-2016
Total Funds: $90,000

Isoform-dependent apoE processing by human induced pluripotent stem cells: A novel pathway linking APOE genotype and Alzheimer's disease risk

Funding Source: University of Wollongong / NHMRC Project Grant Shared Grant
Project ID: RG143042
Investigator/s: A/Prof Kuldip Sidhu
Duration: 1 year: 2015*
Total Funds: $28,944

Towards understanding the role of long non-coding RNA in age-related memory decline – an early marker of Alzheimer's disease

Funding Source: Yulgilbar Foundation
Project ID: RG141699
Investigator/s: Dr Karen Mather
Duration: 1 year: 2014-2015
Total Funds: $20,000

Improving clinical diagnosis of mild neurocognitive disorders

Funding Source: NHMRC Early Career Fellowship
Project ID: RG123148
Investigator/s: Dr Nicole Kochan
Duration: 4 years: 2013-2016
Total Funds: $149,782

Sirtuin single nucleotide polymorphisms in brain ageing

Funding Source: NHMRC Early Career Fellowship
Project ID: RG123293
Investigator/s: Dr Nady Braidy
Duration: 4 years: 2013-2016
Total Funds: $299,564

The Older Australian Twins Study (OATS) of healthy brain ageing and age-related neurocognitive disorders

Funding Source: NHMRC
Project ID: RG122225
Investigator/s: Prof Perminder Sachdev, Dr Margie Wright, Prof David Ames, A/Prof Julian Trollor, A/Prof Wei Wen, Prof Bernhard Baune, Dr Teresa Lee, Dr John Crawford
Duration: 3 years: 2013-2015
Total Funds: $912,023

Project closed & acquitted January 2016

Cognition following non-cardiac surgery and anaesthesia (PhD Project)

Funding Source: NHMRC / DCRC-ABC
Project ID: RG161541-B (ex-RG102939-O)
Investigator/s: Prof Perminder Sachdev, Premilla Chinnappa-Quinn
Duration: 3 years: 2013-2015*
Total funds: $30,000

**Extended to March 2017*

Cognition following non-cardiac surgery and anaesthesia: A study of neuropsychological and functional changes in the first year post-procedure

Funding Source: Australian Society of Anaesthetists / PhD Grant Support
Project ID: RG123624
Investigator/s: Premilla Chinnappa-Quinn
Duration: 3 years: 2013-2015*
Total Funds: $9091

**Extended to March 2017*

Computerised neuropsychological testing for early diagnosis of mild cognitive impairment and dementia

Funding Source: Dementia Collaborative Research Centre – Assessment & Better Care
Project ID: RG133185-C
Investigator/s: Dr Nicole Kochan
Duration: 1 year: 2013-2014*
Total Funds: $50,000

**Extended to June 2016*

The prevention, early detection and effective management of neurocognitive disorders in the elderly

Funding Source: NHMRC
Project ID: RM06756
Investigator/s: Prof Perminder Sachdev, Prof Henry Brodaty, Prof Gavin Andrews
Duration: 5 years: 2010-2014*
Total Funds: $50,000

**Extended to March 2017*

Prevention and management of mental disorders in older Australians

Funding Source: NHMRC
Project ID: RM06714
Investigator/s: Prof Perminder Sachdev, Prof Henry Brodaty, Prof Gavin Andrews, Dr Stephen Lord
Duration: 5 years: 2009-2014*
Total Funds: $2,352,525*

**Extended to December 2015; Project acquitted & closed June 2016*

PHILANTHROPIC

The CHeBA Cerebral Small Vessel Disease (SVD) Fund

Funding Source: John Holden Family Foundation
Project ID: PS41604_PS41625
Awardees: Prof Perminder Sachdev
Duration: 6 years: 2016-2020
Total Funds: $600,000

The Dementia Momentum Initiative, incorporating the Wipeout Dementia Campaign

Funding Source: Roth Charitable Foundation
Project ID: PS38252
Awardees: Prof Perminder Sachdev
Prof Henry Brodaty
Duration: 5 years: 2016-2020
Total Funds: $90,000

Funding Source: Sachdev Foundation
Project ID: PS38252
Awardees: Prof Perminder Sachdev
Prof Henry Brodaty
Duration: 1 year: 2016
Total Funds: $40,000

Funding Source: Vincent Fairfax Family Foundation
Project ID: PS42069_PS42704
Awardees: Prof Perminder Sachdev
Prof Henry Brodaty
Duration: 5 years: 2015-2019 (Final 2 years contingent on meeting outcomes)
Total Funds: $500,000

The Montefiore Chair of Health Brain Ageing at UNSW

Funding Source: The Sir Moses Montefiore Jewish Home
Project ID: PS34587_PS34590
Awardees: Prof Henry Brodaty
Prof Perminder Sachdev
Duration: 5 years: 2011-2015
Total Funds: $665,000

Thomas Foundation Faculty Matching Funds

Funding Source: UNSW Medicine
Project ID: PS39895*
Awardees: Prof Perminder Sachdev
Prof Henry Brodaty
Duration: 3 years: 2015-2017
Total Funds: $335,000

**Amalgamated with PS34586_PS34589 November 2016*

The Thomas Foundation Grant

Funding Source: The Thomas Foundation
Project ID: PS34586_PS34589
Awardees: Prof Henry Brodaty
Prof Perminder Sachdev
Duration: 5 years: 2011-2015
Total Funds: $1,000,000

OTHER

The Healthy Brain Ageing Fund

Funding Source: Miscellaneous
Project ID: PS22384_PS41631 (ex-PS26303)
Awardees: Prof Henry Brodaty
Prof Perminder Sachdev
Duration: Ongoing
Total Funds: $229,364*

**As at 31 December 2016*

Centre for Healthy Brain Ageing Event & Sponsorship Fund

Funding Source: Miscellaneous
Project ID: PS33379_PS33397
Awardees: Prof Henry Brodaty
Prof Perminder Sachdev
Duration: Ongoing
Total Funds: $54,504.60*

**As at 31 December 2016*

APPENDIX F: STATEMENT OF IN-KIND CONTRIBUTIONS

- AMP
- ARIA Restaurant Sydney
- Breathe Fire Specialised Training
- Hurley
- HWL Ebsworth Lawyers
- KPMG
- Murray Fraser, Sprout Daily
- Queenscliff Surf Life Saving Club
- The Bucket List

APPENDIX G: STATEMENT OF FINANCIAL PERFORMANCE

STATEMENT OF FINANCIAL PERFORMANCE FOR THE YEAR ENDED 31 DECEMBER 2016

	Notes	2016 $	2015 $
Funds			
Research Revenue		5,154,650	737,838
Donations		819,627	583,873
Fees		-	-
Faculty Funds	3	-	-
UNSW Contribution - Competitive	1	67,161	229,387
UNSW Contribution - Strategic	2	40,000	240,000
Sundry Other Revenue		1,309	20,260
Total Funds		**6,082,747**	**1,811,358**
Costs			
People Costs		2,520,381	1,672,752
Scholarship Stipends		92,190	71,049
Contract & Consulting Services		377,587	106,567
Repairs and Maintenance		779	120
Consumables		56,770	52,758
Travel		57,305	53,775
Equipment		60,376	25,063
Other Expenses		69,623	36,423
Internal Expense		(39,515)	(61,178)
Total Costs		**3,195,494**	**1,957,329**
Operating result		2,887,254	(145,971)
Opening Balance	1	460,338	606,309
Closing Balance		**3,347,592**	**460,338**

Notes to the Statement of Financial Performance

1. UNSW Contribution - Competitive relates to funding awarded to CHeBA from UNSW through various competitive schemes supporting research activities and infrastructure.
2. UNSW Contribution - Strategic relates to funding provided to CHeBA from UNSW as a strategic investment in the centre's research activities.
3. Faculty Funds - Operating funds provided by the faculty are budget allocations, with no revenue transferred to CHeBA.

APPENDIX H: PUBLICATIONS

Book Chapters

Chenoweth L. 'Personnel recruitment and retention in long-term elder care'. In Boll T, Ferring D, Valsiner J. *Cultures of care: Handbook of cultural geropsychology* (Eds) 1st edition. Section 5, Chapter 17. Information Age Publisher. In press.

Sachdev PS. Vascular cognitive disorders. In: Fillit HM, Rockwood K, Young JB (Eds) *Brocklehurst's textbook of geriatric medicine and gerontology, 8th edition*. Elsevier, Inc: Philadelphia, PA, USA. 2016. ISBN: 9780702061851.

Taylor L, Mohan A, Sachdev PS. Chapter 7: The validity of vascular depression as a diagnostic construct. In: Baune BT, Tully PJ (Eds) *Cardiovascular diseases and depression: Treatment and prevention in psychocardiology*. Springer. 2016; pp. 81-104. ISBN: 9783319324784 / 9783319324807. DOI: 10.1007/978-3-319-32480-7_7.

Theobald A, Daly C, Yang Z, Mather KA, Muenchhoff J, Crawford J, Sachdev P. Sydney Centenarian Study. In: Pachna NA (Ed) *Encyclopedia of geropsychology*. Springer: Singapore. 2016; 1-8. ISBN: 9789812870810. DOI: 10.1007/978-981-287-080-3_140-1.

Journal Articles

Adams HHH, Hibar DP, Chouraki V, Stein JL, Nyquist P, …, Brodaty H, …, Mather KA, …, Sachdev PS, …, Thalamuthu A, …, Wen W, et al. Novel genetic loci underlying human intracranial volume identified through genome-wide association. *Nat Neurosci*. 2016 Dec;19(12):1569-1582. DOI: 10.1038/nn.4398. PMID: 27694991

[Epub 2016 Oct 3].

Ajami M, Pazoki-Toroudi H, Amani H, Nabavi SF, Braidy N, Vacca RA, Atanasov AG, Mocan A, Nabavi SM. Targeting SIRT1 signaling by polyphenols: A 'lock and key' strategy for the treatment of neurodegeneration. *Neurosci Biobehav Rev*. 2016; in press. Accepted Nov 2016.

Balez R, Steiner N, Engel M, Muñoz SS, Lum JS, Wu Y, Wang D, Vallotton P, Sachdev P, O'Connor M, Sidhu K, Münch G, Ooi L. Neuroprotective effects of apigenin against inflammatory activation, neuronal excitability and apoptosis in an induced pluripotent stem cell model of Alzheimer's disease. *Sci Rep*. 2016; 6:31450. DOI: 10.1038/srep31450. PMID: 27514990 [Epub 2016 Aug 12].

Beattie E, Chenoweth L, Moyle W, Robinson A, Horner B, O-Reilly M, Fetherstonhaugh D, Fielding E. Living with dementia in Australia's nursing homes: Multiple lenses on quality of life. *Gerontologist*. 2016; 56:747-748.

Braidy N, Essa MM, Poljak A, Subash S, Aladawi S, Manivasagam T, Thenmozhi AJ, Ooi L, Sachdev PS, Guillemin G. Consumption of pomegranates improves synaptic function in a transgenic mouse model of Alzheimer's disease. *Oncotarget*. 2016 July 28. DOI: 10.18632/oncotarget.10905. PMID: 27486879 [Epub 2016 July 28].

Braidy N, Rossez H, Lim CK, Jugder BE, Brew BJ, Guillemin GJ. Characterization of the kynurenine pathway in CD8+ human primary monocyte-derived dendritic cells. *Neurotox Res*. 2016 Nov; 30(4):620-632. DOI: 10.1007/s12640-016-9657-x. PMID: 27510585 [Epub 2016 Aug 10].

Brodaty H, Connors MH, Loy C, Teixeira-Pinto A, Stocks N, Gunn J, Mate KE, Pond CD. Screening for dementia in primary care: A comparison of the GPCOG and the MMSE. *Dement Geriatr Cogn Disord*. 2016; 42(5-6):323-330. PMID: 27811463 [Epub 2016 Nov 4].

Brodaty H, Woolf C, Andersen S, Barzilai N, Brayne C, Cheung KS, Corrada MM, Crawford JD, Daly C, Gondo Y, Hagberg B, Hirose N, Holstege H, Kawas C, Kaye J, Kochan NA, Lau BH, Lucca U, Marcon G, Martin P, Poon LW, Richmond R, Robine JM, Skoog I, Slavin MJ, Szewieczek J, Tettamanti M, Viña J, Perls T, Sachdev PS. ICC-Dementia (International Centenarian Consortium-Dementia): An international consortium to determine the prevalence and incidence of dementia in centenarians across diverse ethnoracial and sociocultural groups. *BMC Neurol*. 2016 Apr 21; 16:52. DOI: 10.1186/s12883-016-0569-4. PMID: 27098177 [Epub 2016 Apr 21].

Bunce D, Haynes BI, Lord SR, Gschwind YJ, Kochan NA, Reppermund S, Brodaty H, Sachdev P, Delbaere K. Intraindividual stepping reaction time variability predicts falls in older adults with mild cognitive impairment. *J Gerontol A Biol Sci Med Sci*. 2016 Sep 3. pii: glw164. DOI: 10.1093/gerona/glw164. PMID: 27591431 [Epub ahead of print].

Burke C, Stein-Parbury J, Luscombe G, Chenoweth L. Development and testing of the Person-Centred Environment and Care Assessment Tool (PCECAT). *Clin Gerontol*. 2016; 39(4):282-308. DOI: 10.1080/07317115.2016.1172532.

Casey AN, Low LF, Jeon YH, Brodaty H. Residents' perceptions of friendship and positive social networks within a nursing home. *Gerontologist*. 2016 Oct; 56(5):855-67. DOI: 10.1093/geront/gnv146. PMID: 26603182 [Epub 2015 Nov 23].

Casey AS, Low LF, Jeon YH, Brodaty H. Residents' positive and negative relationship networks in a nursing home. *J Gerontol Nurs*. 2016 Nov 1; 42(11):9-13. DOI: 10.3928/00989134-20160901-06. PMID: 27598269 [Epub 2016 Sep 6].

Chan D, Braidy N, Xu YH, Chataway T, Guo F, Guillemin GJ, Teo C, Gai WP. Interference of β-synuclein uptake by monomeric β-Amyloid1-40 and potential core acting site of the interference. *Neurotox Res*. 2016 Oct; 30(3):479-85. DOI: 10.1007/s12640-016-9644-2. PMID: 27364697 [Epub 2016 Jun 30].

Chenoweth L. Developing self-efficacy in caring for people with dementia improves family carer health and well-being. *AJDC* 2016; 54(4):32-35.

Chenoweth L, Stein-Parbury J, White D, McNeill G, Jeon YH, Zaratan B. Coaching in self-efficacy improves care responses, health and well-being in dementia carers: A pre/post-test/follow-up study. *BMC Health Serv Res*. 2016 May 4; 16:166. DOI: 10.1186/s12913-016-1410-x. PMID: 27146060.

Connors MH, Ames D, Boundy K, Clarnette R, Kurrle S, Mander A, Ward J, Woodward M, Brodaty H. Mortality in mild cognitive impairment: A longitudinal study in memory clinics. *J Alzheimers Dis*. 2016 Jul 27; 54(1):149-55. DOI: 10.3233/JAD-160148. PMID: 27472874.

Cross AJ, George J, Woodward MC, Ames D, Brodaty H, Ilomäki J, Elliott RA. Potentially inappropriate medications and anticholinergic burden in older people attending memory clinics in Australia. *Drugs Aging*. 2016 Jan;33(1):37-44. DOI: 10.1007/s40266-015-0332-3. PMID: 26645294.

D'Mello F, Braidy N, Marçal H, Guillemin G, Rossi F, Chinian M, Laurent D, Teo C, Neilan BA. Cytotoxic effects of environmental toxins on human glial cells. *Neurotox Res*. 2017 Feb; 31(2):245-258. DOI: 10.1007/s12640-016-9678-5. PMID: 27796937 [Epub 2016 Oct 29].

Dichgans M, Wardlaw J, Zietemann V, Seshadri S, Sachdev P, Franz Fazekas F, Benavente O, Pantoni L, et al. METACOHORTS for the study of vascular disease and its contribution to cognitive decline and neurodegeneration: an initiative of the Joint Programme for Neurodegenerative Disease research. *Alzheimers Dement*. 2016 Dec; 12(12):1235-1249. DOI: 10.1016/j.jalz.2016.06.004. PMID: 27490018 [Epub 2016 Aug 1].

Delbaere K, Close JC, Brodaty H, Sachdev P, Lord SR. Fall risk and fear of falling in older people: The vigorous, the anxious,

the stoic, and the aware. *Br Med J* 2016; in press. Accepted Dec 2015.

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APPENDIX I: CONFERENCE/PUBLISHED ABSTRACTS

Aerts L, Crawford JD, Kochan NA, Heffernan M, Draper B, Trollor JN, Sachdev PS, Brodaty H. MCI diagnosis: Less is more [Abstract O4-06-05]. *Alzheimer's Association International Conference 2016. 24-28 July 2016; Toronto, Canada. Alzheimers Dement.* 2016; 12(7, Suppl.):P346. DOI: 10.1016/j.jalz.2016.06.641.

Affleck A, Halliday G, Sachdev PS. Anti-hypertensive medications associate with less small vessel disease and Alzheimer pathology. Poster presented at the *Australian and New Zealand Society of Neuropathology (ANZSNP) 34th Annual Scientific Meeting*. Hobart, Australia; 4 Dec 2016.

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Kochan NA, Crawford JD, Brodaty H, Miller-Amberber A, Draper B, Sachdev PS. Influence of linguistic and acculturation characteristics on tradition and computerised neuropsychological test performances in non-native proficient English speakers from the Sydney Memory and Ageing Study [Abstract P2-321]. *Alzheimer's Association International Conference 2016.* 24-28 July 2016; Toronto, Canada. *Alzheimers Dement*. 2016; 12(7, Suppl.):P762-P763. DOI: 10.1016/j.jalz.2016.06.1451.

Lee T, Thalamuthu A, Bowden J, Ames D, Wright M, Sachdev P. Genetic and environmental influences on verbal ability in older adults: Findings from the Older Australian Twins Study. Presented at *46th Annual Behaviour Genetic Association Meeting*. Brisbane, Australia; 23 June 2016. Behav Genet. 2016; 46(6): 793. DOI: 10.1007/s10519-016-9812-4.

Lo J, Sachdev P. STROKOG seminar. Presented at the *International Society of Vascular Behavioural and Cognitive Disorders (VASCOG 2016*). Amsterdam, The Netherlands; 14 October 2016.

Lo JW, Crawford J, Lipnicki D, Kochan NA, Akinyemi R, Bae H-J, Desmond DW, Dong Y-H, Godefroy O, Kandiah N, Köhler S, Lee B-C, Srikanth V, Sachdev PS for the STROKOG collaboration. Profile of cognitive impairment at 3 to 6 months post-stroke or TIA, in diverse geographical and ethno-cultural settings as represented by the STROKOG member cohorts. Poster presented at the *International Society of Vascular Behavioural and Cognitive Disorders (VASCOG 2016)*. Amsterdam, The Netherlands; 14 October 2016.

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O'Reilly M, Fielding E, Chenoweth L, McMaster M, Beattie E. Measuring person-centred care in the nursing home: philosophy, practices and physical environment. *2016 Gerontological Society of America (GSA) Annual Scientific Meeting*. Nov 2016; New Orleans, USA. Gerontologist. 2016; 56(Suppl.3):744. DOI: 10.1093/geront/gnw162.3033.

Sachdev PS, Lipnicki DM, Crawford JD, Kochan NA, Trollor JN, Draper B, Reppermund S, Maston K, Brodaty H. Risk factors for MCI and dementia over 6 years: The Sydney Memory and Ageing Study [Abstract P2-428]. *Alzheimer's Association International Conference 2016.* 24-28 July 2016; Toronto, Canada. *Alzheimers Dement.* 2016; 12(7, Suppl.):P808-P809. DOI: 10.1016/j.jalz.2016.06.1640.

Sachdev PS, Lipnicki DM, Crawford JD, Thalamuthu A, Kochan NA, Lima-Costa MF, et al. Cognitive decline and effects of sex, education and apolipoprotein E genotype on cognitive performance in diverse ethno-cultural and geographical regions internationally: The COSMIC Collaboration [Abstract P4-235]. Alzheimer's Association International Conference 2016. 24-28 July 2016; Toronto, Canada. Alzheimers Dement. 2016; 12(7, Suppl.):P1119-P1120. DOI: 10.1016/j.jalz.2016.06.2327.

Sachdev P, Thalamuthu A, Mather K, Ames D, Wright M, Wen W. White matter hyperintensities have a strong genetic influence. Presented at the *46th Annual Behaviour Genetic Association Meeting*. Brisbane, Australia; 20-23 June 2016. *Behav Genet*. 2016; 46(6): 804. DOI: 10.1007/s10519-016-9812-4.

Senanayake U, Sowmya A, Dawes L, Kochan N, Wen W, Sachdev P. Classification of mild cognitive impairment subtypes using neuropsychological data [Short Paper]. *Proceedings of the 5th International Conference on Pattern Recognition Applications and Methods (ICPRAM 2016)*. 24-26 Feb 2016; Rome, Italy. 2016:620-629. DOI: 10.5220/0005747806200629.

Slot RER, Sikkes SAM, Verfaillie SCJ, Wolfsgruber S, Brodaty H, Buckley RF, …, Sachdev PS et al. Subjective cognitive decline and progression to dementia due to AD and non-AD in memory clinic and community-based cohorts [Abstract P4-153]. *Alzheimer's Association International*

Conference 2016. 24-28 July 2016; Toronto, Canada. *Alzheimers Dement*. 2016; 12(7, Suppl.):P1073. DOI: 10.1016/j.jalz.2016.06.2245.

Yang Z, Wen W, Jiang J, Crawford JD, Reppermund S, Levitan C, et al. MRI markers of dementia in the eighth to eleventh decades of life [Abstract O4-02-02]. *Alzheimer's Association International Conference 2016*. 24-28 July 2016; Toronto, Canada. *Alzheimers Dementia*. 2016; 12(7, Suppl.):P334-P335. DOI: 10.1016/j.jalz.2016.06.613.

APPENDIX J: WORKSHOPS, CONFERENCES & SPEAKING ENGAGEMENTS

Affleck A, Halliday G, Sachdev PS. Anti-hypertensive medications associate with less small vessel disease and Alzheimer pathology. Poster presented at the *Australian and New Zealand Society of Neuropathology (ANZSNP) 34th Annual Scientific Meeting*. Hobart, Australia; 4 Dec 2016.

Agar M, Luckett T, Luscombe G, Phillips J, Beattie E, Pond D, Mitchell G, Chenoweth L. Pragmatic cluster randomised controlled trial of facilitated family case conferencing versus usual care for people with advanced dementia living in aged care – effects on end of life care. Presented at the *Palliative Care Nurses Australia Conference*. Sydney; September 2016.

Beattie E, Chenoweth L, Moyle W, Robinson A, Horner B, O'Reilly M, Fetherstonhaugh D, Fielding E. Living with dementia in Australia's nursing homes: Multiple lenses on quality of life. Presented at the 2016 *Gerontological Society of America Annual Meeting*. New Orleans, USA; November 2016.

Brodaty H, Sachdev P, Daly C. Invited speaker: International prevalence of dementia, cognitive impairment and functional dependence in centenarians. *IPA Asian Regional Meeting.* Taipei, Taiwan; 12 Dec 2016.

Brodaty H. Invited speaker: Can lifestyle prevent Alzheimer's disease? *IPA Asian Regional Meeting*. Taipei, Taiwan; 10 Dec 2016.

Brodaty H. Invited speaker: Integrated care and safety issues in aging mental health. *IPA Asian Regional Meeting*. Taipei, Taiwan; 9 Dec 2016.

Brodaty H. Invited speaker: Innovation in dementia care – where are we headed? *Strengthening Dementia Services Conference 2016*. Melbourne, Australia; 5 Oct 2016.

Brodaty H, Jessop T, Shell A. How you can understand, prevent, and remedy behavioural and psychological symptoms of dementia (BPSD). *HALT Webinar*; 16 June 2016.

Brodaty H. Invited speaker: Exercise and other lifestyle factors – can cognitive decline and dementia be prevented? *ICAD Conference*. Budapest, Hungary. 22 April 2016.

Brodaty H. Invited speaker: Tricky diagnoses – when dementia is not dementia and depression is not depression. Presented at *Alzheimer's Australia NSW: Spotlight on Dementia Forum*. 26 May 2016.

Brodaty H. Invited speaker: An introduction to dementia. Presented at *Dementia Care Commitment*. Little Sisters of the Poor, Randwick; 22 Aug 2016.

Brodaty H. Invited speaker: Maintain Your Brain. Presented at Montefiore Home, Randwick; 31 Aug 2016.

Brodaty H. Invited speaker: Early detection and prevention of Alzheimer's disease. Presented at *Akolade 2nd Annual Dementia Strategy Summit*. Sydney, Australia. 26 Oct 2016.

Chenoweth L. Transitioning to healthier older life. Presented at the *Academic Department for Aged Care*. Prince of Wales Hospital Psychiatric in-service. Sydney; 6 July 2016.

Chenoweth L. Changes in care models and implications for care workers. Presented the *Future of Aged Care Summit*. Sydney; 1 September 2016.

Chenoweth L, Fielding E, Beattie E, AUSQOL Group. Nursing staff attitudes, stress and strain examined. Presented at the *2016 Gerontological Society of America Annual Meeting*. New Orleans, USA; November 2016.

Chenoweth L, Fry M. Overcoming barriers to timely and effective pain relief for people with dementia in the emergency department. Presented at the *2016 Alzheimer's Disease International (ADI) Conference.* Budapest, Hungary; 21-23 April 2016.

Chenoweth L, Agar M, Luckett T, IDEAL study Group. Facilitated case conferencing improves end of life care outcomes in aged care residents with advanced dementia. Poster presented at the *2016 Alzheimer's Disease International (ADI) Conference.* Budapest, Hungary; 21-23 April 2016.

Chenoweth L, Fry M, Arendts G. Improving pain assessment & treatment for people with cognitive impairment in the Emergency Department. Poster presented at the *NHMRC National Institute of Dementia Research (NNIDR) Inaugural Conference.* Brisbane, Australia; 1-4 May 2016.

Daly C. International prevalence of dementia, cognitive impairment and functional dependence in centenarians. Presented in the *International Centenarian Consortium (ICC) Conference 2016*. Porto, Portugal; 15-19 June 2016.

Jeon Y-H, Simpson J, Kendig H, Cunich M, Li Z, Chenoweth L. Does an aged care specific leadership program for middle managers improve work environment, staff retention and care quality and safety? Session- Care - Education and training of the workforce. Presented at the *2016 Alzheimer's Disease International (ADI) Conference*. Budapest, Hungary; 21-23 April 2016.

Kochan NA, Crawford JD, Brodaty H, Croot K, Miller-Amberber A, Draper B, Sachdev P. The influence of linguistic and acculturation characteristics on neuropsychological test performances in linguistic minorities: The Sydney Memory & Ageing Study. Poster presented at the *Alzheimer's Association International Conference (AAIC) 2016*. Toronto, Canada; 24-28 July 2016.

Kochan N. Invited Speaker: Staying brainy. Presented at *Ansarada Corporate*; February 2016.

Lam T, McLean M, Bahl N, Poljak A, Ho KKY, Birzniece V. Testosterone prevents protein loss via the hepatic urea cycle. Presented at the *Endocrine Society of Australia Symposium*. Gold Coast, Australia; 21-24 Aug 2016.

Lee T, Thalamuthu A, Bowden J, Ames D, Wright M, Sachdev P. Genetic and environmental influences on verbal ability in older adults: Findings from the Older Australian Twins Study. Presented at the *46th Annual Behaviour Genetic Association Meeting.* Brisbane, Australia; 20-23 June 2016.

Lo J, Sachdev P. STROKOG seminar. Presented at the *International Society of Vascular Behavioural and Cognitive Disorders (VASCOG 2016)*. Amsterdam, The Netherlands; 14 October 2016.

Lo JW, Crawford J, Lipnicki D, Kochan NA, Akinyemi R, Bae H-J, Desmond DW, Dong Y-H, Godefroy O, Kandiah N, Köhler S, Lee B-C, Srikanth V, Sachdev PS for the STROKOG collaboration. Profile of cognitive impairment at 3 to 6 months post-stroke or TIA, in diverse geographical and ethno-cultural settings as represented by the STROKOG member cohorts. Poster presented at the *International Society of Vascular Behavioural and Cognitive Disorders (VASCOG 2016)*. Amsterdam, The Netherlands; 14 October 2016.

Luckett G, Phillips J, Chenoweth L, Brooks, Cook, Mitchell G, Pond D, Beattie E, Agar M. Implementing facilitated case conferencing for people living in aged care with advanced dementia – benefits, barriers and facilitators. Presented at the *Palliative Care Nurses Australia Conference.* Sydney; September 2016.

Mather K. Invited speaker at the *Genetics & Epigenetics of Longevity Seminar.* University of Valencia, Spain; 1 June 2016.

Mitchell J. Overcoming challenges to implementing person-centred care. Symposium: Person centered care for persons with dementia-effect, understanding and implementation-challenges and possibilities from nurses' perspective. Presented on behalf of Dr L Chenoweth at the *2016 IPA International Congress*. San Francisco, USA; 9 September 2016.

Mitchell J, Chenoweth L, Long J, Braithewaite J, Brodaty H, Feasibility of investigating the social-professional connections of long-term care residents with dementia and neuropsychiatric symptoms. Presented at the *2016 IPA International Congress*. San Francisco, USA; 6-9 September 2016.

Mohan A, Thalamuthu A, Weickert C, Mather K, Sachdev P. A study of gene expression in the ageing human brain. Presented at the *46th Annual Behaviour Genetic Association Meeting*. Brisbane, Australia; 20-23 June 2016.

Muenchhoff J, Song F, Poljak A, Crawford JD, Mather K, Kochan NA, Yang Z, Trollor JN, Reppermund S, Maston K, Theobald A, Richmond RL, McEvoy M, Attia J, Schofield PW, Brodaty H, Sachdev PS. Plasma apolipoproteins and physical and cognitive health in very old individuals. Poster presented at the *Alzheimer's Association International Conference (AAIC) 2016*. Toronto, Canada; 24-28 July 2016.

O'Reilly M, Fielding E, Chenoweth L, McMaster M, Beattie E. Measuring person-centred care in the nursing home: Philosophy, practices and physical environment. Presented at the *2016 Gerontological Society of America Annual Meeting*. New Orleans, USA; November 2016.

Sachdev P. Invited Speaker: Biomarkers for dementia: Implications for practice and policy. Presented at the *ARDSI 20th Annual National Conference*. Mysuru, India; 10-11 Dec 2016.

Sachdev P. Can we really prevent dementia: Examining the evidence. Presented at the *New Zealand Applied Neuroscience Conference*. Auckland, New Zealand; 24-26 Nov 2016.

Sachdev P. Invited speaker: Dementia in the oldest old. Presented at the *Keio Longevity Initiative Seminar Series: Successful Brain Aging Symposium*. Keio University, Japan; 11 Mar 2016

Sachdev P. Invited speaker: Seminar on dementia. Presented at the University of KwaZulu-Natal, Durban, South Africa; 19 Mar 2016.

Sachdev P. Invited speaker: Can we prevent dementia? Presented at the *Psychiatry Symposium*. University of Cape Town, Cape Town, South Africa; 22 Mar 2016.

Sachdev P. Invited Speaker: Maintain Your Brain: An internet based trial for the prevention of dementia. Presented at the *Australian Dementia Forum*. Brisbane, Australia; 1-5 May, 2016.

Sachdev P. Invited Speaker at the *Tourette Syndrome Association of Australia (TSAA) Annual Meeting*. Brisbane, QLD; 14 May 2016.

Sachdev P. Keynote Speaker at the *AASHA Eight to Eighties-Uniting Generations Annual Wellbeing Forum*. Pennant Hills, Sydney; 5 Nov 2016.

Sachdev P. Invited Panel Member: "Careers and Private Practice". Hosted by the *NSW Association of Psychiatry Trainees*. Garvan Institute, Darlinghurst; 28 April 2016.

Sachdev P, Bowden J, Lee T, Wen W, Ames D, Brodaty H, Crawford J, Kang K, Mather K, Lammel A, Thalamuthu A, Trollor J, Wright MJ, OATS Research Team. The Older Australian Twins Study: Findings from the first 10 years. Presented at the *ICTS Satellite Meeting*. Brisbane, Australia; 20 June 2016.

Sachdev PS, Lipnicki DM, Crawford JD, Brodaty H. Validating the VASCOG criteria for vascular cognitive disorders: A comparison with four other sets of criteria for vascular dementia. Poster presented at the *International Society of Vascular Behavioural and Cognitive Disorders (VASCOG 2016)*. Amsterdam, The Netherlands; 14 October 2016.

Sachdev PS, Lipnicki DM, Crawford JD, Thalamuthu A, Kochan NA, Fernanda Lima-Costa M, Brayne C, Lipton R, Katz MJ, Ritchie K, Ancelin M-L, Scarmeas N, Lam L, Guaita A, Kim K-W, Anstey K, Scazufca M, Shuzo K, Pin NT, Brodaty H, Lobo A for the COSMIC collaboration. Cognitive decline and effects of sex, education and ApoE genotype on cognitive performance in diverse ethno-cultural and geographical regions internationally: the COSMIC collaboration. Poster presented at the *Alzheimer's Association International Conference (AAIC) 2016*. Toronto, Canada; 24-28 July 2016.

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