UNSW AUSTRALIA

Annual Report 2015
Centre for Healthy Brain Ageing (CHeBA)

Never Stand Still | Medicine | School of Psychiatry

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Centre for Healthy Brain Ageing (CHeBA)
UNSW Australia

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Contents

Chairperson's Report

"We are proud of the achievements that CHeBA has made since its official launch in October 2012 and look to the year ahead with certainty and optimism."

The year 2015 was a particularly eventful one for the Centre for Healthy Brain Ageing (CHeBA), with its researchers galvanised to action to achieve their vision of healthier brain ageing and better clinical care of age-related brain diseases.

Following two years of steady growth in garnering philanthropic support, **The Dementia Momentum** was launched in March this year - an initiative to further develop its 'big data' research with the goal of reducing dementia incidence globally. We are extremely fortunate to have the passionate support of Richard Grellman AM, Spokesman for The Dementia Momentum, as well as KPMG Sydney, the host of the launch event, and ARIA Restaurant Sydney who has been our partner for the past two years. In addition a number of community groups have enabled this initiative to generate an extremely positive response from both corporations and individuals.

With the increased support for this initiative, CHeBA has been able to expand its programs focusing on the pooling, harmonising and analysing of data from a number of international studies in order to expedite research outcomes. Media coverage of this initiative has also been encouraging, with The Dementia Momentum featuring in the *Australian Financial Review*, the *Sydney Morning Herald* and on ABC television.

CHeBA's expansion and growing public profile has been due to its industrious and focused group of researchers and support staff. Under the guidance of Professors Perminder Sachdev and Henry Brodaty, they share the CHeBA mission of enhancing the evidence base in relation to prevention, early detection and treatment of age-related disorders, in particular brain diseases, and improving the health care of individuals affected by these diseases.

A number of achievements are noteworthy this year, including Dr Karen Mather, the leader of CHeBA's Genetics and Genomics Group, who received the UNSW Medicine Dean's Rising Star Award for significant contributions to research, and Dr Nady Braidy who was awarded the Chilean Connect Postdoctoral Prize to examine whether the South American rodent *Octodon degus* is a unique natural model of Alzheimer's disease.

I feel privileged to lead a devoted Advisory Committee that meets regularly and is motivated to assist the Co-Directors in achieving their ambitions for CHeBA. In 2015, all members of the Advisory Committee renewed their membership for another term, demonstrating their confidence and commitment to CHeBA. We also welcomed Mrs Imelda Roche AO to the Committee. Imelda brings to the Committee her rich experience in business and philanthropy, and the passion for supporting good research.

2015 saw the continuation of CHeBA's highly successful ***Better Brain. Better Life* forums**. These community forums, as well as a series of supporting educational materials on the modifiable risk factors for dementia, are made possible through the support of Genworth. In 2016, CHeBA will expand the reach of these public forums by taking them into corporate workplaces, specifically targeting those in mid-life, which is when behavioural change should begin so as to reduce cognitive decline in late life.

We are proud of the achievements that CHeBA has made since its official launch in October 2012 and look to the year ahead with certainty and optimism. I would like to take this opportunity to extend enormous thanks to everyone who has supported CHeBA in the previous year with a particular thank you to Heidi Mitchell CHeBA's Marketing and Communications Officer whose creative efforts have been central to the success of the Dementia Momentum.

Dagmar Schmidmaier AM

Directors' Report

Research estimates suggest a third of the risk of dementia is related to lifestyle and modifiable health-related factors.

A number of risk and protective factors are already known and recent trials indicate that it is never too late to improve brain health, with significant gains in brain health possible in mid to late life. Since the disease process generally begins 20-30 years before the symptoms become apparent, there is a window of opportunity for its prevention or delaying of the symptoms.

Cardiovascular health in mid-life is one modifiable factor identified by research as critical to brain health in later life. A recent analysis found physically inactive individuals had an 80% increased risk of dementia and smokers a 60% increase. Treating high blood pressure, diabetes and high cholesterol well could have a major impact on the development of new cases of dementia.

Encouraged by the possibilities of modifiable risk factors for reducing dementia rates, CHeBA launched a major initiative in 2015, **The Dementia Momentum**, a movement to bring researchers and the corporate and philanthropic community together to change the future of dementia incidence. The Dementia Momentum seeks to increase the dialogue with the community about this disease and give an opportunity for philanthropists and corporates to invest firmly in social change by advancing the large-scale, "big data" research being conducted at CHeBA.

Having set a substantial goal of raising $10 million over 5 years to advance CHeBA's research into risk and protective factors for dementia, we are thrilled to announce that we have already achieved close to $1.2 million in 2015 thanks to the overwhelming generosity and support of our Members and Friends. In particular, we would like to thank our Platinum Members: Mr Phil Cave and Mrs Judy Harris, the Vincent Fairfax Family Foundation and the Yulgilbar Foundation, and Gold Member, the Roth Family Foundation. We have been inspired by the tireless work of our Spokesman for The Dementia Momentum, Mr Richard Grellman AM, who was a driving force behind the initiative.

Corporate and community support drove two extremely successful fundraising events as part of our ***Wipeout Dementia*** campaign which raised close to $170,000 for The Dementia Momentum. We were delighted to have high-level backing from Australian political leaders with former Prime Minister Tony Abbott participating in the May Surf Off and NSW Premier Mike Baird taking part in the November Surf Off. We look forward to continuing success with the next round of *Wipeout Dementia* in May 2016.

We were encouraged by a number of major, successful funding grants from the NHMRC in 2015 including:

- $6.78 million for researching strategies for early detection and intervention to slow the development of mild neurocognitive disorders and dementia;
- $6.46 million for "Maintain Your Brain", the largest clinical trial in the world to examine a suite of online interventions designed to reduce dementia risk; and
- $2.6 million for CHeBA's contribution to the European Union Joint Programme for Neurodegenerative Disease (JPND), an international collaboration to identify the genes involved in dementia.

"Funding will enable CHeBA to continue its record of ground-breaking research in ageing and the dementias."

Professor Henry Brodaty & Professor Perminder Sachdev

This funding will enable CHeBA to continue its record of ground-breaking research in the fields of ageing and the dementias. In 2015, CHeBA published world-first findings related to gender differences in brain networks in old age and identification of the first genes associated with people's general cognitive function.

2016 promises to be another big year for CHeBA. Plans to grow The Dementia Momentum continue apace and we look forward to new research insights from our international consortia, COSMIC, ICC-Dementia, STROKOG and PROMOTE. Recruitment for our **Maintain Your Brain** trial will commence in 2016, with a planned 18,000 people aged 55-75 years participating. We also look forward to continuing our collaboration with Sir Moses Montefiore Jewish Home (Montefiore Home) focussing on improving quality of life in residential care.

Once again, we gratefully acknowledge our colleagues and supporters for their enthusiastic involvement and participation, without which our work would not be possible. Our talented group of researchers continue to provide new insights into brain ageing. For the fourth consecutive year, our motivated CHeBA Champions raised funds for research into positive brain ageing and awareness for the role of healthy lifestyles to protect the ageing brain. Ms Heidi Mitchell, our Marketing & Communications Officer, worked untiringly in 2015 to launch and drive The Dementia Momentum's funding success and media outreach. We would also like to thank our Centre Manager, Ms Angie Russell and the administrative team Dr Sophia Dean and Ms Kate Crosbie for their diligence, and our dedicated Advisory Committee for their continued support in 2015.

At CHeBA, we are proud of our close engagement with the community and policy makers to ensure that our research makes a real difference to the burden of neurocognitive disorders in older individuals, both in Australia and internationally. Key components of our community outreach are the four public forums that CHeBA organised or was part of, professional development conferences and multiple media appearances by our team. Our goal is to build healthy, resilient communities by using innovative, research-based approaches and public awareness campaigns to drive positive social change in the field of ageing and dementia. In particular, we seek to enhance the capacity of the community to stave off cognitive decline, Alzheimer's and other dementias.

We look forward to continuing to deliver on these goals in 2016.

Sincerely

Scientia Professor Perminder Sachdev & Scientia Professor Henry Brodaty

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 in October 2012. It is headed by internationally acclaimed leaders in the field, Professors Henry Brodaty and Perminder Sachdev.

Our Vision

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

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 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 & 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 post graduate 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.

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 Australia

Professor Terry Campbell

Professor Phillip Mitchell

- Professor Henry Brodaty, Co-Director of CHeBA
- Professor Perminder Sachdev, Co-Director of CHeBA

2015 meeting date: 7 December.

Advisory Committee

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

- Enhance the profile and community awareness of the Centre and its aims
- Facilitate the development of more effective infrastructure for the Centre, such as specialised research facilities and laboratories, IT networks, equipment and training support services
- Facilitate sponsorship for the Centre's activities, through various mechanisms for example, directly through personal networks via donation or service provision and introductions to potential high end donors, and indirectly by creating sponsorship opportunities
- Provide advice specific to areas of expertise of the Committee members, e.g. legal, government relations, business development strategy, marketing strategy and media.

The members of the CHeBA Advisory Committee are:

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

2015 meeting dates: 10 February, 12 May, 25 August, 10 November.

Advisory Committee Profiles

John Gray

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.

Professor Roger Layton AM

UNSW Emeritus Professor of Marketing

Roger has 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

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 a representative to the successor organisation, the Business Advisory Council to APEC.

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.

Dagmar Schmidmaier AM

FALIA

Co-ordinator, 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 M Thomas

KSS FAICD FIFS JP

Principal, JT Consultancy

John has been involved in banking, finance and funds management activities for over 40 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.

Scientia Professor Perminder Sachdev AM

MD PhD FRANZCP FAAHMS

Co-Director, CHeBA

Perminder is Professor of Neuropsychiatry at UNSW Australia and the Clinical Director of the Neurospychiatric Institute (NPI).

Scientia Professor Henry Brodaty AO

MB BS, MD, DSc, FRACP, FRANZCP, FAAHMS

Co-Director, CHeBA

Henry is Professor of Psychogeriatrics, UNSW Australia; Director of the DCRC-ABC; Director, Aged Care Psychiatry and Head of the Memory Disorders Clinic, Prince of Wales Hospital.

Significant Highlights

"If research delivers a way to delay the onset of dementia by just two years, and it is put into practice in 2020, the number of new cases in Australia could be reduced by almost 50,000."

Professor Henry Brodaty

The Dementia Momentum

Spokesman's Report

When Professor Brodaty asked me to support CHeBA in their effort to change the future of dementia incidence in Australia, I had little choice but to agree.

Professor Brodaty had provided invaluable support to myself and my wife, Suellen who was diagnosed with Early Onset Alzheimer's disease in 2011, and I felt a great sense of gratitude for his caring, clear, professional and yet pragmatic approach to our journey.

Richard Grellman AM

"We need help to get resources directed to researching prevention, diagnosis and treatment and corporate Australia is the best hope we have for getting the volume of funds we need quickly, so we can start seeing results." RICHARD GRELLMAN AM

I agreed to become Spokesman for **The Dementia Momentum**, CHeBA's initiative to bring the philanthropic community together to drive momentum in awareness, research and societal change for a brighter future.

My role as Spokesman has given me a public voice to discuss the challenges we face when dealing with dementia. Light needs to be shined on the journey of sufferers and their families, the ever-growing cost implications of this disease and the vital role of our researchers in changing the predictions. I have had the opportunity to tell my story this year, through corporate events, newspaper articles, radio and television interviews. Although challenging at times, I have been richly blessed with the opportunity to do something of practical worth to the cause, particularly given that by this time Suellen was in full time residential care with all of her practical living needs provided by others.

Launched in March 2015 at the offices of one of our corporate supporters KPMG, progress on The Dementia Momentum, I am pleased to say, has been tangible.

A major awareness and fundraising campaign for The Dementia Momentum was also launched in 2015, Wipeout Dementia – a unique event that seems to be gathering a life of its own. Wipeout Dementia is a gruelling 4 week strength for surfing course for senior corporates, culminating in a 'Surf Off' tournament. 1978 World Champion Wayne 'Rabbit' Bartholomew is my fellow Ambassador for this event. We kicked off our first event in May 2015, in which the then Prime Minister Tony Abbott participated and followed this up with our second event in November, with NSW Premier Mike Baird paddling out. Our next event is planned for May 2016. Again, many corporates have generously supported this initiative – totalling close to $170,000 - with all money raised going straight into research.

In November, ARIA Restaurant Sydney provided a private room and full fare for a 30 person luncheon, comprised mainly of senior corporates and business leaders, to raise awareness about The Dementia Momentum. They have generously offered to continue to do so on an annual basis going forward. Similarly, Genworth Mortgage Insurance, AMP and the aforementioned KPMG have been and remain willing to throw their doors open for our functions.

As Spokesman, I have had the pleasure of working with the outstanding folk at CHeBA; in particular with the fertile mind and energetic support of Communications & Marketing Officer, Heidi Mitchell, and the committed Co-Directors Professors Henry Brodaty and Perminder Sachdev. Together, we have undertaken a variety of initiatives, made successful with the support of some wonderful people and organisations.

While we have made significant progress in 2015, much more needs to be done and it is with this reality in mind that all involved with The Dementia Momentum look forward to another productive year.

Richard Grellman AM
Chairman, Genworth Mortgage Insurance Ltd, IPH Ltd & AMP Foundation

Launch of The Dementia Momentum

The Dementia Momentum was officially launched at a corporate event hosted by our partner KPMG Sydney on 25 March 2015, with a number of leading philanthropists attending, including Founding Members and Friends of the initiative.

Professor Perminder Sachdev, Co-Director CHeBA, Richard Grellman, The Dementia Momentum Spokesman, and John Teer, partner at KPMG

"This important social initiative is a bold attempt to bring the right researchers and community donors together to materially increase the pace of clear, clever and relevant work in confronting this disease," said Spokesman for The Dementia Momentum, Mr Richard Grellman AM.

The number of dementia sufferers is increasing rapidly, with figures estimated to rise to 135 million worldwide and to almost 1 million in Australia, at an economic cost of 2-3% of the GDP by 2050. At projected rates, the aged care workforce in Australia will need to triple by 2050 and 500 new nursing home beds for dementia-related care will be needed per month for the next 40 years.

Around the world researchers have documented modifiable risk factors for the different types of dementia and are now designing strategies to delay the onset of dementia or prevent it altogether. CHeBA's intention with The Dementia Momentum is to bring international efforts together to make a truly big impact on dementia research.

"Research is an international enterprise and dementia affects all communities. The future of dementia research is in being able to bring the scores of international studies together for a common purpose," says Professor Perminder Sachdev, Co-Director of CHeBA.

> "To achieve the goals of prevention, early diagnosis and better care, we need a new research strategy to find scalable solutions which can then be translated into real outcomes for the public."
>
> PROFESSOR HENRY BRODATY

> "Richard's commitment to the goals and work of CHeBA following Suellen's diagnosis has been inspiring."
> PHIL CAVE AM AND JUDY HARRIS

"By pooling data, we can create 'big data sets' that produce more robust statistical models involving multiple risk factors and more precise estimates than can be reliably obtained from individual cohort studies."

Having already led a number of international consortia, Professor Sachdev says CHeBA is in an excellent position to make a world-wide difference to prevention, earlier diagnosis, and earlier and more effective interventions.

The Momentum's first Platinum members, Mr Phillip Cave AM and wife Ms Judy Harris, who have contributed $100,000 to the Fund, firmly endorsed the initiative and encouraged more individuals and corporations to get on board in support of Richard Grellman.

"Richard's commitment to the goals and work of CHeBA following Suellen's diagnosis has been inspiring," they said.

Other founding members of The Dementia Momentum include The Roth Charitable Foundation and The AMP Foundation. KPMG and HWL Ebsworth have pledged in-kind support and Friends of The Dementia Momentum (individuals contributing between $500 and $5,000) include BridgeClimb founder Mr Paul Cave AM and Non-Executive Director Mr Graeme Pettigrew.

The launch was covered by the *Australian Financial Review* and *Australian Ageing Agenda.*

2015 Donor Members

Platinum Members

- Mr Phillip Cave AM & Judy Harris
- Vincent Fairfax Family Foundation

Gold Members

- The Roth Charitable Foundation

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- Breakwater Advisory
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- Mr Paul Cave AM
- Mrs Keri Chittenden
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- Mrs Michelle & Mr Tony McGrath
- McGrath Estate Agents - Neutral Bay
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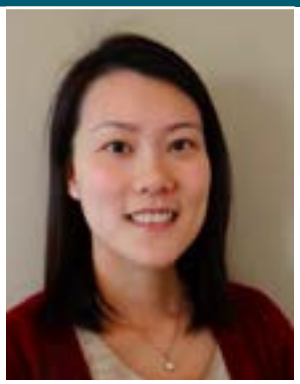
- Ms Nancy Milne
- Morgans Foundation
- Mr Nigel Mukhi
- Mr Donovan Murphy
- Mr Derek Nelson
- Mrs Colleen Nichols
- Parkview Group
- Mr Graeme Pettigrew
- Dr Sally Pitkin
- Mr Don & Mrs Anne Potter
- Mr Douglas Potter
- ProGood
- Mrs Angela Raymond
- The Rotary Club of Rose Bay
- Ms Dagmar Schmidmaier AM
- Mrs Jacqueline Smith
- Sydney Airport
- Ms Gayle Tollifson
- Watson Mangioni Lawyers Pty Limited
- Mrs Sally White OAM
- Mrs Ali Wood & Mr Brian Holder
- Mr David G. Young
- Mr Geoff Zuber

In Kind Supporters

We are extremely grateful to those individuals and organisations that have contributed support for The Dementia Momentum in-kind.

Research funding by The Dementia Momentum



Helen Wu – PhD Student

Part-time PhD candidate Dr Helen Wu is the recipient of a $90,000 grant from The Roth Charitable Foundation (Founding Gold Member, The Dementia Momentum) to investigate novel genetic biomarkers of Alzheimer's disease (AD).

Patients with AD are known to have neuropathology in their brains for over twenty years before any symptoms occur, meaning that by the time the disease is identified, irreversible cognitive damage has occurred. Current methods for detecting early markers, or biomarkers, for AD are highly invasive, expensive, difficult to access or not specific enough to be consistently useful. Since only 1-2% of all cases of AD are clearly genetic, gene-environment interactions (known as epigenetics) are understood to play a major role in the cause and progression of the disease. Micro-RNAs (miRNA), which can be obtained from blood samples, may have an important role in gene regulation and could be a potentially useful biomarker for the early diagnosis of AD.

"The ideal biomarker should identify the neurodegenerative process before cognitive decline has begun and correlate to severity and progression. miRNA may well turn out to be one such marker," explained CHeBA Co-Director Professor Perminder Sachdev. "This would have significant implications for therapeutics, since treatment in the preclinical stage may yield greater benefit as well as reducing the burden on the health system and aged care services."

In 2015, Dr Wu published a systematic review investigating research into miRNAs as potential biomarkers for early diagnosis in the *Journal of Alzheimer's Disease*. Dr Wu found that failure to use a standardised approach is limiting the effectiveness of research, with few studies assessing the same miRNAs and methodological differences making it hard to validate findings.

"We are excited to have Dr Helen Wu on board for this project. With a first class honours in medicine and training in geriatrics, Dr Wu is extremely bright, driven and talented and is sure to make a strong contribution to this novel field of Alzheimer's research," said Professor Sachdev.

Consortia Coordinators

Ms Catriona Daly

One of the most exciting things about being involved with The Dementia Momentum initiative is its focus on real world application, according to Ms Catriona Daly, the new Study Coordinator of the International Centenarian Consortium of Dementia (ICC-Dementia) at the Centre for Healthy Brain Ageing (CHeBA).

Catriona explains that one of CHeBA's strengths lies in its strong social justice focus. It is not just about getting research papers published, it's about improving people's lives and helping them overcome or cope with real problems of ageing by investigating and providing evidence based information and interventions. ICC-Dementia combines international centenarian and near-centenarian studies to describe the cognitive and functional profiles of exceptionally old individuals. CHeBA researchers are systematically exploring the risk and protective factors involved in dementia and longevity, as well as providing real-life models of healthy brain ageing to develop strategies for escaping or delaying the onset of dementia.

"Studying centenarians provides an exciting opportunity to work out how to prevent the onset of dementia for future generations and the use of longitudinal studies means that we are able to access an almost complete picture of a person's health and lifestyle. I hope that this will inform clinical interventions and raise awareness of lifestyle choices which can be altered to ensure successful ageing."

This year, ICC-Dementia expanded its membership to include studies from Poland, Hong Kong, The Netherlands, Spain and the UK, and now comprises seventeen studies in the Asia-Pacific region, Europe and the Americas.

Following a meeting of ICC-Dementia in Sardinia in June, the consortium has gained a renewed momentum. Multiple studies from Europe, Asia, Australia and North America were presented in Sardinia, and it became apparent that there are some pockets in the world in which centenarians appear to be cognitively quite healthy. To understand the basis of the inter-regional differences is a major, and potentially rewarding, challenge.

Ms Daly holds an undergraduate degree in Psychology from the University of Sydney and a Masters of Clinical Psychology from the University of Leiden (The Netherlands). She has also worked in the British health system as a trainee psychologist and has a clinical background working for not-for-profit organisations.

Dr Darren Lipnicki

Understanding the universal and local risk factors for cognitive decline is what drives Dr Darren Lipnicki, Study Coordinator of the Cohort Studies of Memory in an International Consortium (COSMIC) at CHeBA.

COSMIC compares research findings from around the world to identify risk and protective factors associated with cognitive decline and dementia. These findings will have significance for everyone's daily lives.

"If people implement and practice changes in their daily lifestyle, ideally from as early an age as possible, we can reduce the impacts of cognitive ageing on society," explained Dr Lipnicki.

Dr Lipnicki is encouraged by existing findings about the impact of modifiable lifestyle factors.

"There may be some fine tuning of our understanding about how physical activity and diet influence cognitive ageing, but the basics are clear and promoting lifestyle change to reflect these should be a priority."

CHeBA Co-Director and Leader of COSMIC Professor Perminder Sachdev said that Dr Lipnicki's skill-set is an invaluable resource for the success of COSMIC. "Darren has a great mind for detail which, coupled with his capacity to work for hours undisturbed to bring together diverse data sets, is helping COSMIC to realise its goals."

Dr Lipnicki has been a researcher with CHeBA since 2010. He holds a Bachelor of Science (Physiology and Pharmacology) from the University of Western Australia, a Bachelor of Arts with first class Honours in Psychology from Murdoch University and a PhD in Psychology from the Australian National University (ANU). He has also worked for the Centre for Mental Health Research at ANU and held a Humboldt Research Fellowship at the Berlin Center for Space Medicine. He is married and has a young son.

Wipeout Dementia

One of the fundraising highlights of the year for The Dementia Momentum was the launch of the Wipeout Dementia campaign; a four week strength for surfing program culminating in a Surf Off tournament between senior executive competitors.

"With a rapidly expanding ageing population, dementia is set to bring an enormous challenge to health, aged care and social policy. I fully support Richard Grellman in his role with CHeBA to drive positive change for the future of all Australians."

NSW PREMIER MIKE BAIRD

The fundraising event is in honour of Spokesman for The Dementia Momentum Richard Grellman's wife Suellen, who has advanced young onset Alzheimer's disease and now requires full time care and attention.

"We need help to get resources directed to researching prevention, diagnosis and treatment and corporate Australia is the best hope we have for getting the volume of funds we need quickly, so we can start seeing results," said Mr Grellman, who is the former President of the Association of Surfing Professionals (ASP) International Limited.

"The significance of Wipeout Dementia is the tie-in between physical exercise and brain health," he said.

A recent analysis showed that physically inactive individuals had 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.

Following the success of the first event in May 2015, which involved a surfing appearance from then **Prime Minister Tony Abbott**, a second event was held November to further increase appreciation of the massive health and socioeconomic challenge the dementia epidemic poses to Australia.

"Research is incredibly important for all our futures because with life expectancies getting up to the mid-80s and beyond a lot more people are going to end up with dementia of one form or another," said Hon. Tony Abbott.

Nearly $200,000 was raised over the two events, with another event set for May 2016. **NSW Premier Mike Baird** made a guest appearance in the November event surfing for Richard Grellman's 'Evergreens' team.

"With a rapidly expanding ageing population, dementia is set to bring an enormous challenge to health, aged care and social policy. I fully support Richard Grellman in his role with CHeBA to drive positive change for the future of all Australians," Premier Mike Baird said.

Richard Grellman said Wipeout Dementia was an extraordinary success in 2015 and credited the high profile participants for their dedication in raising awareness and funds.

"Our participants have been great, many of them making donations personally and all of them drawing on their extensive professional networks."

1978 World Surfing Champion **Wayne Rabbit Bartholomew AM** joined the Wipeout Dementia campaign as Ambassador and said he was proud to adopt the role to promote healthy brain ageing.

"It was a privilege to sponsor the first Wipeout Dementia event and to be able to participate alongside Richard Grellman in what was truly a quality strength for surfing program and an extremely enjoyable event overall. Watson Mangioni is committed to giving back to the community and to be able to support a campaign that raised nearly $100,000 for dementia research was an honour." CHRIS CLARKE, DIRECTOR, WATSON MANGIONI LAWYERS (MAJOR SPONSOR OF *WIPEOUT DEMENTIA,* MAY 2015)

"Richard Grellman has for the last 15 years been a mentor figure in my life. As Chairman of ASP International, Richard was a great asset, in fact instrumental, in the implementation of the "Dream Tour" concept, ushering in a new era of governance that set Professional Surfing on its ascendancy. Moreover, Richard and Suellen became close personal friends, our social and professional lives interacting on many levels, and I have witnessed the challenges, heartbreak, despair and resignation that the Grellmans' journey has taken them on. I am privileged to be alongside the great man once again," he said.

One of the most effective strategies we can adopt to reduce the risk of cognitive decline and dementia later in life is to become physically active from an early age, and remain active throughout our lives.

The Wipeout Dementia concept is the brainchild of Heidi Mitchell, CHeBA Marketing and Communications Officer, who was inspired by Richard Grellman's passion for surfing and his strong group of surfing friends and colleagues, in their 50s and 60s. Team Captain Rob Gillespie, who managed the Surf Off, credits his mother-in-law Colleen Nichols for coming up with the "Wipeout Dementia" title. The four week strength for surfing course, tailored for the more mature surfer, was delivered by PDHPE teacher Craig Douglass.

Watson Mangioni Lawyers was the sponsor for Wipeout Dementia May 2015.

Flight Centre was the major sponsor for Wipeout Dementia November 2015, with realestate.com.au Pty Ltd a secondary sponsor, and Colliers and ProGood as supporter sponsors.

Hurley, KPMG, Queenscliff Surf Life Saving Club and Surfing NSW provided in-kind support.


DEMENTIA

DEMENTIA


FLIGHT CENTRE
Hurley
DEMENTIA


DEMENTIA


Hurley
DEMENTIA

Wipeout Dementia 2015

Guest Surfers

- Hon Tony Abbott MP
- Hon Mike Baird MP

Participants

- Wayne 'Rabbit' Bartholomew (Ambassador)
- Ian Bennett
- Phil Butt (Gnarly Award for highest fundraiser, November)
- Tony Camphin
- Peter Chittenden (Best Wipeout Award, May)
- Chris Clarke (Player's Player Award, May)
- John Cunningham (Gnarly Award for highest fundraiser, May and Team Captain, November)
- Andreas Faeste
- David Foster
- Ian Freestone (Player's Player Award, November)
- Rob Gillespie (Team Captain)
- Ben Grellman (Coach's Award, May)
- Richard Grellman (Ambassador, Spokesman for The Dementia Momentum and Team Captain)
- Mark Gross
- Michael Gulley
- James Haywood
- Chris Jessop
- Andy Kennard (Wave of the Day Award, November)
- Warren King
- Stephen Lennard
- Philip Macken
- Hamish McLennan
- Doug Miller-Davie
- Paul Oesterheld
- David Smith
- Richard Stubley
- Mark Westfield (Best Wipeout Award, November)
- David Young

First Findings From COSMIC Published in PLOS One

By applying standardised criteria to international studies in the COSMIC consortium, CHeBA researchers have provided a more reliable estimate of mild cognitive impairment (MCI) prevalence.

The first findings from COSMIC were published in the November 2015 edition of eminent journal *PLOS ONE*. The researchers found that after applying standard criteria to 11 studies from USA, Europe, Asia and Australia, estimates of overall MCI prevalence in people over the age of 60 years ranged between 6 to 12%, a much narrower range than previously published estimates of 5 to 36.7%.

> "This is the first time that data from so many studies from diverse countries have been brought together and the data harmonised so that direct comparisons make sense." PROFESSOR PERMINDER SACHDEV

The lack of uniform criteria for diagnosing MCI has previously resulted in a wide range of unreliable estimates for global prevalence of the disease, with significant implications for health policy and planning.

MCI refers to a decline in cognitive performance from a previous level of functioning, but not to the degree to impair the individual's independent functioning. People with MCI are at an increased risk of progressing to dementia, with about 6-10% being diagnosed with dementia per year of subsequent follow-up. Since it needs to be differentiated from age-related changes in cognition, the diagnosis of MCI is complex and, according to COSMIC leader Professor Perminder Sachdev, even minor differences in definition and the diagnostic tests used can significantly alter the rates of estimated prevalence.

This is the first time that data from so many studies from diverse countries have been brought together and the data harmonised so that direct comparisons make sense. The studies show that, as expected, MCI becomes more common with age, and not having completed high school increases its risk. Interestingly, the prevalence was not different in White and Chinese populations.

COSMIC

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

- Our first project "The prevalence of Mild Cognitive Impairment in diverse geographical and ethnocultural regions: The COSMIC collaboration" was published in ***PLOS ONE.***
- Our second project was approved by COSMIC's Scientific Steering Committee and is underway. This project aims to compare neuropsychological test performance across different cohorts, and to investigate cognitive decline and its associated risk and protective factors. 14 studies have provided data for this project, including a number of the original member studies who did not contribute to the first project. Data from this project will be presented at the Alzheimer Association International Conference in Toronto, Canada, in July 2016.
- Three new studies became full members of COSMIC in 2015. Each study was from a country not yet represented, including Indonesia (ACtive Aging Research), India (MYSORE), and Germany (LEILA75+).

ICC-Dementia

Formed in 2012, ICC-Dementia is a dementia work group of the International Consortium of Centenarian (ICC) studies brought together to apply standard diagnostic criteria for dementia to centenarian cohorts around the world. The group will combine data from population-based, longitudinal cohort studies to identify common risk and protective factors and biomarkers for dementia (in particular Alzheimer's disease (AD) and vascular dementia (VaD)), mild cognitive impairment (MCI), age-related cognitive decline and geriatric depression. The group hopes to find factors that predict successful brain ageing into the 11th decade of life that are robust across cohorts. This will spearhead an international effort to promote successful brain ageing. Currently, ICC-Dementia includes studies from Australia, The United Kingdom, Poland, Italy, The Netherlands, Portugal, Hong Kong, Japan, Germany, Sweden, and the USA.

Highlights

- A new coordinator, Ms Catriona Daly, was appointed to this consortium.
- Seventeen studies from around the world have signed memoranda of understanding for participation in the ICC Dementia. Data has been received from 15 of these.
- A paper describing the methodology of the consortium is in press with *BMC Neurology*.
- A second paper, looking at the international prevalence of dementia, is currently being written up.
- Data harmonisation of numerous variables across studies is well underway.
- Regular teleconferences are being held to progress the first project, which will examine prevalence of dementia in the various cohorts. Fifteen studies have thus far contributed data to this project.
- A meeting of the ICC was held in Sardinia from 18-20th June 2015.
- The next meeting of the ICC will occur in Porto, Portugal, between June 15-19th 2016.

STROKOG

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 post-stroke cognitive impairment and ask questions in relation to risk and protective factors. We anticipate that the findings of STROKOG will help guide and optimise preventative strategies and health policy, both in Australia and internationally. Currently, STROKOG includes studies from Australia, Hong Kong, Singapore, Korea, China, Poland, France, Finland, Ireland, the UK, Sweden, Germany, South Africa, Nigeria and the USA.

Highlights

- STROKOG was officially launched at the VASCOG meeting in Tokyo, Japan in October.
- Specific research questions and projects are currently being developed and agreed upon by a STROKOG governance committee comprising the leaders of contributing studies.
- A methodology paper is in preparation, and the first project - examining the prevalence of cognitive disorders in post-stroke patients - is currently being evaluated.
- 26 studies have now agreed to participate in STROKOG.

PROMOTE

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

- We have collected data from Hong Kong, South Korea, Malaysia and Australia.
- A keynote presentation was given at the APRU Ageing in the Asia-Pacific Research Symposium in Sydney on 29th September 2015.

Funding Success

"Our work will make a significant impact on the diagnosis of neurocognitive disorders in the early stages, and the postponement of dementia in Alzheimer's disease and vascular cognitive disorder."

PROFESSOR PERMINDER SACHDEV

In 2015, CHeBA continued its record of grant success with significant funding awarded by the NHMRC, JPND and Sachdev Foundation.

Early Detection and Interventions for Mild Neurocognitive Disorders and Dementia

In March, the Minister for Health, the Hon Sussan Ley MP, announced that CHeBA will receive an NHMRC program grant worth $6.78 million for researching strategies for early detection and intervention to slow the development of mild neurocognitive disorders and dementia.

According to the 2012 report from the Australian Institute of Health and Welfare, direct health and residential care costs of dementia currently exceed $4.9 billion per annum, not including the indirect costs in foregone earnings, carer time and expense. If dementia rates continue to rise at predicted rates with the ageing population, the cost will total 3.6% of the GDP by 2051. Mild neurocognitive disorders are not included in these figures and comprise an additional hidden burden. Without research into risk factors and strategies for prevention and early diagnosis, the economic and social cost of dementia will be devastating.

"Our work will make a significant impact on the diagnosis of neurocognitive disorders in the early stages, and the postponement of dementia in Alzheimer's disease and vascular cognitive disorder," said chief investigator Perminder Sachdev.

Maintain Your Brain

In August, CHeBA researchers received $6.47 million in grant funding from the NHMRC for the largest clinical trial in the world of online tools designed to reduce dementia risk.

Lead investigator Scientia Professor Henry Brodaty said the 'Maintain Your Brain' trial will recruit 18,000 people aged 55-75. Half of the trial participants will be given information on managing dementia risk factors, while the rest will get extra support through online tools connecting them with medical specialists and tailored health interventions.

> "If older people increased their efforts to address these risks factors by just 5 or 10%, several million people could keep dementia at bay." PROFESSOR HENRY BRODATY

Professor Brodaty said there remains a lack of understanding in the community regarding dementia risk factors, such as lack of physical activity, obesity, depression, smoking and excessive consumption of alcohol.

"The people in our trial will be young enough still to be able to prevent the accumulation of more pathology in their brain, and old enough that we can study the outcomes to benefit future generations," he said.

Twenty specialists from around Australia will be involved in this study including experts in exercise, cognitive training, diet, IT platform design, general practice, research design and prevention, hypertension and depression, and consumer representation. Alzheimer's Australia Ambassador, Ita Buttrose, is patron of the "Maintain Your Brain" study.

> "Centenarians are examples of successful ageing, many of whom have avoided age-related disease until very late in their lives." DR KAREN MATHER

Sachdev Foundation Funding

In June, CHeBA researchers received $40,000 from the Sachdev Foundation to conduct whole genome sequencing of centenarians.

With age a major risk factor for dementia, the study of centenarians, who are aged 100 years or more, may provide invaluable insights into biological and lifestyle factors related to cognitive ageing.

"Centenarians are examples of successful ageing, many of whom have avoided age-related disease until very late in their lives," said study leader and leader of CHeBA's Genetics & Genomics Group, Dr Karen Mather.

"Our ultimate aim is to understand the molecular pathways underlying successful ageing and to translate the genetic findings from this cutting-edge research project into new strategies for improving the health outcomes and quality of life of older adults.

Dr Karen Mather

The whole genome sequencing data generated by this project will form a cornerstone of future studies examining successful ageing and longevity within NSW, Australia and internationally.

"It will place us at the forefront of centenarian genetics research and facilitate new collaborations with international research groups," said CHeBA Co-Director Professor Perminder Sachdev.

"Understanding the genetics of Alzheimer's disease is one of the best ways of improving our knowledge of the underlying mechanisms of disease development."

PROFESSOR PERMINDER SACHDEV

European Union Joint Programme for Neurodegenerative Disease (JPND)

In November, CHeBA researchers received $2.6 million in grant funding from the NHRMC as part of an international collaboration to identify the genes involved in dementia.

Led by Co-Director Professor Perminder Sachdev, the funding will support two Australian studies which will be part of the European Union Joint Programme for Neurodegenerative Disease (JPND). As one of the world's largest neurodegenerative research programmes, the JPND includes a number of consortia of international collaborators to identify risk and protective factors for neurodegenerative diseases, such as dementia, as well as trialling advanced experimental models.

"These two major studies will focus on understanding the genetic basis of Alzheimer's disease and other dementias," Professor Sachdev said.

"We know that genes play a major role in the development of Alzheimer's disease, but we have only identified genes that account for less than half of the genetic risk of developing this disease," said Professor Sachdev.

"This funding will allow us to more effectively understand the 'missing' heritability and identify the genes involved in dementia. It will also enable us to partner with large European research consortia, thereby greatly enhancing the power of the investigations."

CHeBA's research team will consist of *Professor Perminder Sachdev, Professor Henry Brodaty, Associate Professor Wei Wen, Dr Karen Mather, Dr Anbu Thalamuthu and Dr Nicola Armstrong (Murdoch University).*

Co-Directors Appointed Australian Academy of Health and Medical Sciences Fellowships

In 2015, both CHeBA Co-Directors, Professor Perminder Sachdev and Professor Henry Brodaty, received the prestigious honour of being appointed as Fellows of the Australian Academy of Health and Medical Sciences.

The role involves assisting the Academy to provide impartial leadership in health care research by assessing current knowledge, conducting studies and considering policy issues in disease prevention and health service provision.

Professor Perminder Sachdev

Professor Henry Brodaty

Gender Differences in Brain Networks Continue Into Old Age: NeuroImage

Alistair Perry

A brain mapping study led by researchers from CHeBA and QIMR Berghofer has found new evidence of a neural basis for the difference behaviours in men and women and that gender differences in brain networks continue through old age.

The findings were published in the prestigious journal, *NeuroImage*, in July 2015.

For the first time, the researchers created a complex map of connections in the healthy elderly brain, known as a connectome, using advanced imaging technology and sophisticated computer models. CHeBA lead investigator and PhD student Alistair Perry said the study found stronger neural networks in elderly women around verbal and language areas of the brain.

"In men there was not such a clear distinction but we found greater connections to the regions of the brain related to reward centres and behaviour regulation," Mr Perry said.

The study also lays the groundwork for new research into Alzheimer's disease and frontotemporal dementia. Mr Perry said the next step would be to use the same methods to map the connectome of those with mild cognitive impairment.

Research Student Completions

Ms Sri Chandana Kanchibhotla, Master by Research

Thesis: Investigating the genetics of the microstructure of the corpus callosum in the ageing brain

Supervisors: Perminder Sachdev, Karen Mather, Peter Schofield (NeuRA)

The corpus callosum is an important brain structure comprised of white matter, responsible for communication between the two hemispheres of the brain. Age-related changes in the corpus callosum have been associated with cognitive impairment and neurodegenerative disease. My research concluded that the microstructural integrity of the corpus callosum in older adults is generally under moderate heritability. A top-up scholarship from the *Dementia Collaborative Research Centre* supported my project.

Ms Kanchibhotla now works as a research assistant with CHeBA's Genetics & Genomics Group.

Dr Amanda Olley, PhD

Thesis: A decision making model of Obsessive Compulsive Disorder (OCD): A neuropsychological and functional neuroimaging investigation

Supervisors: Perminder Sachdev, Gin Malhi (University of Sydney)

We proposed a conceptual shift in OCD research towards an integrated decision making model to account not only for the behavioural phenomena of doubt and indecision, but also the neuropsychological and neurobiological deficits reported in OCD. The research skills that I garnered from completing the study were essential in fostering my research career. A Psychiatry and Neuroscience Scholarship from the School of Psychiatry allowed me to focus on my research while also working part-time as a clinical neuropsychologist

Dr Olley is now lead clinical neuropsychologist at the KaRA Institute of Neurological Diseases in Sydney. She is a supervising clinical neuropsychologist in the School of Psychology, UNSW Australia and lecturer in the School of Psychology, Charles Sturt University.

Dr Katrin Seeher, PhD

Thesis: The psychosocial effects of becoming a carer: Predicting psychological distress and caregiver burden in family members and friends of older people with normal cognitive function, mild cognitive impairment and dementia over time

Supervisors: Professor Henry Brodaty, Associate Professor Lee-Fay Low, Dr Simone Reppermund

Professor Henry Brodaty, Dr Katrin Seeher and Dr Simone Reppermund

My most important finding was that the long-term psychological well-being of family members and friends in general was very good and affected only minimally by the deterioration of the older person over time. However, if family members or friends perceived those changes as stressful or were facing secondary role strain or self-rated health problems then their psychological distress increased over time. The positive implications for this are that the negative effects of long-term caring can potentially be prevented, or at least ameliorated, by promoting good physical health and improving coping abilities and stress appraisals through early carer interventions.

I was fortunate to receive a Dementia Collaborative Research Centre (DCRC) PhD scholarship which enabled me to study with some of Australia's best dementia researchers. Funding from the Australian Association of Gerontology, Postgraduate Research Support Scheme (Travel), Alzheimer Association International Conference Travel Fellowship supported additional data collection and allowed me to present my findings at two of the most important international dementia conferences.

Dr Seeher is now a Consultant for the Global Dementia Observatory (World Health Organization), an international surveillance and knowledge platform of key dementia indicators. The main purpose of the Observatory will be to monitor dementia numbers and care resources, as well as dementia policy development and planning. She is also a visiting academic with the School of Psychiatry, UNSW Australia and the Dementia Collaborative Research Centre.

Our Community

"Our group is closely engaged with the community as well as policy makers to ensure that our research makes a real difference to the burden of neurocognitive disorders in older individuals, both in Australia and internationally."

Professor Perminder Sachdev

CHeBA Champions

In 2015, 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 and in 2015 a video campaign was started in which PJ will appear. This campaign will launch in 2016.

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.

New additions to the CHeBA Champions in 2015 included Tanya Duckworth and Lara Molle who participated in this year's City 2 Surf event.

Hailey Maxwell

A CHeBA Champion since the inception of the program in 2012, Hailey has made a number of lifestyle changes toward improving her brain health in later life.

In 2015 Hailey ran the North Face 100 – an ultra marathon event over 100km. Hailey has raised over $15,000 for CHeBA's research.

"The knowledge and support that CHeBA has given me allows me to help educate others and inspire them to think about making changes to help prevent or delay dementia."

Warren King

Fellow CHeBA Champion, Warren King, surpassed his fundraising goal for CHeBA's research when he completed the 2015 Ironman Asia-Pacific Melbourne on March 22, three minutes faster than his target time of 11 hours.

"It wasn't easy but all the training definitely paid off and the motivation to finish was always there because of the support and generous donations so many people had made."

A keen surfer, Warren also competed in the May 2015 Wipeout Dementia event.

ARIA Restaurant Sydney Hosted Corporate Lunch

On 6 November 2015, ARIA Restaurant Sydney continued its incredibly generous support by hosting the third annual lunch to enhance CHeBA's links with Australia's corporate philanthropic leaders.

At a time when Alzheimer's disease and other dementias have reached epidemic proportions, some of Sydney's leading business professionals came together for the annual charity lunch generously hosted by ARIA Restaurant Sydney on Friday, 6 November to support The Dementia Momentum initiative.

Guest speaker and Spokesman for The Dementia Momentum, Richard Grellman AM, spoke openly about his personal experience. His wife of over 40 years, Suellen, was diagnosed with young-onset Alzheimer's disease 4 years ago and is now in full-time care.

Richard told the group that 12 of the residents where his wife Suellen lives have dementia and have significant needs in terms of support for everyday living. Most have lost their ability to communicate verbally.

Richard called upon corporate Australia to help support vital research to create a brighter future for all Australians and to help spare others this isolating, uncertain experience.

Co-Director of CHeBA, Professor Henry Brodaty , who also spoke at the event, said that by the 2060s, when over a quarter of the population will be older than 65 years and one in 12 will be over 80, spending on dementia will outstrip any other health condition.

"CHeBA's research aims to determine which risk and protective factors for Alzheimer's disease and other dementias are global," said Professor Brodaty.

"To achieve the goals of prevention, early diagnosis and better care, we need a new research strategy to find scalable solutions which can then be translated into real outcomes for the public. We propose to deliver this through our initiative, The Dementia Momentum."

Master of Ceremonies fellow Co-Director Professor Perminder Sachdev AM said it was his hope that corporate Australia would be inspired by Richard to become a part of The Dementia Momentum.

> "Treating Alzheimer's and other forms of dementia is the biggest healthcare challenge for our society."
> RICHARD GRELLMAN AM

Better Brain. Better Life Forums

The *Better Brain. Better Life* forums, supported by platinum sponsor Genworth since 2014, are a series of public forums with talks by leading experts in ageing to promote strategies for better brain health.

> "The message of these talks is not only to showcase the complexities of the brain and CHeBA's latest research, but to also show that it is never too early and never too late to be proactive about brain health." PROFESSOR HENRY BRODATY

On 4 March 2015, CHeBA ran a *Better Brain. Better Life* forum as the first event in the Seniors' Month program at Rockdale City Council.

The forum was opened by General Manager of Rockdale City Council, Meredith Wallace, who delivered a supportive community address and reiterated Rockdale City Council's commitment to hosting educational forums for seniors. Attendees were entertained by Walkley-Award winning journalist and author of the blog *Coming of Age*, Adele Horin, who gave a delightful personal insight into the art of ageing well and encouraged the audience to involve themselves in a variety of volunteering activities. Associate Professor Belinda Goodenough provided fascinating statistics about the brain and encouraged everyone to adopt strategies to assist in preventing or delaying the onset of age-related cognitive disorders, such as dementia.

This year CHeBA partnered with Leagues Clubs Australia and delivered their first forum at the Mounties Leagues Club in Mt Pritchard on 19 August 2015. This is the first time the public forum series has been held in Western Sydney.

The forum was opened by Chief Executive Officer of Mounties, Mr Greg Pickering, who delivered an interesting address and confirmed his support of free educational forums for its members and guests. MC for the event, Associate Professor Belinda Goodenough, delivered an expert talk providing a strong argument for evidence-based strategies to maintain brain health. Dr Nicole Kochan spoke on maximising memory, neurogenesis and how to implement memory strategies for a better life. The forum also included presentations from internationally acclaimed experts in the field of ageing research, CHeBA's Co-Director Professor Henry Brodaty and CHeBA collaborator Professor Maria Fiatarone-Singh from the University of Sydney, who discussed the role of muscle strength and cardiovascular fitness in reducing dementia risk and improving brain function.

Ellie Comerford, Managing Director and CEO of Genworth Financial presented via a video feed stating Genworth's support of the forum and a series of four educational booklets supplementing the *Better Brain. Better Life* forum series. The booklets cover four evidence-based modifiable risk factors associated with healthy brain ageing: physical exercise, complex mental activity, nutrition, and vascular health. These booklets can be viewed at: **https://cheba.unsw.edu.au/content/resources**.

Genworth

LEAGUES CLUBS AUSTRALIA

The Brain Dialogues

CHeBA's Blog, The Brain Dialogues, continued to have a strong readership in 2015.

The blog covers a variety of aspects of brain health, CHeBA's researchers and their activities and our fundraising initiatives. Particular interest was shown for Professor Perminder Sachdev's article titled 'What is Successful Ageing', Kate Crosbie and Heidi Mitchell's article on 'Doubling the Data Through Twins Research' and Monica Cations' blog on 'Keeping Fit to Delay Dementia'. Also popular was the new 'Meet Our Researcher' series which will continue in 2016. To follow The Brain Dialogues go to **https://cheba.unsw.edu.au/content/blog**

City 2 Surf

The unforgiving 14km terrain of the City 2 Surf is a highlight of the year for CHeBA with so many people showcasing their incredible spirit and drive to support and promote the healthy brain ageing message.

2015 was a significant and emotional year at the startline for Team CHeBA, with many new recruits joining those who have participated alongside Co-Directors Professor Perminder Sachdev and Professor Henry Brodaty in previous years in order to honour a parent or grandparent with dementia.

2015 was also the first year that son of Henry Brodaty, Dave, joined the City 2 Surf group. For Dave, participating with Team CHeBA was not just to support his father but to improve his health for the sake of his daughters.

Over 60 people tackled the challenging course for CHeBA. Many of these people were first timers to the event including Megan Tracey and Susan Coorey.

Top times included Professor Julian Trollor who completed in 64 minutes, Ashton Trollor in 65 minutes, Richie Dolan in 69 minutes, Hailey Maxwell in 70 minutes, Monique Cusack in 71 minutes, Rob Kift in 72 minutes, Dr Nicky Kochan in 74 minutes, Heidi Mitchell in 75 minutes and Raymond Chan in 79 minutes. Despite injuries, new members to Team CHeBA Beverly and Carlos Hurtado finished in around the 90 minute and 80 minute mark respectively.

CHeBA's positive ageing heroes are Graham Gates (who has now completed the course for the third time for CHeBA at age 87 and was one of our top fundraisers), Col Blake (who has completed *every* City 2 Surf since the very first event in 1971 and was also one of our top fundraisers) and Derek Nelson (a member of the Legends group who, at age 81, still manages to run the entire course). We thank these gentlemen for the incredible inspiration!

A heartfelt thanks to everyone for the strong support for the cause and a special thanks to Monica Cations, Rosi Benninghaus and friends, for ensuring the team were well fed at the after-celebration at Bronte Park.

$20,000 was raised by Team CHeBA in the 2015 City 2 Surf which went towards The Dementia Momentum.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Donor Support & Partners

Major Donors

The Centre for Healthy Brain Ageing has been able to conduct significant research into the ageing brain with the support of our two major donors, Thomas Foundation and Montefiore Home, who have partnered with CHeBA since the launch of the Centre in 2012.

The Thomas Foundation supports CHeBA's research with the objective of providing better assessment and care for people with Alzheimer's disease and other dementias.

A number of projects were funded by the Thomas Foundation in 2015, including transcranial direct current stimulation combined with cognitive training; epigenetic and genetic factors associated with Alzheimer's disease, metabolomic screening for discovery of low molecular weight blood-based biomarkers, and understanding the role of RNA in age-related memory decline.

CHeBA and Montefiore Home share a mutual goal of improving the quality of life of the older population and Professor Henry Brodaty is the Montefiore Chair of Healthy Brain Ageing. We are enormously grateful to Montefiore Home, David Freeman AM and his team for the ongoing support and interest in CHeBA's research.

Government & Grant Funding

- Alzheimer's Australia Dementia Research Foundation
- Alzheimer's Australia NSW
- Australian Research Council (ARC)
- Dementia Collaborative Research Centre – Assessment & Better Care
- Genworth
- IRT Research Foundation
- National Health & Medical Research Council (NHMRC)
- Rebecca L. Cooper Medical Research Foundation
- The Roth Charitable Foundation
- The Sachdev Foundation
- UNSW Australia
- UNSW Medicine
- Vincent Fairfax Family Foundation
- Yulgilbar Foundation

Individual Donors

We thank the following individuals who made generous donations to CHeBA, separate to The Dementia Momentum (see page 13), in 2015:

- Emma Baker
- Gwenda D. Beckitt
- Mabel Cheng
- DBC Lawyers
- Sue Edwards
- Heather Irwin
- Robert Jordan
- Catherine Kalokerinos
- Patrick D. Lee
- Macquarie Group Foundation
- Alistair McDonald
- Primrose Jane Moss
- Thomas Regan
- Jennifer Rigg
- Seqirus (Australia) Pty Ltd
- Inderjit Singh
- Dr Emily Stockings
- Nicholas J. Willcocks
- John Woolford
- Liz Woolfson
- Zixuan Yang
- Ana M. Young

Our Partners

DCRC
Dementia Collaborative Research Centres

The **Dementia Collaborative Research Centre** based at UNSW is one of three DCRCs funded by the National Health and Medical Research Council. They conduct research to improve the diagnosis, reduce the risk of dementia, and improve the lives of those people living with dementia, their families and carers through over 160 research projects with more being added all the time. Each DCRC has links to other research centres around Australia. The DCRC-ABC is an important component of CHeBA. While it has its own independent management and funding, it contributes to the greater whole and provides important opportunities for collaboration. The Director of the DCRC-ABC, Professor Henry Brodaty, is Co-Director of CHeBA.

NPI
Neuropsychiatric Institute

The **Neuropsychiatric Institute (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 NPI offers a number of specialised programs. It is also at the fore-front of research into neuropsychiatric disorders. The Director of NPI, Professor Perminder Sachdev, is Co-Director of CHeBA.

CHeBA's Research

"International collaboration represents the next phase of medical research in which biomedical scientists, much like physicists, work collaboratively on problems too large to be solved by individual researchers."

Professor Perminder Sachdev

Research Highlights

A multidisciplinary centre, CHeBA staff collaborate across groups and key studies to effectively tackle research questions about cognitive ageing from a range of perspectives, using a diverse set of skills and approaches.

CHeBA groups include: Epidemiology, Genetics & Genomics, Molecular Biology & Stem Cells, Neuroimaging, Neuroinflammation, Neuropsychiatry, Neuropsychology and Proteomics.

Among other sources, data is drawn from CHeBA's three large, longitudinal studies: The Sydney Memory and Ageing Study (MAS), the Older Australian Twins Study (OATS) and the Sydney Centenarian Study (SCS).

Key research findings in 2015 include:

- Decline in cognition is a robust predictor of mortality in older people without dementia at a population level. This relationship is not accounted for by co-morbid depression or other established biomedical risk factors, highlighting the importance of considering cognitive health in older people (Connors et al., *Age and Ageing*).
- As older people develop mild cognitive problems, they also show increased 'neuroticism' (associated with worry and anxiety) and greater degrees of negative emotions (Waggel et al, *International Journal of Geriatric Psychiatry*).
- Ageing is characterised by chronically elevated inflammatory markers (IMs). The neuroanatomical correlation patterns of two proinflammatory cytokines and two vascular IMs might be reflective of the effects of neurodegenerative and vascular pathological processes in the ageing brain (Zhang et al., *Neurobiology of Aging*).
- Structural MRI distinguishes amnestic Mild Cognitive impairment (MCI), but not non-amnestic MCI, from cognitively normal elderly individuals. The structures that best distinguish amnestic MCI from cognitively normal differ in those <85 years from those ≥85 years, suggesting different neuropathological underpinnings of cognitive impairment in the very old (Yang et al, *Current Alzheimer's Research*).
- Being overweight or obese is associated with poorer brain health, in particular a greater decline in the volume of the hippocampus, a part of the brain critical for memory acquisition. These results are consistent with those of previous animal and human studies and further stress the importance of reducing the rate of obesity through education, population health interventions and policy (Cherbuin et al, 2015).

Sydney Centenarian Study participants Margaret Sommerville and Major Cyril Bunny

- Lower intakes of nutrient-dense foods and higher intakes of unhealthy foods are each independently associated with smaller hippocampal volume. To our knowledge, this is the first human study to demonstrate associations between diet and hippocampal volume concordant with data previously observed in animal models (Jacka et al, 2015).
- Concerns about memory problems in non-demented community-dwelling individuals were better predictors of dementia on follow-up if they came from a family member or friend (informant) than from the individual themselves (Slavin et al, 2015).
- Impaired fasting glucose (IFG) represents an intermediary condition between normal fasting glucose and diabetes mellitus. IFG in older adults is associated with IFG have higher disease burden, cardiovascular risk, and systemic inflammation. However, we did not find higher rates of 2-year mortality in this group (Samaras et al, 2015).
- Using a potential natural model for Alzheimer's disease (the Chilean rodent ***O. degus***), our data suggests that alterations in the enzyme serine racemase may be associated with the development and progression of Alzheimer's disease. Deregulation of amino acid levels is likely to contribute to the pathological changes reported in Alzheimer's disease, including excitotoxicity, oxidative stress, and neuronal cell death.
- Our data indicate that transition metals may be enriched with age in the brains of ***O. degus***, and metal dyshomeostasis in specific brain regions may be associated with the development and progression of Alzheimer's disease pathology in ageing individuals. Our study provides further evidence for altered biometal trafficking in the pathogenesis of Alzheimer's disease.
- Brief reaction time measures can provide information on risk of imminent dementia and functional decline within four years in older adults at a population level, with mean reaction time the stronger predictor (Kochan et al., *The American Journal of Geriatric Psychiatry*).
- MIC-1/GDF15 serum levels were negatively associated with brain grey matter volumes both cross-sectionally and longitudinally. Grey matter volume is one of the mediators in previously observed relationships of MIC-1/GDF15 serum levels with cognitive performance in MAS. The results were published in *PLOS ONE*.
- MIC-1/GDF15 serum levels were inversely associated with brain white matter (WM) integrity. The FA value is another mediator in the associations between MIC-1/GDF15 serum levels and cognitive performance. MIC-1/GDF15 serum levels can be considered as a marker of early stage WM degeneration in the ageing population. The findings have been published in *Psychoneuroendocrinology*.
- MIC-1/GDF15 has been proposed as a potential biomarker of cognitive/brain ageing and dementia. Findings were accepted for publication as a review paper in *Current Opinion in Psychiatry*.
- In the Sydney Centenarian Study (SCS):
  - About 55% of people 95 years and above meet criteria for dementia.
  - Rates of heart disease and diabetes were lower than in octogenarians, but hearing and visual deficits were common in centenarians.
  - Rates of psychological distress were low and satisfaction with life high (mean 5.91 out of a maximum of 7).
  - White matter lesions are very common and extensive in centenarian brains, but they do not relate to cognitive impairment.

Research Spotlight: Professor Lynn Chenoweth continues strong collaboration with Montefiore Home

With an established track record of research, training and translation in the fields of aged care nursing, care models and healthy ageing, Professor Lynn Chenoweth strengthened CHeBA's collaborative partnership with major donor Montefiore Home in 2015.

Through a salary paid by CHeBA and funding support from Montefiore Home, Professor Chenoweth ran a number of studies in 2015 with important implications for aged care provision. Professor Chenoweth's findings were disseminated widely through journal articles, conference presentations, published reports and in-house training.

> "Strong collaborative partnerships, such as CHeBA's relationship with Montefiore Home, are crucial to developing responsive research programs, translating key research findings and evaluating scalable implementation measures." PROFESSOR HENRY BRODATY

CHeBA and Montefiore Home links

- Montefiore funding for research projects addressing a wide range of issues including:
  - Person-centred care audits of aged care facilities
  - Modelling and implementing person-centred care and lifestyle services to improve care outcomes
  - Evaluation of a PAINAD screening tool to assist emergency nurses to improve pain assessment and analgesic responses for elderly people with cognitive impairment
  - Improving quality of palliative care and wellbeing for people with advanced dementia living in residential aged care through a facilitated case conference intervention
  - Adapting smart technology to assist individuals in in-home aged care and residential aged care services
  - Investigating the experiences of people with dementia living in retirement villages.
- CHeBA researchers contribute to a regular column in *Montefiore Life* magazine.

Brain Bank

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.

Progress

In 2015, 4 new brains were donated to the CHeBA Brain Donation Program. 8 additional research participants have signed up to donate to the program.

ILP Student Research

Medicine students complete an Independent Learning Project (ILP) as part of their degree to develop fundamental research skills and learn about current issues affecting health. An understanding of brain ageing research will help students in their future careers as health practitioners.

Geraldine Koo – Can blood vessels in your eye predict age-related decline and disease?

Lawrence Hui and Geraldine Koo

"Retinal imaging can be used as a 'window' to observe the vascular health of the eye and brain. My research into this exciting field uses a subset of the Sydney Memory and Ageing Study participants who underwent retinal imaging.

My project looks at whether retinal measures are linked to cognitive ageing, brain structure, stroke and/or dementia. Through this work I hope to contribute to our understanding of vascular ageing and explore whether retinal imaging would be useful as a clinical screening tool"

Lawrence Hui – Identifying genes linked to healthy ageing

"Life expectancy in most countries has increased over the last century. Longevity has been found to occur within families, with siblings of centenarians living longer than controls. In my project I am looking for genes that influence a 'healthy ageing index' which is constructed from a battery of tests including blood pressure, respiratory capacity and cognitive performance. By studying the genetics of healthy ageing in the Sydney Memory and Ageing Study I hope to gain a better understanding of the molecular pathways involved, which may inform novel strategies to improve health in older adults"

Improvements Needed in Computerised Neuropsychological Assessment Devices

CHeBA researchers Dr Nicole Kochan and Dr Nicola Gates have found that computerised neuropsychological assessment devices (CNADs) need to improve in order to reach the same level of reliability as traditional pen and paper assessments.

The review, published in the March 2015 edition of *Current Opinions in Psychiatry*, analysed 17 CNADs developed since 2012 when the standards were published. The researchers found that the field has not significantly advanced, with the majority of recommendations inadequately addressed by current CNADs.

"Proponents of CNADs assert that technology-based assessments improve upon traditional neuropsychological tests. However, there remain fundamental questions of validity, reliability, normative data and administration, raising the question of whether CNADs are appropriate alternatives," say co-authors Dr Gates and Dr Kochan.

A range of issues were found to limit the reliability of CNADs, including the application of existing CNADs to new clinical populations, insufficient clinical guidelines, small sample sizes used for normative data, and individual patient factors, such as language and sensory skills and familiarity with technology.

Dr Gates argues significant research-based improvement is needed before CNADs are as reliable as traditional testing methods.

"We recommend clinicians and researchers make informed decisions about CNAD suitability for their clients and their individual requirements based upon published psychometric and other test information," said Dr Gates.

Neuropsychiatry Forums in 2015

The Neuropsychiatry Group in conjunction with the NPI continues to be at the forefront of training in Neuropsychiatry and will help develop the neuropsychiatry training curriculum for the RANZCP.

1. The Neuropsychiatry Training Weekend: Neuropsychiatry Narratives 17 & 18 April

CHeBA and the Neuropsychiatric Institute co-hosted the Second Neuropsychiatry Training Weekend. The event was a great success with the majority of participants reporting a rewarding professional development experience. The neuropsychiatric approach has become increasingly relevant in recent years to general psychiatrists, psychiatric trainees, neurologists and neuroscientists alike, and this weekend was packed with lectures aiming to provide a foundation of knowledge relevant to such an approach. Participants were given access to key readings from each of the speakers; all opinion leaders in their respective areas of practice and research, allowing them to build on the content delivered in the weekend in their own time.

The program comprised five themes: secondary psychoses, immunology and the mind, social cognition in the clinic, neuropsychological conundrums, and an interactive neuroimaging

workshop led by Dr Frank Gaillard, a neuroradiologist who developed *Radiopaedia*, a website for teaching radiology through illustrative cases. It ended with a clinical forum with discussion of complex clinical cases. Speakers at the 2015 Neuropsychiatry Training Weekend were Professors Perminder Sachdev, Rhoshel Lenroot, Andrew Lloyd and Russell Dale, Associate Professor Oliver Piguet, and Drs Umesh Babu, Bruce Chenoweth, Frank Gaillard, Ilana Hepner, Nicole Kochan, Teresa Lee and Adith Mohan. Dr Paul Silberstein returned in 2015 to join the complex clinical case panel.

2. Keynote Speeches from RANZCP Travelling Professor Charles F. Reynolds III as Keynote Speaker 17 & 18 September

We were delighted to host 2015 RANZCP Travelling Professor Charles F. Reynolds III MD as the Keynote speaker for two forums run in affiliation between CHeBA, the NPI and the Aged Care Psychiatry Service.

Professor Reynolds is the UPMC Endowed Professor in Geriatric Psychiatry at the University of Pittsburgh and directs the NIMH sponsored Center of Excellence in the Prevention and Treatment of Late Life Mood Disorders and the UPMC/Pitt Aging Institute. He is widely recognised as a leading teacher and innovator in the field of old age psychiatry.

Professor Reynolds III addressed the following forums:

- **Prevention of Depression: Current Opinion Forum 17 September**

This forum explored current opinion on the prevention of depression. Topics ranged from depression prevention among young people and in late life, to prevention of bipolar disorder, to prevention of suicide. Speakers included: Professors Gavin Andrews, Michael Berk, Helen Christensen, Philip Mitchell and Jane Pirkis, and Dr Yael Perry.

- **Depression in Late Life: Current Status 18 September**

Key issues addressed included melancholia, the neurobiology of late life depression, pseudodementia and pseudodepression, suicide in late life, bipolar disorder in late life, internalising disorders in late life, and psychosocial treatment. Speakers included: Professors Gavin Andrews, Henry Brodaty, Colleen Loo, Sharon Naismith, Gordon Parker and John Snowdon, and Drs Chanaka Wijeratne and Viviana Wuthrich.

Dr Julia Muenchhoff: Towards early detection of Alzheimer's disease

Dr Julia Muenchhoff was awarded a Rebecca L. Cooper Foundation Medical Research Grant of $21,000 for her project *Apolipoprotein levels and post-translational modifications as blood biomarkers for early stages of Alzheimer's disease* in 2015.

Dr Muenchhoff's research takes a novel approach to identify blood-based biomarkers which could potentially aid diagnosis at the stage of mild cognitive impairment (MCI), often a pre-cursor to Alzheimer's disease (AD), and therefore also improve future drug and therapeutic strategies to treat AD.

According to Dr Muenchhoff, "the ability to diagnose Alzheimer's disease at an early stage prior to extensive neuronal damage is essential in order to realise the full potential of disease modifying treatments". At present, many drug candidates may have failed due to their administration only after the disease had progressed too far.

"We also expect that our novel approach will identify modifications to proteins that are relevant to Alzheimer's disease pathology. Once identified, we can study what consequences these modifications might have for the function of the protein. This could improve our understanding of the progression of the disease, which is still not well understood."

Preliminary findings confirmed a number of previously identified potential protein biomarkers for AD and MCI. Levels of two proteins - fibronectin and C1 inhibitor –previously associated with AD were found for the first time to change in MCI. The results were published in the *Journal of Alzheimer's Disease*.

Although preliminary, these findings are a step towards improving early detection and diagnosis of Alzheimer's disease, says Professor Perminder Sachdev, Co-Director of CHeBA. "Studies like this point researchers towards those proteins that deserve further investigation and weed out others that are unlikely to be useful markers," he said.

This study has generated further evidence towards the possibility of a blood test for early stages of Alzheimer's disease, however the authors caution that further studies are needed to validate these findings.

Dr Karen Mather: Rising Star

Dr Karen Mather was awarded the competitive UNSW Medicine Dean's Rising Star Award for "significant contributions to research" on 18 November 2015.

Dr Mather is the leader of CHeBA's Genetics & Genomics Group. Her recent research includes investigating the biological determinants of memory loss, an early symptom of Alzheimer's disease, as well as being heavily involved in the genetics components of CHeBA's international consortia, which aim to increase our understanding of healthy and pathological ageing.

Dr Karen Mather and Head of the School of Psychiatry, Professor Philip Mitchell

CHeBA Collaborators

Industry

- Anglican Retirement Villages
- Baptist Community Services
- 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)
- International Society of Vascular Behavioural and Cognitive Disorders (VASCOG)

National

COMMONWEALTH

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

WESTERN AUSTRALIA

- Edith Cowan University, Perth
- Murdoch University, Perth

TASMANIA

- University of Tasmania, Hobart

ACT

- Australian National University, Canberra

NEW SOUTH WALES

- University of Newcastle, Newcastle
- University of New England, Armidale
- University of Wollongong, Wollongong

Sydney

- 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
- Garvan Institute
- Macquarie University
- National Drug & Alcohol Research Centre (NDARC), UNSW
- Neuropsychiatric Institute (NPI), Prince of Wales Hospital
- Neuroscience Research Australia (NeuRA), UNSW
- School of Biotechnology and Biomolecular Sciences (BABS), UNSW
- School of Medical Sciences, UNSW
- School of Psychology, UNSW
- St Vincent's Centre for Applied Medical Research
- St Vincent's Hospital
- University of Sydney
- University of Technology Sydney
- Western Sydney University

SOUTH AUSTRALIA

Adelaide

- Flinders University
- University of Adelaide

VICTORIA

Melbourne

- The Florey Institute of Neuroscience and Mental Health
- La Trobe University
- Monash University
- National Ageing Research Institute
- Royal Melbourne Hospital
- University of Melbourne

QUEENSLAND

Brisbane

- Griffith University
- QIMR Berghofer Institute, Brisbane
- Queensland University of Technology
- St Andrew's Medical Institute
- University of Queensland

International

AFRICA

- University of Ibadan, Nigeria
- University of Natal Kwazulu, South Africa

ASIA-PACIFIC

- Beijing Normal University, China
- Capital Medical University, China
- Peking University, China
- Shanghai Jiaotong University, China
- Institut de Recherche pour le Développement (IRD), Tahiti, French Polynesia
- Institut Louis Malardé, Tahiti, French Polynesia
- Chinese University of Hong Kong, Hong Kong
- Hong Kong Polytechnic University, Hong Kong
- The University of Hong Kong, Hong Kong
- CSI Holdsworth Memorial Hospital, India
- Atma Jaya Catholic University, Indonesia
- 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
- National Neuroscience Institute, Singapore
- National University Health System, Singapore
- Mahidol University, Thailand

MIDDLE EAST

- Baqiyatallah University of Medical Sciences, Iran
- Sultan Qaboos University, Oman

EUROPE

- Innsbruck Medical University, Austria
- Karolinska Institutet, Finland
- University of Helsinki, Finland
- CHU Amiens-Picardie, France
- French National Institute of Health and Medical Research (INSERM), France
- University Aix-Marseille, France
- Lille University Hospital*, France*
- Forschungszentrum Juelich, Germany
- Heidelberg University, Germany
- Ludwig Maximilians University Munich, Germany
- Max Planck Institute of Psychiatry, Germany
- Neuroscience Network Düsseldorf, Heinrich Heine University, Germany
- University of Leipzig, Germany
- University of Marburg, Germany
- University of Athens, Greece
- Golgi-Cenci Foundation, Italy
- Mario Negri Institute for Pharmacological Research, Italy
- University of Udine, Italy
- Jagiellonian University, Poland
- University of Porto, Portugal
- University of Valencia, Spain
- University of Zaragoza, Spain
- Lund University, Sweden
- University of Gothenburg, Sweden
- Leiden University, The Netherlands
- Maastricht University, The Netherlands
- University of Groningen, The Netherlands
- VU University, The Netherlands

UK

- Cambridge University, England
- Cognitive Function & Ageing Studies, England
- King's College London, England
- Leeds-Beckett University, England
- Newcastle University, England
- University College London, England
- University of Bradford, England
- University of Leeds, England
- Royal College of Surgeons in Ireland, Ireland
- University of Aberdeen, Scotland
- University of Edinburgh, Scotland
- Swansea University, Wales

NORTH AMERICA

- Dalhousie University, Canada
- Université de Montréal, Canada
- Stanford University, California, USA
- University of California, California, USA
- University of Colorado, Colorado, USA
- University of Georgia, Georgia, USA
- James A Haley VA Hospital, Florida, USA
- Johns Hopkins Medicine, Maryland, USA
- Mayo Clinic, Minnesota, USA
- Magill University, Canada
- 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

Consortia

International research consortia provide opportunities for researchers to share and compare data from existing studies, allowing systematic examination of brain ageing issues on a larger scale.

"International collaborations provide the ability to replicate findings in different geographical and ethnic groups, and also determine which risk and protective factors are truly universal." PROFESSOR PERMINDER SACHDEV

Researchers at CHeBA are studying the process of human ageing to determine the factors that influence the trajectory of healthy ageing and cause age-related diseases, including dementia. At CHeBA, we are taking this line of investigation to the next level by making it international. Many research groups from around the world have asked similar questions and established cohorts in their local area. Since dementia and ageing are universal concerns, CHeBA researchers seek to harness the power of these international studies by bringing them into large consortia. These consortia not only provide large sample sizes necessary to address some of the questions, they also provide the ability to replicate the findings of one study in another in a different geographical and ethnic group, and also determine which risk and protective factors are truly universal.

CHeBA leads a number of international consortia: COSMIC, ICC-Dementia, STROKOG and PROMOTE (see pages 21-23). Additionally, CHeBA is a member of the following consortia:

- CHARGE (Cohorts for Heart and Ageing Research in Genetic Epidemiology)
- ENIGMA (Enhancing Neuro Imaging Genetics through Meta-Analysis)
- PERADES (Defining Genetic, Polygenic and Environmental Risk for Alzheimer's disease)
- EuroDiscoTWIN (European Discordant Twin Study)
- BRIDGET
- EADB.

Study Finds the First Genes Associated with General Cognitive Function

Researchers have identified genes associated with people's general cognitive function – how we process information.

An international team including researchers from CHeBA found significant small signals from four genetic regions that were associated with having stronger thinking skills. These regions contained genes that have previously been associated with neurological and psychiatric states.

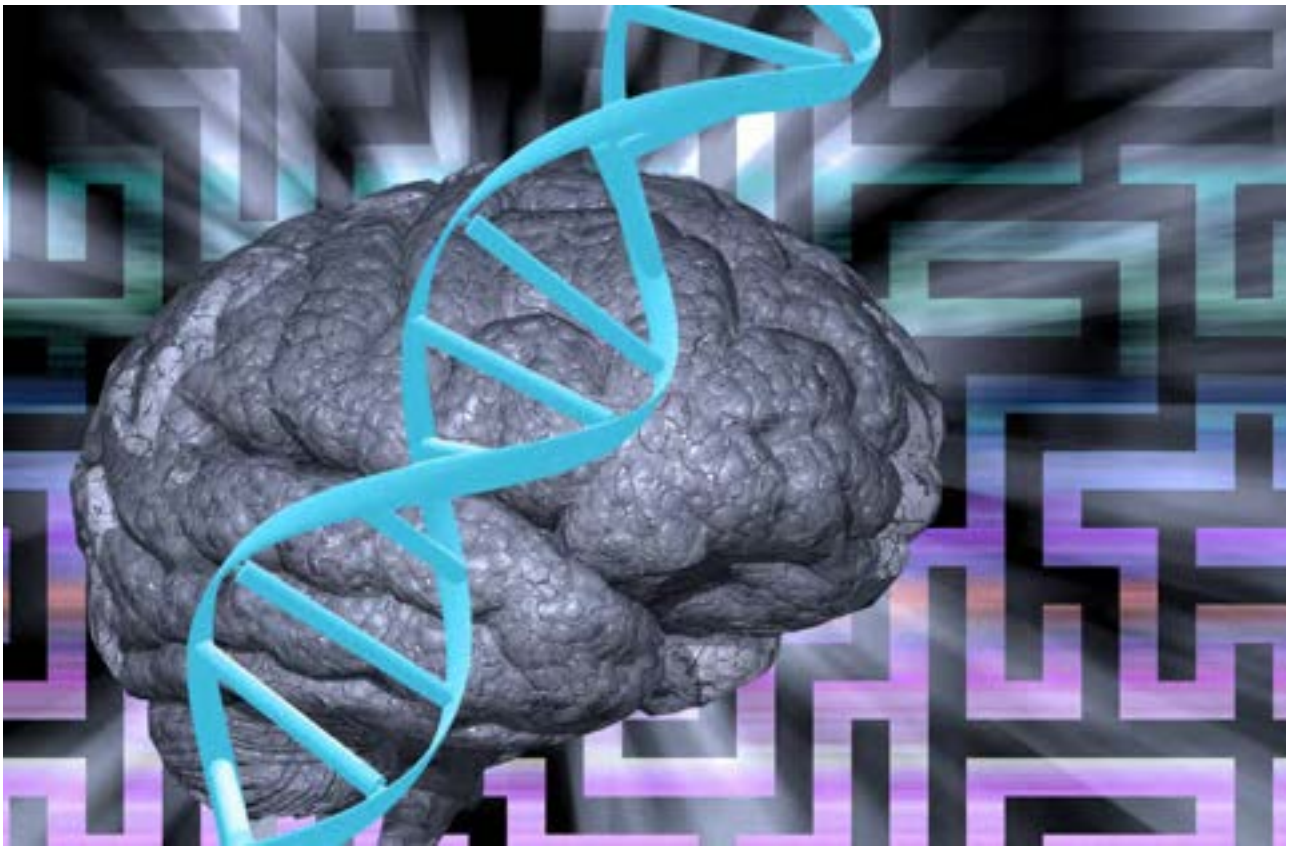
The study, published in *Molecular Psychiatry in February 2015*, was conducted under the auspices of the CHARGE (Cohorts for Heart and Aging Research in Genetic Epidemiology) Consortium. It analysed data from 54,000 people aged more than 45 years old who had taken part in 31 cohort studies including CHeBA's Sydney Memory & Ageing Study and the Older Australian Twins Study.

Using DNA data, the scientists found general cognitive function was 28 percent heritable in people aged more than 45 years old.

Co-Director of the Centre for Healthy Brain Ageing, Professor Perminder Sachdev said "This study sets the parameters within which gene discovery should be pursued. The discovery of specific genes that influence cognitive function in later life may be related to brain development, maintenance or degeneration, and knowledge of their specific roles can help understand the mechanisms of disease, and ultimately find strategies to alter these mechanisms."

Professor Sachdev said that CHeBA contributes a number of international collaborations to accelerate positive outcomes in ageing research, particularly in relation to Alzheimer's disease and other dementias.

The study involved researchers in Australia, Austria, Croatia, Finland, France, Germany, Holland, Iceland, Ireland, Norway, Sweden, the UK and the US.



ENIGMA Findings Published in Nature

An international study including CHeBA researchers provided insight into the causes of variability in human brain development. Reported in *Nature* in January 2015, the identification of five genetic variants that influence the size of structures within the brain may help us determine the genetic processes that underlie neuropsychiatric diseases.

Almost 300 scientists from 193 institutes shared results from analyses of genetic data and MRI scans from more than 30,000 individuals, including data from CHeBA's Sydney Memory and Ageing Study and the Older Australian Twins Study.

CHeBA's Co-Director Professor Perminder Sachdev said that the study focused on the portions of the human brain known as the subcortical regions, which are associated with movement, learning, memory and motivation.

"One of the identified genetic variants confirms a previously established influence on the volume of the hippocampus, a key region in forming and storing memory. What is novel is the discovery of 5 genes that influence the volume of the putamen and caudate, two key structures in the regulation of movement and emotion."

"This study is the triumph of international collaboration, with data contributed by over 200 investigators that brought together 50 cohorts from all over the world," Professor Sachdev said.

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)

Project description: This project examines the effect of acute illness requiring hospitalisation on a 6 year cognitive and functional trajectory. It will utilise cognitive and functional data from the Sydney Memory and Aging Study and the Older Australian Twins Study combined with linked data regarding hospitalisations from self-report questionnaires and NSW hospital records via the Centre for Health Record Linkage (CHeReL). Linear mixed modeling will be used to examine the extent to which acute hospitalisation events are able to predict the pattern and extent of decline in cognition and functional ability from baseline to follow-up assessments at two, four and six years.

Aims:

- To observe the effect of acute physical illness requiring hospitalisation on cognitive and functional trajectory over several years in longitudinal cohort studies of cognitive ageing.
- To examine whether variables describing the nature of the illness and hospitalisation influence the level of decline in cognition and function over time.
- To 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.

Design & method:
Acute physical illness will be defined as any illness that requires a minimum of one overnight stay in an acute hospital bed. Admissions involving a primary psychiatric or neurological diagnosis as a reason for admission or admissions to rehabilitation or non-acute facilities will be excluded. Hospital admissions without an overnight stay such as day surgery or dialysis will also be excluded. Participants are drawn from MAS and OATS. Hospitalisation data regarding the admission timing and length, intensive care admission, diagnosis and a variety of other information will be available for each MAS and NSW OATS participant through the NSW Admitted Patient Data Collection (ADPC) and the NSW Emergency Department Data Collection (EDDC) via the Centre for Health Record Linkage (CHeReL).

Linear mixed modeling (LMM) will be used to examine the extent to which the occurrence of acute physical illness requiring hospitalisation predicts the pattern and extent of decline in cognitive and functional ability from baseline to follow-up assessments at two, four and six years. The model will include risk-factor variables (e.g. APOε4 carrier status, MCI), as well as the interaction between these and variables describing the nature of the illness and hospitalisation. Participants' sociodemographic characteristics (including age, sex and years of education) will also be included as independent variables. In addition to examining the overall linear decline years, possible non-linear patterns of decline will be investigated by the inclusion of squared and cubed values of time.

Progress to date: A systematic review of studies investigating cognition following hospitalisation is being prepared to be submitted for publication. An ethics approval was obtained, in collaboration with two other studies, to obtain hospital linked data for two existing CHeBA databases that will enable hospitalisation data to be accessed for the Sydney Memory and Ageing Study and the Older Australian Twins Study. This data has been accessed via CHeReL in NSW.

Benefits: The large amount of detailed health information we will be acquiring from CHeReL will provide the opportunity for other researchers to further investigate the health status of the study participants from MAS and OATS and associations with cognition, morbidity and mortality. The research findings will have implications for the management of hospital patients on discharge and for subsequent cognitive evaluation of these patients who may present to GPs and specialists with memory and other cognitive problems. Depending on the factors associated with cognitive decline, a set of physical health risk factors will be defined and moderating variables will be delineated which will guide doctors about which of their elderly patients are at greatest risk of cognitive decline. Furthermore, information will be disseminated about expected trajectories over short and long-term intervals so that physicians and surgeons can advise patients and provide appropriate management plans on discharge and beyond. Eventually, guidelines and care pathways in hospitals can be optimised to identify those patients most at risk of cognitive decline and moderate factors affecting cognitive trajectory to minimise long-term cognitive effects from their admission, overall improving in-patient standard of care.

Output: A systematic review manuscript is in preparation.

Funding: This study is being funded by the Australian Society of Anaesthetists and the NSW DCRC.

Date commenced: October 2013

Expected date of completion: January 2019

Abeta (Aβ) peptides in plasma

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

Other investigators: Dr Amelia Assareh (BABS, UNSW, formerly CHeBA), Ms PC Ng (formerly Brain & Ageing Research Program), Associate Professor George Smythe (SOMS, UNSW)

Project description: Correlation of plasma Aβ with cognition and brain volumetrics in mild cognitive impairment (MCI).

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.

Design & method: Cross-sectional design using W1 MAS data and ELISA assays to quantify plasma levels of Aβ peptides 1-40 and 1-42. A longitudinal design aspect was used to study association of W1 plasma Aβ peptides with progression to MCI in W2.

Progress to date: Manuscript titled "The relationship between plasma Aβ levels, cognitive function and brain volumetrics: Sydney Memory and Ageing Study" has been accepted for publication in *Current Alzheimer Research,* 2016*, 13,* 243-255.

Benefits:

- Potential biomarkers to assist in diagnosis of predisposition to MCI and/or AD, especially if used for tracking longitudinally or in conjunction with additional proteomics or metabolomics markers to improve sensitivity and specificity.
- Explore the possibility that plasma Aβ peptide levels are correlated with brain volumetric and cognitive changes, to explore disease mechanisms.

Output: 5 conference presentations, 4 invited oral presentations, 2 publications, 1 manuscript in press.

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

Date commenced: July 2007

Expected date of completion: February 2016

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, John Crawford, Julia Muenchhoff, 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)

Project description: Relatively little is known about the effects on plasma Aβ by variables such as cognitive, physiological or disease factors, or drugs, nutrients or supplements taken to treat

neurodegenerative diseases or their comorbidities. To establish Aβ levels as a biomarker of dementia therefore warrants further study in large cohorts that have longitudinal data. Several forms of Aβ are gaining acceptance as biomarkers of AD neuropathology, including soluble CSF levels and plaque as measured by PET scanning. Others such as plasma Aβ are potential (though controversial) biomarkers and located in a convenient sample type for screening. The numerous "potential" covariates will require large sample sizes for sufficient statistical power, and multiple cohorts for robustness and test of reproducibility across studies.

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 four neurodegenerative conditions tested.

Design & method: Multicohort longitudinal study using existing ELISA data on plasma levels of Aβ peptides 1-40 and 1-42.

Progress to date: Analysis of the relationship between plasma Aβ Levels, cognitive function and brain volumetrics undertaken for the Sydney MAS. Initiating data access approval for other studies.

Benefits:

- Potential biomarkers to assist in diagnosis of predisposition to MCI and/or AD.
- Better understand factors that affect plasma Aβ peptide levels and the specificity of Aβ peptide levels for neurodegenerative diseases.

Output: Paper submitted to *Current Alzheimer Research*.

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

Date commenced: 2015

Expected date of completion: Ongoing

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

CHeBA staff: Julia Muenchhoff, Anne Poljak, Fei Song, Nady Braidy, Nicole Kochan, Wei Wen, John Crawford, Julian Trollor, Henry Brodaty, Perminder Sachdev

Other investigators: 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)

Project description: Quantification of apolipoprotein levels in MCI and Alzheimer's disease plasma in a variety of population based cohorts, from Sydney and elsewhere in Australia.

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.

Design & method: Both cross-sectional and longitudinal designs are used. Cohorts include: Sydney MAS (all 4 waves), Hunter Community Study (HCS), Dominantly Inherited Alzheimer's disease Network (DIAN), Older Australian Twins Study (OATS) and Sydney Centenarian Study (SCS). Cellular and animal models of ageing and AD are in the planning phase.

Progress to date: Experiments are ongoing, with numerous conference presentations, several published manuscripts, and both local and international collaborators involved.

Benefits:

- Potential biomarker panel to assist in diagnosis of predisposition to MCI and/or AD.
- Identify robust biomarkers, which show consistent change across studies.
- Understand the effect of plasma apolipoprotein changes on cognition and brain volumetrics.

- Determine how plasma apolipoprotein levels change with age, particularly advanced old age.
- Understand the role of specific apolipoproteins (ApoA1, ApoD, ApoJ and ApoH) in the ageing brain.

Output: 1 conference presentation, 2 publications, 4 manuscripts in preparation.

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

Date commenced: 2006

Expected date of completion: Ongoing

Assessment and management of the cognitively impaired older person 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)

Project description: Receiving care from an Emergency Department (ED) team with limited skills in care of the person with dementia requiring acute treatment care carries a high risk that symptoms like pain that can be missed or misinterpreted. Untreated or poorly managed pain in people with dementia can escalate suffering, precipitate delirium and agitation. The study comprised three stages: assessing the prevalence of ED patients >64 years presenting to the ED with a suspected long bone fracture and in pain, a comparative study of pain assessment and analgesic response by ED staff to pain in people >64 years with and without cognitive impairment, and a clinical trial of a dementia-specific pain assessment tool for use by ED nurses in all people >64 years. The prevalence study findings showed that 50-80% of all ED patients present for pain relief, of whom most are older than 65 and 25-28% have dementia. The comparative study revealed far longer wait times (up to 148 minutes) for pain assessment and analgesia for people with a cognitive impairment, compared with people over 65 without cognitive impairment (68 minutes). The subsequent trial of ED nurses' use of the Pain Assessment in Advanced Dementia tool (PAINAD) with people >64 years presenting to the ED with a suspected long bone fracture and in pain, produced a significant improvement in their attention to pain and improved time to analgesia for the cognitively impaired group. The wait time to analgesia reduced significantly by 17 minutes on average in 602 ED patients with dementia and pain associated with a long bone fracture.

Aim: To 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.

Design & methods: The study was conducted in eight tertiary hospital EDs in NSW and comprised three stages: assessing the prevalence of ED patients >64 years presenting to the ED with a suspected long bone fracture and in pain, a comparative study of pain assessment and analgesic response by ED staff to pain in people >64 years with and without cognitive impairment, and a clinical trial of use of the PAINAD by ED nurses in all people >64 years.

Progress to date: All three study stages have been completed and all data analysed and reported. The study findings provide the justification for further investigation through a NHMRC funded clinical trial of the PAINAD and protocols for staff and patient carers that are informed by the PAINAD.

Benefits: The study's evidence clearly demonstrates that there is inadequate and inappropriate pain relief for people with cognitive impairment in the ED, which results in adverse events, hospital readmissions, increased functional decline, cognitive decline, behavioural changes and co-morbid mental illness. These negative outcomes are fundamentally attributable to poor pain management and a lack of family/carer engagement in the pain management process in the ED. Pain assessment and management for these vulnerable patients can be improved by educating all ED nurses and physicians in use of the PAINAD, and by establishing protocols for more accurate clinical assessment and management of pain and for family members/carers prompting ED staff in better assessment and responses to pain in the person with a cognitive impairment.

Output: 4 journal publications, 3 conference presentations, 1 conference presentation accepted for 2016.

Funding: Montefiore Home funding (administered by CHeBA) supports Professor L. Chenoweth's research position with CHeBA, Emergency Care Institute of NSW (not administered by CHeBA).

Date commenced: May 2013

Expected date of completion: May 2016

Brain proteomics: Differential expression of the proteome in AD brain

CHeBA staff: Anne Poljak, 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)

Project description: Proteomic expression difference profiling in Alzheimer's disease cortical brain regions.

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.

Design & method: Case control design using Brain Bank tissue (Victorian Brain Bank Network and NSW Brain Bank) from age-matched normal control and AD brain tissue in 65-75 year and ≥90 year age groups. An iTRAQ proteomics approach will be employed.

Progress to date: Tissue samples have been fractionated into 5 subcellular fractions and proteomics experiments performed using iTRAQ methodology.

Benefits:

- Proteomics is a discovery-based approach, and as a research tool may provide a signpost for novel proteins and pathways to provide insight into AD pathogenesis
- By identifying deregulated proteins, which may not have previously been linked to AD, the potential exists for discovery of novel mechanisms of disease causation. Furthermore, these data will provide the impetus and rationale to follow new research leads.

Output: 5 conference presentations, 4 invited oral presentations, 3 publications, 2 manuscripts in preparation.

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

Date commenced: 2007

Expected date of completion: Ongoing

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)

Project description: Over half of the residents in aged care homes have dementia and another quarter have some degree of cognitive impairment. In the latter stages of dementia special care is needed to ensure a comfortable end**.** This cluster randomised controlled trial evaluated facilitated case conferencing for end of life care in people with advanced dementia. Ten residential aged care facilities (RACFs) in Sydney and Brisbane received facilitated case conferences and ten continued usual care. Facilitated case conferences were managed by registered nurses who received one week's intensive training to fulfil the role of Palliative Care Planning Coordinator (PCPC) 0.4 full-time equivalent (FTE) over 18 months. The PCPC's role was to: 1) use evidence-based 'triggers' to identify residents with advanced dementia likely to benefit from a case conference; 2) organise, set an agenda, chair and document case conferences with optimal involvement from family, multi-disciplinary facility staff and external health professionals (e.g. general practitioners [GPs]); 3) develop and oversee implementation of palliative care plans; and 4) train other RACF staff in person-centred palliative care. Effectiveness of the intervention was evaluated by comparison with ten other facilities which continued usual care. Outcomes included 3-monthly measures of resident quality of life, prevalence of hospitalisations, emergency department (ED) presentations and other potentially non-palliative interventions (e.g. ventilation), and family and nurse ratings of end of life care one month after residents died. Effectiveness of the intervention and perceptions of other factors associated with high quality care were evaluated qualitatively by means of semi-structured interviews with PCPCs, families, facility staff and GPs.

Aims: The aim of the study was to improve the quality of palliative care and wellbeing for people with advanced dementia living in residential aged care through a facilitated case conference intervention.

Design & method: Parallel cluster randomised phase III study comparing a facilitated case conference (FCC0 approach to palliative care for people with end-stage dementia and usual care in 20 randomly assigned aged care homes in Sydney and Brisbane. FCC comprised 3 components: 1) training of a Palliative Care Planning Coordinator (PCPC) at each home, 2) ongoing support of the PCPC to promote case conferencing (CC) and person-centred palliative care, and 3) provision of a written framework with supporting clinical pathways to guide CC and ongoing palliative care over the final months of life.

Progress to date: 20 randomly assigned aged care homes recruited in excess of its target of 272 residents and families. In total, PCPCs organised and supported 138 case conferences for 117 residents over the course of the project, with input from registered nurses (RNs) (99% of case conferences), assistants in nursing (AINs) (61%), physiotherapists and aides (35%), recreational officers (21%), enrolled nurses (19%) and diversional therapists (10%). Around 50% of case conferences organised by PCPCs involved a GP, 10% a geriatrician, and one an aged care psychiatrist. Case conferences resulted in advance care plans in 62% of cases, medication reviews in 48%, and comprehensive medical assessments in 20%. PCPCs conducted a total of 117 training sessions for other staff within their 10 facilities; most commonly covering topics relating to dementia care, person-centred care and palliative care (17 sessions each).

Benefits: The case conferencing resources developed and trialed in this study will be made available on the website of the national CareSearch Palliative Care Knowledge Network, already the home of the Residential Aged Care Palliative Approach Toolkit. The existing Toolkit resource provides general guidance for palliation and case conferencing in aged care, but does not focus on the needs of residents with advanced dementia. Web-based, rather than hard-copy format, has been chosen because it enables ready access for providers throughout Australia and can be updated regularly to ensure currency with emerging evidence for best-practice care and other resources

Output: 1 journal publication, 2 conference presentations, 1 conference presentation accepted for 2016, Toolkit of FCC resources (http://www.caresearch.com.au/CareSearch/tabid/2718/Default.aspx).

Funding: Montefiore Home funding (administered by CHeBA) supports Professor L. Chenoweth's research position with CHeBA, Department of Health and Ageing (not administered by CHeBA).

Date commenced: March 2013

Expected date if completion: June 2016

Defining the role of inflammation in depression during ageing

CHeBA staff: Perminder Sachdev, Julian Trollor

Other investigators: Professor Bernhard Baune (University of Adelaide)

Project description: This study builds on two well-characterised ageing cohorts, with the aim to assay systemic inflammatory biomarkers (proteins and gene-expression) derived from bloods to determine contribution of these biomarkers to depression. Samples were collected at the time of in-depth assessments, including a psychiatric assessment. These assessments establish current and previous diagnoses and severity of depressive symptoms. Serum has been collected for both cohorts across multiple time-points, and genome-wide genotype data are already available. Through the prospective study of inflammatory signalling proteins and depression diagnosis, we will clarify the biological role of inflammation in these mood states. In order to capitalise on the rich resources available in the fourth wave of MAS (DNA, RNA, serum), we will take a cross-sectional approach with the aim to identify gene expression that predicts protein levels, and extend these findings to the genetic data by identifying expression quantitative trait loci (eQTLs) for these gene systems. Based on our findings we will target genetic analyses to variants that show evidence for being functional. We will investigate if these eQTLs predict lifetime depression in this sample, and utilise machine-learning methods to determine the best prediction model (using gene expression, proteomic, and genetic data) we have available with our data. This predictive model will then be tested in the OATS sample with targeted gene expression and protein assays run and analysed.

Aims:

- To 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).

- To investigate the molecular underpinnings of inflammation during aging by using genetic, gene expression, and proteomic data.
- To 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).

Design & Method: Use longitudinal study to develop a predictive model of lifetime depression using quantitative genetics, and then test in another cohort.

Progress to date: Genetic analyses have been performed; data analysis is proceeding.

- Review of underpinning genetic factors of inflammation on cognitive ageing published in *European Neuropsychopharmacology*.
- Characterised whole genome gene expression patterns in peripheral blood samples from MAS cohort.
- Investigated shared genetic overlap between depression and cardio-metabolic genes which is highly relevant for at risk states during ageing

Benefits:

- The first of its kind to address the question of bi-directionality between inflammation and depression in ageing.
- Improved understanding of the biological and molecular underpinnings of inflammation and depression
- Could lead to early identification of risk factors and to novel and improved pharmacotherapies for depression in late life.

Output: 1 review paper published (*European Neuropsychopharmacology*).

Funding: NHMRC (administered by University of Adelaide).

Date commenced: January 2014

Expected date of completion: December 2016

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, Anbu Thalamuthu

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

Project description: There is a large variation in published prevalence rates for mild cognitive impairment (MCI), from around 3% to 35%. Some of this variation may stem from true geographic or racial/ethnic differences, but the majority is likely due to differences in methodology between studies.

Aims: To make 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.

Design & method: Data were provided by 11 COSMIC studies from the USA, Europe, Asia and Australia. We developed protocols for harmonising data on neuropsychological test performance, functional status and subjective memory complaints, and then used the harmonised data to make classifications of MCI.

Progress to date: The determination of the prevalence of MCI has been completed and a paper published.

Benefits: MCI imposes a health burden of its own and increases the risk of dementia. It is thus important to reliably estimate the prevalence and incidence of MCI around the globe.

Output: 1 journal publication (*PLOS ONE*).

Funding: NHMRC Program Grant ID 568969, direct donations to The Dementia Momentum initiative (from March 2015), Vincent Fairfax Family Foundation (from October 2015).

Date commenced: 2013

Expected date of completion: December 2016 for incidence component

Determine the rates and patterns of cognitive decline in ageing populations from different geographical regions (using data from COSMIC)

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

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

Project description: The rapidly growing global population of elderly individuals is accompanied by increasing individual and societal impacts of normal cognitive ageing and neurocognitive disorders like dementia. Little is known about how rates and patterns of cognitive decline are similar or different in different geographical regions and ethnicities.

Aims: To investigate age-related changes in neuropsychological test performance and cognitive status in cohorts from different geographical regions and ethnicities, and to determine if there are differences between these.

Design & method: Both cross-sectional and longitudinal analyses of cognitive domain scores, and of scores for individual tests that are common among the cohorts (including Trail Making, Boston Naming and semantic fluency).

Progress to date: Analyses of common neuropsychological tests from among 14 COSMIC cohorts with longitudinal data have been completed. A conference abstract has been submitted (for AAIC 2016) and a paper is being prepared.

Benefits: Understanding the rate and pattern of cognitive decline that occurs with ageing is important for population health policies, and knowledge of regional and ethnic differences will help create tailored approaches.

Output: Conference abstract submitted for 2016; manuscript in preparation.

Funding: NHMRC Program Grant ID 568969, direct donations to The Dementia Momentum initiative (from March 2015), Vincent Fairfax Family Foundation (from October 2015).

Date commenced: 2014

Expected date of completion: December 2016

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

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

Other investigators: Dr Russ Pickford (BMSF, UNSW)

Project description: Correlation of plasma lipids with cognition and brain volumetrics in mild cognitive impairment (MCI).

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.

Design & method: Cross-sectional design using W1 MAS data and coupled mass spectrometry techniques to quantify plasma lipid levels

Progress to date: The lipidomics technique is currently being optimising in collaboration with the BMSF.

Benefits:

- Potential biomarkers to assist in diagnosis of predisposition to MCI and/or AD, especially if used for tracking longitudinally or in conjunction with additional proteomics or metabolomics markers to improve sensitivity and specificity.
- Explore the possibility that plasma lipid levels are correlated with brain volumetric and cognitive changes, to explore disease mechanisms.

Output: None to date.

Funding: Australian Postgraduate Award PhD Scholarship to support salary for Mr Matthew Wong.

Date commenced: August 2015

Expected date of completion: August 2018

Epigenetic and genetic factors and AD development

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

Other key investigators: Dr Nicola Armstrong (Murdoch University), Professor Bernhard Baune (University of Adelaide), Associate Professor John Kwok (NeuRA, UNSW), Professor Peter Schofield (NeuRA, UNSW), Dr David Stacey (University of Adelaide)

Project description: This project aims to determine the key epigenetic factors involved in the development of Alzheimer's disease (AD) focusing on DNA methylation and small RNA molecules, known as microRNAs (miRNAs). However, ultimately, all aspects of genetic and epigenetic variation interact with each other. This newly generated epigenetic data will be integrated with existing CHeBA genetic and gene expression information to gain a more comprehensive understanding of AD.

Aims:

- To unravel the relationships between DNA methylation, miRNAs, the genome and gene expression in early AD.
- To determine the role of miRNAs as a biomarker of memory loss, an early marker of AD.

Design & method: Initially, DNA methylation and miRNA profiles will be compared across three groups, AD, mild cognitive impairment and controls.

In addition, the data will be integrated with existing information collected on genetic variants and gene expression. Further experiments will be planned.

Progress to date: The three groups of participants have been selected from Sydney MAS participants at Wave 4. miRNA profiles for these groups of participants have been collected.

Benefits: An improved understanding of the genetic and epigenetic factors that are associated with the development of AD will increase our knowledge regarding the early molecular changes observed in AD. This work ultimately may suggest novel interventions or treatments to prevent AD, slow down its progression and/or delay its onset.

Output: None to date.

Funding: This work is supported by the Mason Foundation (NA & KM) and the Roth Charitable Foundation (HW PhD scholarship). Sydney MAS is supported by the NHMRC Program Grant 568969. Karen Mather was kindly supported by the Thomas Foundation and by the NHMRC Capacity Building Grant 568940.

Date commenced: January 2015

Expected date of completion: Ongoing

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

Project description: There are many Assistive Robotic devices that are being used to assist people in daily living activities and to enhance the quality of life of senior citizens and people with disabilities. The project team has been developing the Smart Hoist in collaboration with the Illawarra Retirement Villages, as well as the Smart Wheelchair, the Smart Walker, and the Telepresence Robot. The assistive technologies for navigation, localization and shadowing (Follow-Me), is new, being developed, and aims to offer many benefits to older citizens in receipt of aged care services. Complementing each other, these intelligent assistive technologies improve the assurance that older people need to engage in a multitude of daily life activities and are very robust and safe to use by older people. The study is evaluating the suitability and acceptance of these three technologies through an Expert Advisory Group (EAG) and focus groups comprising residents, carers and management, drawn from two rural aged care facilities and in the homes of a number of older people who access in-home aged care. These technologies will be critically evaluated against the in-home care and residential care needs to identify the potential applications that will have immediate impact on care services, and will be tailored to meet these needs. An exemplary prototype device "Follow-Me trolley" will be cooperatively developed with the IRT project participants to incorporate the selected subset of features of the navigation, localization and shadowing technologies. The Follow-Me trolley prototype platform will be used to comprehensively demonstrate the benefits of the technologies, specifically covering the usability, adaptability, efficiency and user-friendliness aspects.

Aim: This project aims to realise practical improvements to in-home aged care services and residential aged care services through assistive technologies.

Design & methods: This is a three-phase study over two years, using mixed methods. In phase 1 the expert advisory group (EAG), comprised of aged care residents, carers, managers and staff, will collaborate with the research team (robotic engineers, industrial designer, aged care nursing) to understand and scope out the current in-home care and residential care needs that could be potentially addressed by the proposed technologies. In phase 2, a refined design of the Follow-Me trolley will be built incorporating user preferences customising the device to consumer needs that is suitable to be used within aged care homes and in homes in the community. In parallel to this development, the research team will identify the potential users willing under informed consent to be trial participants and finalise the evaluation methods and data collection tools. In phase 3, the selected features of the three technologies will be assessed with users and adjusted as required to ensure it meets the user needs over a two month period prior to the instrumentation trial in two aged care homes and in the homes of 6 older people receiving aged care services. Evaluation of the utility and effectiveness of the three technologies for users (residents and carers) and their satisfaction with the technologies will be undertaken following the trial.

Progress to date: The activities outlined in the first two phases have been completed, and phase 3 is now underway.

Benefits: This research will transfer the outcomes of ten years of research funded through the Australian Research Council on three important assistive robotic technologies: navigation, localization and shadowing, to aged care practice through a "user-centred" deployment and evaluation of Follow-Me assistive robotic trolley in both in-home and residential aged

care services. The primary outcome of the project, a successful demonstration of the utility of these technologies, will pave the way for adapting these technologies to many other applications in the future, leading to novel, innovative strategies for delivering in-home care and residential care services and a significant positive impact on the quality of care.

Output: 1 conference presentation.

Funding: Montefiore Home funding (administered by CHeBA) supports Professor L. Chenoweth's research position with CHeBA, Illawarra Retirement Trust (not administered by CHeBA).

Date commenced: March 2015

Expected completion date: March 2017

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)

Project description: Dementia Care Mapping (DCM) is an established care home intervention used to support the implementation of person-centred care training (PCCT). Whilst DCM has been used in dementia care for nearly 20 years, there is limited robust evidence of its efficacy in relation to clinical outcomes such as reduction of behaviours staff find challenging. Reported practice implementation benefits include improvement of resident well-being and increased staff skills. However, there is very limited robust evidence for effectiveness and no examination of its cost-effectiveness. Therefore, a definitive pragmatic RCT of DCM is being conducted in the UK in 50 aged care homes. Investigation focuses on whether the study intervention reduces behaviours staff find challenging as measured by the Neuropsychiatric Inventory (NPI) score over time, if it has an impact on the use of antipsychotic and other psychotropic drugs, if it improves resident quality of life, care quality and care staff well-being and role efficacy measured by the number and types of adverse events occurring and quality of staff/resident interactions over time, and to explore if there are any differential predictors of the effects of the intervention (i.e. treatment-covariate interactions) and the process, challenges, benefits and impact of implementing the intervention in order to refine implementation guidance.

Aims:

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

Design & method: Cluster randomised controlled trial (RCT) (follow-up over 16-months), cost-effectiveness analysis and process evaluation.

Progress to date: The DCM intervention has been completed in all 50 randomly assigned aged care homes with room for improvement. The trial is in its post-test phase and the 16 month follow-up stage will commence at the end of March 2016.

Benefits: This study will provide convincing evidence of the utility of DCM as an effective method of instituting a person-centred approach to dementia care, with direct benefits to people with dementia and the staff who care for them.

Output: 1 journal publication submitted, 1 conference presentation.

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).

Date commenced: January 2013

Expected date of completion: June 2017

Examine the risk and protective factors for dementia that are consistent across the world and those that differ (using data from COSMIC)

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

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

Project description: This project extends upon our investigation into the rates and patterns of cognitive decline in various international cohorts by investigating the effects of risk and protective factors. These are yet to be fully understood, and there is little known about if and how they differ between different geographical regions and ethnicities. Important factors include sex, education, apolipoprotein E (ApoE) status, general health, psychiatric status, and vascular risk factors.

Aims: To examine risk and protective factors for cognitive decline and dementia, and determine the extent to which these differ between cohorts from different geographical regions and ethnicities.

Design & method: Both cross-sectional and longitudinal analyses of associations between each of cognitive performance and dementia and various risk and protective factors will be conducted. Data on risk and protective factors will be harmonised to enable comparisons of rates among cohorts and overall effects on cognition.

Progress to date: Associations with cognitive decline patterns determined for 14 COSMIC cohorts have been established for the risk and protective factors: sex, education and (ApoE) genotype. A conference abstract has been submitted (for AAIC 2016) and a paper is being prepared.

Benefits: Knowing the risk and protective factors will facilitate the prevention of late-life cognitive decline and minimise its impacts. Understanding differences between regions and ethnicities will help in developing more tailored and effective interventions.

Output: 1 conference abstract submitted for AAIC 2016; manuscript in preparation.

Funding: NHMRC Program Grant ID 568969, direct donations to The Dementia Momentum initiative (from March 2015), Vincent Fairfax Family Foundation (from October 2015).

Date commenced: 2014

Expected date of completion: December 2016

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, Darren Lipnicki, John Crawford, Nicole Kochan, Anbupalam Thalamuthu, Kristan Kang

Other investigators: STROKOG collaborators

Project description: Differences in diagnostic criteria and populations have produced a wide range of prevalence estimates for post-stroke cognitive impairment. This project initiates the first step in harmonising data from the STROKOG studies and we aim to describe the prevalence and profile of post-stroke cognitive impairment across various geographical regions and ethnic backgrounds.

Aims:

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

Design & method: Cross-sectional analyses from up to 27 studies that include a detailed neuropsychological battery of tests and for which cognitive function was assessed between 1 to 6 months will be performed. Data will then be pooled and harmonised. Prevalence estimates of post-stroke cognitive impairment will be estimated using common methodology and criteria.

Benefits: Applying uniform methodology and criteria to harmonised data will greatly reduce the variation in prevalence of post-stroke cognitive impairment. A pooled sample that consists of studies conducted in different geographical and ethical settings will also allow distinct group or individual characteristics to be considered and compared.

Output/Planned Output:

- STROKOG consortium discussed in a special session of the VASCOG World Conference in Tokyo (16 September 2015)
- Protocol paper to be submitted for journal publication (May 2016)

- Presentation at AAIC meeting in Toronto (July 2016)
- Preliminary analyses to be presented at VASCOG meeting in Amsterdam (October 2016) and submitted for journal publication (November 2016)
- Consolidated report (December 2016)

Funding: Vincent Fairfax Family Foundation.

Expected date of commencement: In planning 2015, official start date February 2016

Expected date of completion: December 2016

Genetic and epigenetic markers of late-life depression

CHeBA staff: Ruby Tsang (PhD student), Perminder Sachdev, Simone Reppermund, Karen Mather, Anbu Thalamuthu

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

Project description: Late-life depression is associated with increased mortality, greater functional impairment and elevated risk of cognitive impairment. Moreover, there is limited understanding of the biological underpinnings of the disorder. Heritability estimates of late-life depression vary greatly; however, all prior studies suggest that there is a significant genetic component.

Design & method: Using the Older Australian Twins Study, heritability for late-life depression and depressive symptoms will be estimated and bivariate genetic correlations calculated between these measures and related phenotypes such as anxiety.

Progress to date: This work is ongoing.

Benefits: This work will potentially provide information regarding the contribution of genetics to late-life depression.

Output: None to date.

Funding: OATS is supported by the NHMRC Project Grant 1045325. Karen Mather was kindly supported by the Thomas Foundation and the NHMRC Capacity Building Grant 568940. Ruby Tsang has a Viertel PhD Scholarship from the Alzheimer's Australia Dementia Research Foundation.

Date commenced: December 2015

Expected date of completion: June 2017

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)

Project description: We study genetic influence on fibre tract connectivity between brain regions by using OATS wave 1 DTI scans. Both binary and number-of-fibre weighted connectivity parameters are calculated and a network can be constructed for each brain. We will construct a network that represents the genetic correlations between each region. The genetic influence on the connections is then estimated by using the connectivity properties between the regions.

Aims: We hypothesize 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.
- We will also investigate whether the connections between network hub regions are genetically stronger than those of non-hub regions, including feeders and non-feeders.

Design & method: We are studying over 400 twins aged 65 years and over (age range 65-88) with their DWI (diffusion weighted imaging) scans using probabilistic models to investigate the genetic patterning of the white matter fibre tracts. We then compute a series of network measures and examine their heritability and establish a multi-variant SEM (structural equation model) and examine the relationship between age, sex and various types of cognition.

Progress to date: We have used FSLs network functions for this study. We have tested the initial results of the relationships between cognition and age and have found some significant correlations.

We have generated all of the connectivity matrices for all 399 subjects using various parcellation schemes of AAL (automated anatomical labelling), including 90, 256 and 512 parcellations (ROIs or nodes).

Benefits: Our study demonstrates a complex but patterned genetic architecture of the older human brain. An understanding of this pattern will assist in the refinement of phenotypes for the discovery of the genetic blueprint of the human brain.

Output: 1 manuscript in preparation.

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

Date commenced: July 2015.

Expected date of completion: April 2017

Genetics and epigenetics of longevity

CHeBA staff: Perminder Sachdev, Karen Mather, Anbu Thalamuthu, Mary Revelas (PhD student), Jessica Lazarus (PhD student)

Other key investigators: Dr Nicola Armstrong (Murdoch University), Professor John Attia (University of Newcastle), Associate Professor John Kwok (NeuRA, UNSW), Dr Chris Oldmeadow (University of Newcastle), Professor Peter Schofield (NeuRA, UNSW)

Project description: As our population ages, a better understanding of the factors involved in longevity is required. Heritability studies suggest longevity has a genetic component, with siblings of centenarians having a greater likelihood of living to 100 than the general populace. Longevity is often linked to healthy ageing, with many centenarians delaying or avoiding age-related diseases.

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

Design & method: Genome-wide genotyping, whole genome sequencing and DNA methylation data from the Sydney Centenarian Study (SCS) and other cohorts will be used to identify genetic and epigenetic variants linked to longevity.

Progress to date: In 2015, medicine student, Lawrence Hui, completed his Independent Learning Project by undertaking a candidate gene study examining healthy longevity. Mary Revelas (PhD student) is performing candidate gene studies for longevity in order to undertake a meta-analysis with previous published longevity study results. Jessica Lazarus (PhD student) is undertaking a DNA methylation study using participants from SCS and OATS. We have identified ~50 SCS participants for whole genome sequencing.

Benefits: As our population is ageing, increased knowledge regarding the genetic determinants of longevity will shed light on the underlying biological processes involved and may suggest strategies and targets for interventions to promote healthy ageing.

Output: 2015 Medicine Independent Learning Project Report; poster presentation at the International Society for Neurochemistry, Cairns, 2015 (Lazarus et al.).

Funding: This work is supported by the Sachdev Foundation. The Sydney Centenarian Study is supported by the NHMRC Project Grant 630593 and Program Grant 568969. Karen Mather was kindly supported by the Thomas Foundation and by the NHMRC Capacity Building Grant 568940.

Date commenced: January 2015

Expected date of completion: Ongoing

Genetics of apolipoproteins

CHeBA staff: Karen Mather, Anbupalam Thalamuthu, Anne Poljak, Perminder Sachdev

Other key investigators: 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), Dr Fei Song (formerly CHeBA), Dr Margaret J. Wright (QIMR Berghofer Institute, Brisbane, Australia)

Project description: Apolipoproteins are important transporters of lipids in the circulation and lymphatic systems. Apolipoprotein levels in the Sydney Memory and Ageing Study have been previously associated with cognitive performance and decline. However, little is known about the contribution of genetic variation to apolipoprotein levels, especially in older adults.

Aims: To identify genetic variants associated with plasma apolipoproteins in mid to late life.

Design & method: Plasma apolipoproteins were measured using an immunoassay method. Heritability of seven plasma apolipoproteins in older adults was assessed using data collected from the Older Australian Twins Study. A genome-wide association study using three cohorts of middle-aged to older adults, the Sydney Memory and Ageing Study,

the Older Australian Twins Study and the Hunter Community Study was undertaken.

Progress to date: Analyses are complete and a manuscript examining the genetics of apolipoprotein H is currently under review.

Benefits: Potential benefits from this work include a better understanding of the contributions of genetics to plasma levels of apolipoproteins.

Output: This work was presented at the Alzheimer's Association International Conference in Copenhagen in 2014. A manuscript examining the genetics of apolipoprotein H levels is currently under review.

Funding: Sydney MAS is supported by the NHMRC Program Grant 568969. OATS is supported by the NHMRC Project Grant 1045325. Karen Mather was kindly supported by the Thomas Foundation and by the NHMRC Capacity Building Grant 568940.

Date commenced: February 2013

Expected date of completion: June 2016

Genetics of white matter hyperintensities

CHeBA staff: Karen Mather, Wei Wen, Anbu Thalamuthu, Perminder Sachdev

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

Project description: White matter hyperintensities (WMHs) are regions of hyperintensity observed on neuroimaging scans of middle-aged to older adults and are associated with negative health outcomes such as cognitive and physical impairments. The aetiology of white matter hyperintensities is unclear but is thought to be ischemic in origin. Heritability studies suggest genetic variation also plays a role. WMHs can be sub-classified into deep and periventricular, dependent upon their brain location. Deep and periventricular WMHs may have different aetiology and functional consequences but no studies have yet undertaken a genome-wide approach to find genetic variants.

Aims: To identify genetic variants associated with total, deep and periventricular WMHs.

Design & method: WMH burden was estimated from neuroimaging scans of participants from the Sydney Memory and Ageing Study (Sydney MAS), the Older Australian Twins Study (OATS) and the PATH Through Life Study (administered by the Australian National University). Candidate gene analyses were undertaken using data from the PATH study. Genome-wide association analyses (GWAS) were undertaken in Sydney MAS and OATS. Meta-analyses will be undertaken using GWAS data contributed from ours and other studies.

Progress to date: Part of this work was used in Dr Assareh's PhD thesis in 2011. In an extension of this work, other cohorts (both national and international) are being invited to contribute to a GWAS meta-analysis examining deep and periventricular WMHs.

Benefits: Potential benefits from this work include a better understanding of the contributions of genetics to WMHs.

Output: Part of this work was used in Dr Assareh's PhD thesis and led to a published paper examining candidate genes for WMHs in the PATH study (Assareh et al., 2014).

Funding: Sydney MAS is supported by the NHMRC Program Grant 568969. OATS is supported by the NHMRC Project Grant 1045325. Karen Mather was kindly supported by the Thomas Foundation and the NHMRC Capacity Building Grant 568940.

Date commenced: 2010

Expected date of completion: Ongoing

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, Anbu Thalamuthu, Perminder Sachdev

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

Project description: Genetics influences brain structure and function, as shown by heritability studies. The ENIGMA consortium, comprised of a number of international studies, seeks to find genetic variants associated with different brain measures, such as subcortical volumes.

Aims: To identify single nucleotide polymorphisms (SNPs) for various brain measures.

Design & method: A genome-wide association study was performed on subcortical volumes using the Sydney Memory and Ageing Study and the Older Australian Twins Study. Our data contributed to a meta-analysis of GWAS results at the discovery stage. We are also contributing to other studies examining the genetics of other brain measures.

Progress to date: GWAS results for subcortical volume measures from CHeBA studies contributed to a published manuscript in 2015. We are also contributing to other analyses.

Benefits: Identification of genetic variants associated with various brain measures may lead to a greater understanding of how genetics (i) influences brain structures over the lifespan and (ii) contributes to the development of psychiatric and neurodegenerative disease.

Output: A manuscript detailing the results of meta-analyses for subcortical volumes was published in 2015 in the eminent journal, *Nature* (Hibar et al.).

Funding: Sydney MAS is supported by the NHMRC Program Grant 350833. OATS is supported by the NHMRC Project Grant 1045325. Karen Mather was kindly supported by the Thomas Foundation and by the NHMRC Capacity Building Grant 568940.

Date commenced: June 2012

Expected date of completion: Ongoing collaboration

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, Anbu Thalamuthu, Wei Wen, Nicole Kochan, Teresa Lee

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

Project description: Heritability studies suggest genetic variation plays a major role in many age-related measures, including cognitive performance. The CHARGE consortium, comprised of a number of international studies, seeks to find genetic variants associated with different cognitive measures such as processing speed and general cognitive ability and other ageing-related measures.

Aims: To identify single nucleotide polymorphisms (SNPs) associated with cognitive performance and other measures.

Design & method: Genome-wide association studies (GWAS) have been performed on various measures using the Sydney Memory and Ageing Study and the Older Australian Twins Study. Our GWAS data has contributed to meta-analyses of GWAS results either at the discovery or replication stage of CHARGE studies.

Progress to date: For several of these studies, analyses have been completed and manuscripts have been written and are currently under peer review or are published. For others, the CHARGE consortium is still assessing the results.

Benefits: Identification of genetic variants associated with various measures such as cognitive performance may lead to clarification of the biological underpinnings underlying these measures. For the cognitive analyses, these results may potentially lead to targeting of those at risk of age-related cognitive decline and the development of novel preventative or therapeutic strategies.

Output: Currently, papers are under review/accepted and include GWAS meta-analyses of general cognitive ability (Davies et al., 2015) and verbal declarative memory (Debette et al., 2015).

Funding: Sydney MAS is supported by the NHMRC Program Grant 568969. OATS is supported by the NHMRC Project Grant 1045325. Karen Mather was kindly supported by the Thomas Foundation and by the NHMRC Capacity Building Grant 568940.

Date commenced: January 2012

Expected date of completion: Ongoing collaboration

Heritability and genetic influence of brain structures

CHeBA staff: Wei Wen, Anbupalam Thalamuthu, Karen Mather, Jiyang Jiang (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)

Project description: A greater understanding of the genetic contributions to the structure of the human brain at older ages will assist in the elucidation of the pathways associated with normal and pathological brain ageing. Prior research suggests brain structures have moderate to strong heritability. However, few studies have examined the heritability of the shape of subcortical structures. Nor have the genetic correlations between bilateral hemispheric structures been considered. In 2013, we started a comprehensive heritability and genetic correlation analysis of cortical and sub-cortical structures of the human brain, utilising neuroimaging data from the MAS and the OATS. The study of twins offers an excellent strategy to examine the relative contributions of genetic and environmental influences on brain structures.

Aims: To estimate heritability and genetic correlations of cortical, sub-cortical structures and structural and functional networks of the human brain.

Design & method: We are studying over 400 twins aged 65 years and over (age range 65-88) with high resolution magnetic resonance imaging (MRI) to investigate the genetic patterning of the cerebral cortex and seven subcortical structures, using cortical thickness and surface deformation as the imaging phenotype in a vertex-wise approach.

Progress to date: We have mapped heritability for both the cortex and subcortical structures. Both the cortex and subcortical structures were examined. For the latter, three dimensional surface information was extracted. Bilateral symmetry for genetic influences was examined. Shared genetics between cortical areas and subcortical structures were investigated.

Benefits: Our study demonstrates a complex but patterned genetic architecture of the older human brain. An understanding of this pattern will assist in the refinement of phenotypes for the discovery of the genetic blueprint of the human brain.

Output: One manuscript is completed and will be submitted early in 2016.

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

Date commenced: July 2013

Expected date of completion: April 2016

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, Keenie Daly, John Crawford, Nicole Kochan

Other investigators: Study leaders and other researchers from among 16 ICC-Dementia member cohorts.

Project description: Globally, the centenarian population is rapidly increasing. Although the prevalence of dementia increases exponentially with age, normative data for centenarians remain scant. ICC-Dementia seeks to harmonise centenarian and near-centenarian studies internationally to describe the cognitive and functional profiles of exceptionally old individuals across diverse ethnoracial and sociocultural groups. Prevalence and incidence rates, as well as risk factors, for dementia will be examined. Additionally protective factors for exceptional brain ageing will be investigated.

Aims:

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

Design & method: Sixteen longitudinal studies of cognitive ageing have submitted data to ICC-Dementia. Studies are eligible to participate if they meet the following criteria: (i) the focus is on individuals aged ≥95 years; (ii) a minimum sample of 80 participants; (iii) assessment includes measures of cognitive function; and (iv) informed consent allows for de-identified data sharing. Variables are being harmonised across studies so the meaningful comparisons can be made.

Component 1: Prevalence rates of dementia in centenarians.

Cross-sectional analyses of 15 longitudinal population-based studies of cognitive aging, within ICC Dementia, are being performed. We endeavour to apply common criteria across studies to define cognitive impairment, functional dependence and subsequently, dementia prevalence. These prevalence estimates will be tested against existing frameworks for diagnosing dementia in a research setting to test the sensitivity, reliability and validity of our approach. The recruitment method utilised by each study will also be taken into account during analyses.

Component 2a: Risk factors for dementia and cognitive impairment in centenarians.

Component 2b: Protective factors for exceptional longevity and maintenance of cognitive functioning into the 10th and eleventh decades of life.

Data harmonisation across studies is taking place. Member studies are invited to guide research projects on common risk and protective factors of their choice, once a repository of harmonised variables has been created.

Progress to date: Data harmonisation across studies is taking place, to form harmonised variables for cognitive impairment, functional dependence and dementia status. Normative definitions of impairment are also being discussed. A draft paper is in progress.

Benefits:

- Clearer understanding of dementia prevalence for the oldest old.
- Provision of a new way of identifying dementia in research populations.
- Ability to inform predictions about the cognitive and functional state of centenarians, across diverse geographical and ethno-racial settings.
- Greater understanding of the risk and protective factors involved in cognitive functioning at the extreme end of the lifespan.

Output/Planned Output:

- Initial protocol paper is in press with *BMJ Neurology*.
- A prevalence paper will be submitted for journal publication in 2016.
- A presentation has been accepted for the International Centenarian Consortium (ICC) conference in Porto in July 2016.

Funding: The Thomas Foundation (Keenie Daly salary, conference attendance and paper publication), Vincent Fairfax Family Foundation (from October 2015).

Date commenced: July 2015

Expected date of completion: July 2016 (Component 1); Ongoing (Component 2a and b)

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, Henry Brodaty, Perminder Sachdev

Project description: Aliquoting and cataloguing of biospecimens from CHeBA cohorts to enable easy access for researchers and transfer of sample subsets from current ultra-low temperature freezers to vapour phase liquid nitrogen tanks for safe long-term storage. As such, this will facilitate many new research projects using CHeBA biospecimens both within UNSW and with external collaborators.

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.

Design & method: Aliquot large volume samples into smaller volume and catalogue all samples in a custom-designed, dedicated database for CHeBA biospecimens. Once aliquoting is complete, subsets of samples can be moved to vapour phase liquid nitrogen tanks.

Progress to date: A technical assistant was hired. All samples have been moved onto the UNSW main campus into alarmed freezers in dedicated freezer rooms. Sample aliquoting has commenced with MAS samples and a database has been created.

Benefits:

- Samples ready for distribution to researchers.
- Safe long term storage of samples.

Output: N/A.

Funding: UNSW MREII 2015.

Date commenced: 2015

Expected date of completion: 2016

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)

Project description: Early and accurate detection of subtle cognitive changes associated with mild neurocognitive disorders and early dementia is essential so that patients can access timely and appropriate services and treatment, and make important lifestyle decisions. A clinical assessment along with neuropsychological testing is considered the 'gold standard' for accurate diagnosis of cognitive impairment. Yet a number of barriers exist which limit access to specialised neuropsychological assessments and also diminish the accuracy of the assessment when they are available. Firstly, clinical diagnoses of mild neurocognitive disorders using neuropsychological assessment is challenging in Australia because of a lack of local normative data to enable accurate evaluation of older persons' cognitive performance on traditionally used tests. Secondly, accurate evaluation of cognitive test performance is even more challenging for individuals who come from culturally and linguistically diverse (CALD) backgrounds. Thirdly, neuropsychological assessment is only available in specialist settings due to the requirement for specialist training, high costs and lengthy administration times. This underscores the need for the development of brief computerised neuropsychological tests which may be more sensitive to a variety of subtle cognitive changes (such as response times), have the potential for use in non-specialist or primary care settings and may be appropriate for CALD persons because of the reduced linguistic and cultural content.

The overarching purpose of this project is to improve accuracy of detecting subtle cognitive changes associated with mild neurocognitive disorders in older adults using neuropsychological assessment methods, including developing appropriate normative data and new computerised cognitive tests.

Aims:

- To 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.
- To facilitate interpretation of neuropsychological test performance in persons from CALD backgrounds by investigating the influence of cultural, linguistic and educational factors.
- To 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.
- To 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.

Design & method: Data for this project will be primarily drawn from the Sydney Memory and Ageing Study (MAS), which has a longitudinal prospective design.

Component 1: Australian normative data

This study uses demographic and neuropsychological data from Wave 1 of MAS to construct normative data. Native English speakers (those that learned English before age 10) (N=878) from the baseline MAS cohort are being used in the development of normative data. The sample of NESB participants (N=159) will be used to investigate cultural, educational and linguistic influences on neuropsychological test performance. Twelve tests have been administered to the MAS participants from seven cognitive domains. Multiple measures are available for each test. Multiple linear regression analyses are used to examine the influence of demographic variables (age, years of education, sex) on raw scores for each test. For the analysis of the NESB sample, education, linguistic and cultural factors are entered into a multiple regression analyses to evaluate the relative influence of these various factors for each of the cognitive measures.

Component 2: Computerised neuropsychological test battery

The newly developed computerised *Sensus* battery consists of 4 tasks:

- Simple Reaction time (RT)

- Complex RT
- Computerised version of the Stroop test
- A visuospatial memory task which requires the individual to learn the positions of various everyday objects on the screen.
- *Sensus* is administered via a touch screen computer and responses are made by tapping the screen with a stylus pen or by voice recording. It typically takes 30 minutes and is largely self-administered under the supervision of a trained research psychologist.
- Participants from the MAS cohort completed the *Sensus* battery at Wave 1 and Wave 2 along with traditional neuropsychological tests. The MAS cohort was dementia-free at Wave 1. Participants were evaluated every two years and incident dementia diagnoses were established by consensus using an expert panel of clinicians including geriatric psychiatrists, neuropsychiatrists and neuropsychologists. A clinical validation study is also being undertaken. S*ensus* is administered to patients of the Prince of Wales Memory Disorders Clinic to establish its clinical feasibility and validity in patients with amnestic Mild Cognitive Impairment and Alzheimer's disease.

Progress to date:

Component 1:

Normative data analyses completed in the native English speaker sample, beta version of normative software program completed, and main manuscript are in preparation. Specific demographic and linguistic associations of cognitive performance on traditional neuropsychological tests CALD individuals have been identified. We identified two main factors that influenced performance on tests in CALD individuals: 1) the degree of English language dominance and acculturation in day-to-day life, and 2) the individual's past and current exposure to English. In the main, these factors affected verbally-based test performance but not exclusively.

Component 2:

1022 MAS participants completed the *Sensus* battery demonstrating its feasibility in this older age group. In the first study, we observed strong concordance between test performance on *Sensus* tests and traditional neuropsychological tests of attention/processing speed, executive abilities and memory, supporting its construct validity as a cognitive measure. In examining diagnostic accuracy of the battery, a global *Sensus* score successfully discriminated those with dementia from those that were cognitively normal (at Wave 2) with 90% accuracy. Classification of individuals with Mild Cognitive Impairment based on the global *Sensus* score was also achieved with moderately high accuracy. In predicting future dementia over 6 years, global *Sensus* score performed significantly better than routine clinical screening tests such as the MMSE and ratings of activities of daily living made by a knowledgeable family/carer/friend, and the brief computerised tests were as effective as a more detailed and lengthy traditional neuro-psychological paper and pencil test battery. A manuscript reporting these results is in preparation.

We also examined the utility of two brief reaction time measures from the *Sensus* battery for estimating risk of future dementia over four years in the old age cohort. Risk of future dementia was increased by 40-60% for each unit (standard deviation) that the individual was slower or more variable in their performance on the reaction time tasks. The increased risk of a shorter time to dementia diagnosis for those with slower and more variable reaction times remained even after controlling for other known dementia risk factors such as age, depression, cerebrovascular disease, genetic susceptibility and lower overall cognitive function. Furthermore, the 4-minute reaction time task was on par with lengthier neuropsychological batteries for predicting decline in ability to perform instrumental activities of daily living. A manuscript reporting these results has been accepted for publication in the *American Journal of Geriatric Psychiatry*.

Recruitment for the clinical study conducted at the Prince of Wales Hospital is near completion. The results will be analysed and published.

Benefits: The new normative data are expected to enhance accuracy of diagnosis of mild neurocognitive disorders in clinical and research settings in Australia, and possibly in other English-speaking countries such as Britain. The findings obtained from the project will also potentially provide information on the most effective types of measures for identifying neurocognitive disorders in the elderly and for flagging the likelihood of future cognitive decline, as well as suggesting more appropriate methods of assessing cognitive functioning in older adults of CALD backgrounds than are traditionally used. The findings will be widely disseminated to clinical and research communities in Australia and overseas. The findings will be translated into a set of recommendations for neuropsychologists and clinical psychologists who assess ethnic and linguistic minority clients. The benefits of computerised testing of cognition include greater accessibility (particularly for those in remote areas where there are no specialist services), reduced burden on the individual because of briefer testing, greater accuracy of data collected and improved sensitivity compared to current cognitive screening

measures. Furthermore, computerised tests have potential scalability for pragmatic, time- and cost-effective screening of at-risk individuals from a broad section of the population including those from CALD backgrounds in a variety of settings (primary care, research or clinical trials) because they are brief, do not require linguistic content or high levels of expertise for administration.

Output:

- 2 peer-reviewed journal papers: Kochan et al. (2015), *American Journal of Geriatric Psychiatry;* Gates & Kochan (2015), *Current Opinion in Psychiatry.*
- 7 conference abstracts/presentations, 1 invited oral presentation.
- Medscape Medical News: Fluctuations in reaction time linked to dementia risk. Variations in reaction time to same tasks seen as a sign of subtle, early cognitive decline (to be published January 2016).

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

Date commenced: March 2012

Expected date of completion: December 2016

Inflammatory markers and brain structure

CHeBA staff: Jiyang Jiang (PhD student), Wei Wen, Julian Trollor, Perminder Sachdev

Other investigators: Professor Bernhard Baune (University of Adelaide), Associate Professor David Brown (St Vincent's Centre for Applied Medical Research)

Project description: Drawing on the established pathways linking the periphery with the central nervous system (CNS), previous studies at the cellular level demonstrated the impact of peripheral inflammation on ageing brains. By applying magnetic resonance imaging (MRI) techniques, recent epidemiological studies have evidenced similar associations. However, the clinical utility of circulating levels of inflammatory markers as biomarkers in the diagnosis and prognosis of structural alterations in ageing brains has been restricted by inconsistent findings and relatively small effect size.

Macrophage inhibitory cytokine-1/growth differentiation factor 15 (MIC-1/GDF15) is a divergent transforming growth factor-β (TGF-β) superfamily cytokine. Available studies have linked its blood concentration and polymorphisms with unfavourable outcomes, including cancer, cardiovascular disease, and all-cause mortality. Studies of animal models have also demonstrated its role in damaged brain tissue. However, the relationship of MIC-1/GDF15 concentration with human brain structures has not been extensively explored.

Aims:

- To 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 MIC-1/GDF15. The aim is to find a robust circulating biomarker of brain structural measures in non-demented older individuals.
- To 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.
- To 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.
- To examine the relationship of serum levels of CRP and IL-6 with human brain volumes and brain network properties.

Design & method: Blood was collected after an overnight fast, clotted, aliquoted and frozen at -80°C. sVCAM-1, PAI-1 and SAA concentrations were processed by commercially available sandwich enzymelinked immunosorbant assay (ELISA) kits. Cytometric bead array (CBA, BD Biosciences, San Diego, CA, USA) was used to measure IL-1β, IL-6, IL-8, IL-10, IL-12p70 and TNFα levels. The MIC-1/GDF15 serum levels concentration was determined using an ELISA in St Vincent's Centre for Applied Medical Research. T1-weighted, T2-weighted FLAIR and DTI were also acquired and processed by FSL and FreeSurfer. Grey matter (GM) volumes of cortical and subcortical structures, white matter hyperintensity (WMH) volumes, and fractional anisotropy (FA) values, were extracted at both Wave 1 and 2 of MAS. Linear regression analyses were performed in both voxel-wise and region of interest (ROI) investigations.

Four population-based cohorts with both genetic data and MIC-1/GDF15 blood levels have been contacted for the genome-wide meta-analysis. They include Framingham Offspring Study and three cohorts located in Sweden.

Progress to date:

MIC-1/GDF15 serum levels were negatively associated with brain GM volumes both cross-sectionally and longitudinally. The GM volume is one of the mediators in previously observed relationships of MIC-1/GDF15 serum levels with cognitive performance in MAS. The results were published in *PLOS ONE*.

MIC-1/GDF15 serum levels were inversely associated with brain white matter (WM) integrity. The FA value is another mediator in the associations between MIC-1/GDF15 serum levels and cognitive performance. MIC-1/GDF15 serum levels can be considered as a marker of early stage WM degeneration in ageing population. The findings have been published in *Psychoneuroendocrinology.*

The idea of MIC-1/GDF15 as a biomarker of cognitive/brain ageing and dementia has been discussed in a review paper accepted for publication in *Current Opinion in Psychiatry*.

In addition, all four candidate cohorts are positive about participating in the genome-wide meta-analysis. Two have shared genome-wide association results, and the other two are processing the data. We anticipate the final number of participants will be approx. 7,000.

Benefits: Our study identified the significant relationships of MIC-1/GDF15 with brain structural measures, which may suggest a robust biomarker and a possible therapeutic target for brain atrophy in ageing. The genome-wide meta-analysis will expand our knowledge in the polymorphisms of circulating MIC-1/GDF15 levels, as there is only one such study with ~3900 participants so far.

Output: 2 journal papers published in 2015 (*PLOS ONE*, *Psychoneuroendocrinology*); 1 review accepted (*Curr Opin Psychiatry*).

Funding: NHMRC.

Date commenced: March 2013

Expected date of completion: March 2016

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 (conjoint)

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

Project description: Apolipoprotein-E (*ApoE)* genotype is the single most important risk factor for late-onset Alzheimer's disease (AD) (Corder et al., 1993). Although there are several postulated pathways by which *ApoE* may affect neurobiology, the exact pathways by which different *apoE isoforms* influence AD remain unknown. Brett Lab has recently reported that *ApoE* is proteolytically cleaved in the human brain in an *ApoE* isoform-dependent manner (Elliott et al., 2011). Moreover, they showed that proteolytic processing of *ApoE* generates a stable ~25 kDa fragment (referred to from here on as "ApoE25") that is present at lower levels (i.e. 50% reduced) in brain tissue from *ApoEε4* as compared to *ApoEε3* subjects. We, and others, have attempted to isolate and sequence human brain *ApoE* proteolytic fragments but due to the complexity of brain tissue and the extent of additional post-translational changes, meaningful peptide sequence data that would conclusively characterise *ApoE* fragments (and indicate the processes leading to their generation) has not been reported. The AD field has also suffered from the lack of a relevant *in vitro* humanised system that recapitulates the ApoE fragmentation seen in the human brain. In a new collaboration, we have recently discovered that cell culture medium from human iPSC-derived neurons contains *ApoE* fragments that appear by western blotting to be identical to those we have previously detected in the brain. This is the first *in vitro* humanised system shown to generate *ApoE* fragments similar to those seen in the brain. We hypothesise that ApoE25 may play a neuroprotective role in the brain and that this contributes to the association of *ApoE* genotype with AD risk. In this proposal we plan to characterise ApoE25 generated by iPSCs and assess its potential neuroprotective properties.

Aims:

- We hypothesise that ApoE25 may play a neuroprotective role in the brain and that this contributes to the association of *ApoE* genotype with AD risk.
- We plan to characterise ApoE25 generated by iPSCs and assess its potential neuroprotective properties.

Design & method:

- Generate iPS neurons, astrocytes and microglia
- Purify and sequence iPSC-derived ApoE25
- Enzyme inhibitors to shortlist candidate enzymes that generate ApoE25
- Generate r-ApoE25 and assess biological activities
- Knockdown candidate enzymes / assess ApoE25 modulation

Progress to date: ApoE25 identified in iPSC clones derived from AD patients with patterns similar to that found in the human brain.

Benefits: This project will be the first to identify the pathway leading to ApoE25 generation in an in vitro humanised system. Moreover, it will be the first to provide direct evidence for a biological/neuroprotective role for ApoE25 and thereby potentially reveal a new therapeutic target for AD. Given that several independent laboratories around the world have detected ApoE25 in the human brain, the novel data resulting from this project would represent a major advance for the AD field.

Output: A paper submitted for publication.

Funding: NHMRC grant administered by University of Wollongong.

Date commenced: February 2015

Expected date of completion: February 2018

Longevity, ageing and transcriptomics

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

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

Project description: Long-lived individuals are examples of successful ageing, many of whom have avoided age-related disease until very late in their lives. This project seeks to identify RNA differences between long-lived individuals (aged 95+) and younger controls using the cutting edge technique of RNA sequencing in RNA derived from peripheral blood samples. In a separate PhD project, transcriptome changes across the lifespan in the ageing human brain will be investigated.

Aims:

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

Design & method: RNA was extracted from peripheral blood samples from the Sydney Memory and Ageing Study and the Sydney Centenarian Study. RNA sequencing was undertaken, data cleaned and analyses undertaken. RNA will be extracted from brain samples aged from 40+ and sequencing performed.

Progress to date: The blood-derived RNA sequencing has been completed and the data cleaned. Initial analyses have been undertaken. Different analysis methods have been used to optimize the quality of the results. The brain samples to be used are still being finalised.

Benefits: Potentially this work will identify RNA biomarkers of longevity and ageing, which may aid in the identification of those who are at risk for age-related decline and disease and also increase our understanding of the ageing process.

Output: The analyses are being undertaken and a manuscript is being prepared. Dr Mather presented a poster presentation at the American Society of Human Genetics annual conference in Baltimore, USA, in 2015.

Funding: The Sydney Memory and Ageing Study is supported by the NHMRC Program Grant 568969. The Sydney Centenarian Study is supported by the NHMRC Project Grant 630593 and the Program Grant 568969. Karen Mather was kindly supported by the Thomas Foundation and by the NHMRC Capacity Building Grant 568940.

Date commenced: December, 2013

Expected date of completion: Ongoing

Maintain Your Brain

CHeBA staff: Henry Brodaty, Perminder Sachdev, Gavin Andrews (conjoint)

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), Associate Professor Michael Valenzuela (University of Sydney)

Project description: As dementia is primarily a disease of late-life, delaying the onset by targeting modifiable risk factors can have a major impact on Alzheimer's disease (AD) rates. Postponing onset by even two years could reduce AD prevalence by up to 20% and a 5-year delay could potentially halve AD prevalence. Interventions geared at reducing modifiable risk factors would result in significant impacts on worldwide prevalence.

The project is based on addressing modifiable risk factors for dementia in general and AD in particular, namely physical inactivity, cognitive inactivity, depression, being overweight and obesity, diabetes (type 2), high blood pressure and smoking. Our intervention modules

will be customised to individual risk profiles using modified tools developed by our team to assess the risk of developing AD and dementia.

Aims: To 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. We will examine the cost-effectiveness of the program with a view to making this a national and potentially a globally suitable program.

Design & method: We will invite 18,000 people from the 150,000 persons aged 55-75 years who are participants in the *45 and Up Study* and meet our eligibility criteria. Participants agreeing to be in the trial will be screened, asked to complete a risk factor profile and then randomised into two groups. The intervention group will be emailed a recommended menu of intervention modules tailored to individuals based on their risks. Modules will be completed in 3 monthly blocks sequentially over the first 12 months followed by boosters at 2 weeks and then monthly. The four main modules comprise a tailored graded physical exercise program, computerised cognitive training, dietary advice and internet delivered cognitive behaviour therapy for depression (or stress reduction). Participants randomised to the control group will receive information about how to manage risk factors.

Progress to date: Ethics application has been submitted and is under consideration, module leaders are fine-tuning their interventions and assessment procedures are in preparation for pilot testing, the IT team is designing and building the platform.

Benefits: Success with this project will delay cognitive decline and the onset of dementia. It will be a scalable intervention nationally and internationally.

Output: None to date.

Funding: NHMRC Dementia Research Team Grant.

Date commenced: December 2015

Expected date of completion: December 2020

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

CHeBA staff: Julia Muenchhoff, Anne Poljak, Perminder Sachdev

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

Project description: Blood contains a mixture of high molecular weight components, such as proteins, and low molecular weight metabolites, such as carbohydrates, organic and amino acids. The low molecular weight metabolites could be valuable biomarkers for mild cognitive impairment (MCI) and/or Alzheimer's disease (AD), as pathologically distinct diseases might be characterised by unique metabolite profiles.

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.

Design & method: A combination of targeted GC-MS and non-targeted NMR-based methods for blood samples to detect and quantify a large variety of metabolites will be developed and applied. Blood samples from cognitively healthy, MCI and AD participants from MAS will be assayed in a cross-sectional and longitudinal design to compare the metabolite profile across these groups.

Progress to date: Targeted GC-MS and non-targeted NMR-based methods have been developed and tested in a preliminary study using blood samples from a small number of MCI, AD and cognitively normal (CN) individuals. This showed significant differences between people with AD and CN in the NMR spectra (15 AD, 10 CN) as well as in the concentrations of the amino acids quantified by GC-MS (15 AD, 15 CN). Differences between MCI and CN samples were less pronounced and did not reach significance, suggesting we are detecting a change later in the disease process. These exciting preliminary results warrant analysis of a larger number of samples by NMR and GC-MS. We have been in the process of selecting blood samples for this analysis, carefully choosing MCI and AD patients for who we have the most amount of medical information available, as well as blood samples from age-matched healthy study participants for comparison. We were able to source more than 200 samples, which are scheduled for analysis in 2016.

Benefits:

Potential metabolite biomarker panel to assist in diagnosis of predisposition to MCI and/or AD.

Identify metabolites and thereby metabolic pathways that are deregulated in MCI and/or AD.

Output: 1 publication in peer-reviewed journal and 1 conference presentation

Funding: Thomas Foundation

Date commenced: 2014

Expected date of completion: Ongoing

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

CHeBA staff: Helen Zong Ying 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)

Project description: MicroRNAs (miRNA) are a class of non-coding RNA known to regulate protein expression post-transcriptionally, which are currently being explored as biomarkers of diseases. With respect to AD, it has been hypothesised that down-regulation of specific miRNAs may lead to up-regulation of AD-relevant genes such as amyloid precursor protein (*APP*). Peripheral blood miRNAs are ideal biomarker candidates, as they are easily accessible, non-invasive, and cost-effective.

Aims: The objective of this collaborative study between UNSW and SJTU is to examine the differences in miRNA expression among Chinese and Australian patients with mild cognitive impairment (MCI) and Alzheimer's disease (AD) compared to cognitively normal controls.

Design & method: We will select age and gender matched patients (n=96) from Chinese and Australian cohorts with AD, MCI and normal cognition. We aim to compare the raw miRNA data between the two cohorts to determine differences and similarities between the two racially diverse groups. Individual miRNAs that have significantly different expression levels between AD/MCI compared to normal controls from the Australian cohort will be selected for further cross-validation in the Chinese cohort. Similarly, significant miRNAs found in the Chinese cohort will be cross-validated in the Australian cohort.

There will be two reciprocal visits for investigators, which allows for the opportunity to share and consolidate knowledge in miRNA data processing and bioinformatics between two leading research centres. Given one of the constraints of miRNA biomarker studies to date is variability in methodology, this inter-centre, international collaboration may help develop consensus on standardised data processing and statistical analyses of miRNAs and lead to further collaborations to facilitate validation studies with larger study cohorts.

Progress to date: RNA samples from the Australian cohort of patients with AD, MCI and normal cognition (n=48) have been processed and microRNA expression array performed. Data analysis is currently in progress. Results will then be compared with the Chinese cohort and further validation analyses on individual miRNAs performed. Dr Wu will be taking maternity leave from April 2016.

Benefits: The expected outcomes of this study include at least one joint co-authored publication of miRNA expression among Australian and Chinese patients with AD/MCI compared to cognitively normal controls. The miRNAs that are cross-validated and able to differentiate AD or MCI from normal controls in both the Chinese and Australian cohorts are potential candidate biomarkers for AD and will be the focus of future studies. This has significant impact for the field of AD biomarker research. Further collaborative work to determine the intrinsic characteristics and downstream targets of these dysregulated miRNAs will provide insight into the pathobiology of AD and inform therapeutic targets.

Output: 1 systematic review published (*J Alzheimers Dis*.).

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

Date commenced: February 2016

Expected date of completion: December 2016

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)

Project description: A consortium of aged care provider senior nurses and aged care nurse researchers has been formed to develop nursing competencies for care of the older person, since none currently exists for the Australian setting. The initial focus will be on the aged care sector, followed by competencies for the acute care sector.

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

Design & method: The project is being conducted over 2 years using mixed methods, including a review of all published aged care nurse competencies in a wide range of practice domains, a Delphi panel process with nurses who care for older people and aged care experts, focus groups with nurses with different roles in care of the older person and surveys with a wide range of nurses.

Progress to date: An extensive literature review has been undertaken which has informed broad and specific domains of nursing practice for which competencies are being considered by the Delphi panel. A workshop with aged care nurses and managers has identified the most salient of the domain of practice and a list of competencies is being considered alongside the reviewed literature.

Benefits: Nursing care of the older person, including the person with dementia, will be progressed through the development of a group of essential competencies that are required to meet the nursing care needs of all older people, while also supporting their rights to quality aged care services.

Output: Chenoweth, L. Abstract. Competencies for aged care nursing. *NSW Nurses and Midwifery Board Annual Better Practice Conference*. Sydney, October 16, 2015. Podcast access: **http://www.nswnma.asn.au/education/podcasts/**

Funding: Montefiore Home funding (administered by CHeBA) supports Professor L. Chenoweth's research position with CHeBA; Anglican Retirement Villages, Uniting Care, BaptistCare, Scalabrini Villages, Hammond Care, University of Wollongong (none administered by CHeBA).

Date commenced: December 2015

Expected date of completion: December 2017

Oxidative stress in AD

CHeBA staff: Anne Poljak, Nady Braidy, Nicole Kochan, Wei Wen, John Crawford, Julian Trollor, 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)

Project description: Quantification of oxidative stress and glycation markers (*o*- and *m*-tyrosine, carboxymethy-lysine) in Mild Cognitive Impairment (MCI) and Alzheimer's disease (AD) plasma in a variety of population based cohorts, from Sydney and elsewhere in Australia.

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.

Design & method: Both cross-sectional and longitudinal designs are used. Cohorts include: Sydney MAS (all 4 waves), Hunter Community Study (HCS), Dominantly Inherited Alzheimer's disease Network (DIAN), Older Australian Twins Study (OATS) and Sydney Centenarian Study (SCS). Cellular and animal models of ageing and AD are in the planning phase.

Progress to date: Experiments are ongoing, with numerous conference presentations, several published manuscripts, and both local and international collaborators involved.

Benefits:

- Potential biomarker panel to assist in diagnosis of predisposition to MCI and/or AD.
- Identify robust biomarkers, which show consistent change across studies.
- Understand the effect of plasma protein oxidation changes on cognition and brain volumetrics.
- Determine how plasma protein oxidation levels change with age, particularly advanced old age.
- Understand the role of specific mechanisms of oxidation; hydroxyl radical *vs* glycation, in ageing and neurodegenerative disease.

Output: 4 conference presentations, 4 invited oral presentations, 1 publication, 1 manuscript in preparation.

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.

Date commenced: 2004

Expected date of completion: Ongoing

Plasma proteomics biomarkers

CHeBA staff: Julia Muenchhoff, Anne Poljak, Tharusha Jayasena (PhD student), Nicole Kochan, Julian Trollor, 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 Mark Raftery (BMSF, UNSW), Associate Professor Peter W. Schofield (University of Newcastle), Dr Fei Song (formerly CHeBA), Associate Professor George A. Smythe (SOMS, UNSW)

Project description: Plasma protein profiling of Mild Cognitive Impairment (MCI) and Alzheimer's disease (AD) in a variety of population based cohorts, from Sydney and elsewhere in Australia

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.

Design & method: Both cross-sectional and longitudinal designs are used. Cohorts include; Sydney MAS (all 4 waves), Hunter Community Study (HCS), Dominantly Inherited Alzheimer's disease Network (DIAN), Older Australian Twins Study (OATS) and Sydney Centenarian Study (SCS). Proteomics (iTRAQ) screening is initially used, followed by western blot and multiplex ELISA of specific proteins of interest, such as the apolipoprotein family.

Progress to date: Experiments are ongoing, with numerous conference presentations, several published manuscripts, and both local and international collaborators working on current projects or validating proteomics data.

Benefits:

- Potential biomarker panel to assist in diagnosis of predisposition to MCI and/or AD.
- Identify robust biomarkers, which show consistent change across studies.
- Understand the effect of plasma proteome changes on cognition and brain volumetrics.

Output: 11 conference presentations, 4 invited oral presentations, 4 publications, 4 manuscripts in preparation.

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.

Date commenced: 2006

Expected date of completion: Ongoing

Personality and Total Health (PATH) Through Life project

CHeBA staff: Perminder Sachdev, Wei Wen, Karen Mather, Anne Poljak, 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)

Project description: The PATH Through Life Project, run by the Centre for Research on Ageing, Health and Wellbeing (CRAHW), Canberra, is a large, on-going, population-based, longitudinal cohort study comprising 7,485 participants ranging from early to late adulthood. PATH has resulted in over 170 publications, and is unique among cohort studies in its age range and duration of follow-up.

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.

Design & method: PATH Through Life is a longitudinal study of 7,485 adult community residents randomly selected from the Electoral Rolls of Canberra and Queanbeyan. There are 3 epidemiological cohorts (20-24, 40-44 and 60-64 years). The Principal Investigator of the Project is Professor Kaarin Anstey (ANU). The project plans to interview participants every four years for 20 years to monitor changes in their lives, and their health and well-being. Longitudinal analyses will help to explain what factors influence change over time in the health areas of interest, and the interrelationships between them, at the individual level.

Progress to date: As of 2015, four waves of data have been collected. CHeBA collaborates on the neuroimaging, genetics and clinical chemistry components of the study.

Benefits:

- Obtaining measures of genetic, biological (including MRI), psychosocial and lifestyle risk and protective factors for mental health and wellbeing.
- Assessment of participants across the full adult lifespan, permitting investigation of developmentally significant, but under studied periods such as midlife.
- Recruitment and follow up of a young-old population, providing important pre-clinical data for studying the development of age related changes in memory and cognition.

Output: Full details, see **http://crahw.anu.edu.au/research/projects/personality-total-health-path-through-life#**

Funding: NHMRC (administered by ANU).

Date commenced: 1999

Expected date of completion: Ongoing

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)

Project description: 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.

Aims:

- To 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.
- Using the findings of this research, the goal is to 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.

Design & method: Two stages over 12 months. Stage One for feasibility testing of the 11 QIs (one of the indicators from the original 12 QIs is not relevant for nursing homes) and Stage Two for face validity of the 11 QIs. Member researchers from each country are responsible for collecting Stage One data for their own country. The aim is to recruit 50 nursing home residents with any type of dementia (for longer than 6 month stay in the nursing home) from each country and for Stage Two 10-15 experts in dementia care and research from the Asia-Pacific region (psychiatrists, nurses and allied-health professionals) met at the International Psychogeriatric Association Regional Conference in Beijing on the 23rd-26th of October 2014. Three focus groups were made available during the conference. The focus groups were chaired and documented by the researchers and content analysis will be used.

Progress to date: We have collected data from Hong Kong, South Korea, Malaysia and Australia, and waiting for data to be sent from China. Both Singapore and Thailand are yet to start data collection. The plan is to complete data collection by July 2016.

Benefits: A set of quality indicators can guide service providers to ensure best practice in dementia care in residential facilities.

Output: Symposia presentations at International Psychogeriatric Association Conferences in South Korea in 2013 and in Beijing in 2014, keynote presentation (HB) at APRU Ageing in the Asia-Pacific Research Symposium, Sydney 2015.

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

Date commenced: July 2014

Expected date of completion: July 2016

Proteomics of natural and non-natural animal models for AD

CHeBA staff: Anne Poljak, Nady Braidy, Tharusha Jayasena, Perminder Sachdev

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

Project description: Proteomic expression difference profiling in transgenic AD models and 'natural' models for AD

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.

Design & method: *O. degus* were obtained from a breeding colony at the animal facility of the University of Valparaiso, Chile and maintained in a temperature controlled room (23 ± 1 °C), under a 12hr: 12hr light/dark cycle, with water and food provided *ad libitum.* At the time of this study, 32 Male *O. degus* were grouped by age: 1, 3, 5 and 7 years old (n = 8 per group). Ages were selected to represent the development of AD-like pathology (which normally starts to appear at ~ 3 years). Twelve transgenic female (APPsw/Tg 2576) and twelve 3xTG mice (Taconic form, NY, USA) were used. These animals were obtained from a breeding colony at the animal facility of the Sultan Qaboos University, Oman (SQU/AEC/2010-11/3).

Progress to date: Tissue samples have been fractionated into 5 subcellular fractions and proteomics experiments performed using iTRAQ methodology.

Benefits:

- Proteomics is a discovery-based approach, and as a research tool may provide a signpost for novel proteins and pathways to provide insight into AD pathogenesis.
- By identifying deregulated proteins, which may not have previously been linked to AD, the potential exists for discovery of novel mechanisms of disease causation. Furthermore, these data will provide the impetus and rationale to follow new research leads.

Output: Samples currently available.

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

Date commenced: 2015

Expected date of completion: Ongoing

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

CHeBA staff: Tharusha Jayasena (PhD student), Anne Poljak, 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)

Project description: Develop an MRM mass spectrometry based quantitative method for assaying all 7 human sirtuins, and apply this approach to study changes in sirtuin expression levels in ageing and disease. Both human plasma and cerebrospinal fluid (CSF) samples, as well as cell culture and animal models, will be used.

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 CSF and variation with age and in AD and MCI.

Design & method: Stable isotope based MRM mass spectrometric quantitative assay for human sirtuins, based on sirtuin specific peptides will be used to assay tissue extracts and fluids such as CSF and plasma. Immunohistochemistry approaches will be used to explore brain distribution of sirtuins.

Progress to date: Experiments are ongoing, results have been presented at conferences and a review paper has been published. The MRM methods paper has been submitted for publication.

Benefits: Understanding the role of all 7 mammalian sirtuins in ageing and neurodegenerative diseases of ageing. These proteins are epigenetic regulators that may be influenced by cellular energy status and exogenous polyphenolic compounds. Modulation of their actions by lifestyle changes presents a potential approach to improving health in old age.

Output: 7 conference presentations, 4 published research papers, 3 manuscripts in preparation.

Funding: NHMRC, Rebecca L. Cooper Medical Research Foundation, UPRA PhD scholarship to Tharusha Jayasena.

Date commenced: 2008

Expected date of completion: Ongoing

The Older Australian Twins Study (OATS)

CHeBA staff: *Investigators:* Perminder Sachdev, Henry Brodaty, Julian Trollor, Wei Wen, Teresa Lee, Karen Mather, John Crawford, Anbupalam Thalamuthu; *Study Coordinator:* Jocelyn Bowden; *NSW Research Assistant:* Tanya Duckworth; *NSW Admin Assistant:* Suzy Forrester; *Data Manager:* Kristan Kang; *Other Researchers:* Julia Muenchhoff, Anne Poljak, Jiyang Jiang (PhD student), Jessica Lazarus (PhD student)

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Project description: OATS is one of the largest and most comprehensive ageing studies with older twins undertaken in Australia. The aim of OATS is to examine the genetic and environmental factors that may influence cognitive decline and dementia in later life. OATS is a multi-centre, longitudinal study incorporating identical and non-identical twin pairs aged 65 years and older. We commenced in New South Wales in 2007 and in Queensland and Victoria in 2008. Baseline, two-year and four-year follow-up data have been collected on a wide range of parameters designed to measure change in cognition and physical health over time. 623 participants were recruited initially, with 390 participants re-tested at their four-year follow up. Participants undergo rigorous medical and cognitive function tests, with many participants also providing bloods samples and having a magnetic resonance imaging (MRI) scan of their brain. Information about environmental factors, such as medical and psychosocial history, lifetime physical and mental activity, and nutrition is collected as well as feedback from an informant (the participant's spouse or relative who knows him/her well) about their memory, thinking skills and activities of daily living. In 2015 we received NHMRC funding to undertake a new OATS sub-study investigating the deposition of amyloid plaques in the brain using positron emission tomography (PET) scans. Amyloid plaques are thought to predict memory decline with age. Performing these scans in twins will help us to establish how these amyloid plaques relate to performance in memory and thinking ability. We also aim to determine if there is a genetic component, and if there are any potentially modifiable environmental factors that may be contributing to the development of the plaques.

Aims:

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

Design & method: Participants were recruited, mainly through the Australian Twins Registry (ATR), during Wave 1 of the study. The Wave 3 assessments repeat some aspects of the Wave 1 and 2 assessments, but were more focused on current events and what happened between assessments. Assessments were performed by the Research Assistant (RA) either in participants' homes or at one of the research facilities (duration 3-4 hours). MRI imaging was performed at a local neuroimaging facility if the participant agreed to a scan. Blood was collected by an experienced phlebotomist at an established collection centre in each state, or at the participants own home. Blood samples were processed using our existing collaboration with South Eastern Area Laboratory Services (SEALS). Where appropriate, cognitive

diagnosis (normal, mild cognitive impairment and dementia by subtype) were made by two experienced clinicians (Professors Trollor & Sachdev) and a senior neuropsychologist (Dr Lee) after presentation of the data at consensus case conference.

Interview, medical assessment and neuropsychological assessment include:

- Demographics: age, sex, education, marital status, occupation (current or retired), relationship between participant and informant.
- Interval psychiatric and medical history, including history of current medications, and modified Structured Clinical Interview DSM-IV.
- Medical examination including height and weight to allow BMI calculation, blood pressure and heart rate.
- Motor examination (timed walk test, lateral stability, speech, hand grip test, parkinsonian features), spirometry test and visual acuity.
- Assessment of subjective memory impairment, current and retrospective cognitive activities, social and physical activity, and family history questionnaire. Life time experiences, social networks and successful ageing are also examined through various modified questionnaires.
- Depression Scale 15 item, Kessler Psychological Distress Scale, World Health Organisation Disability Assessment Schedule II, Positive and Negative Affect Scale, Satisfaction with Life Scale, and Assessment of Quality of Life.
- Repeat detailed neuropsychological examination for performances in Attention, Memory, Visuospatial function, Language, Executive function, Speed of Information Processing, simple and complex reaction time, fine motor skills.
- Informant Questionnaire about the Participant: Cognitive Decline in the Elderly to confirm change in vascular risk factors, interval HRT use, Change In Cognition with Age Questionnaire, Clinical Dementia Rating Scale, Bayer ADL, Neuropsychiatric Inventory, and Apathy Evaluation Scales.
- Informant Questionnaire: Assessment of Quality of Life, Kessler Psychological Distress Scale, World Health Organisation Disability Assessment Schedule II, and, if caring for the participant, an in-house developed assistance and burden rating scale.

Blood tests and genetics:

- Blood is collected in consenting participants to investigate correlates of cognitive function (FBC, clinical chemistry screen, TSH, fasting cholesterol, homocysteine, Vitamins B12, and folic acid). Serum/plasma biomarkers of oxidative stress include biomarkers of lipid peroxidation, markers of DNA/RNA oxidation and markers of protein oxidation/nitrosylation. Inflammatory markers measured include pro- and anti-inflammatory markers.

Amyloid imaging PET scans:

- The Amyloid Imaging study is being conducted in partnership with the Austin Hospital in Melbourne. The target sample size is 100 twin pairs (60 MZ and 40 DZ pairs). Existing OATS participants and new OATS participants will be recruited through the ATR to meet this target. Participants will be required to undertake a PET scan at the nuclear medicine Departments of either the Austin Hospital in Melbourne or the Prince of Wales Hospital in Sydney. The PET scan requires an intravenous cannula to be inserted into a vein in the participant's arm for the injection of a small amount (<5 micrograms) of 18-F radiolabelled NAV tracer. The NAV-PET scan commences approximately 50 minutes after the injection and lasts approximately 20 minutes. This visit will take about 3 hours. In addition to the PET scan, participants are required to undertake the neurocognitive and medical assessments described above, and complete the various questionnaires. As with previous waves, participants can also elect to have an MRI and/or provide a blood sample.

Progress to date

- 4-year follow-up assessment data (Wave 3) were completed in December 2015 with 390 participants having a Wave 3 assessment. Blood samples were collected from 349 participants, and MRI scans from 237 participants. Wave 3 data will be cleaned and released in mid-2016.
- Amyloid imaging commenced in Victoria in July 2015. Fifteen participants had PET scans and neuropsychological assessments by the end of the year. NSW will commence PET scans in early 2016.
- Continued collaboration with the international consortia including ENIGMA (Enhancing Neuroimaging through Genetic Meta-analysis), CHARGE (Cohorts for Heart & Ageing Research Genetic Epidemiology) and EuroDiscoTWIN (diabetes and other hereditable conditions in twin cohorts).
- There have been 13 requests for access to OATS data in 2015. 11 are new requests, and 2 are updated project requests.
- To date, 63 OATS participants have agreed to be brain donors. Two participants unfortunately passed away during 2015 and generously bequeathed their brains to the study.

- The OATS Online assessments are ready to proceed with the exception of a suitable neuropsychological assessment tool. The current online assessments are being used as part of the Amyloid Imaging project.
- Ongoing studies include:
  - Genetics: genome-wide association studies (GWAS); candidate gene studies; gene expression using RNA sequencing and arrays; epigenetic studies using DNA methylation and looking at non-coding RNA; DNA sequencing, both whole exome and genome sequencing; and heritability.
  - Neuroimaging: voxel-wise analysis for subcortical structures, cortical structures and white matter integrity; investigation of lunar infarcts; and incidental findings in MRIs. Wave 3 MRI data processing will continue in 2016.
  - Neuropsychology: heritability of episodic memory and heritability of language functions; and expanding the collaboration with neuroimaging and genetics themes.
  - Funding from UNSW is continuing to help us re-organise the stored blood samples in 2016 which will improve accessibility for future studies.

Findings:

- Many OATS participants have donated a genetics sample to the study. We have a number of researchers, students and international collaborations working on projects using this data. These projects include examination of the genetics of longevity, changes in RNA, and how these may impact on age-related cognitive decline and dementia. In one study, researchers looked at data from ~700,000 individual genetic variants from more than 1,000 people 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.
- Master's student, Sri Chandana Kanchibhotla, completed her Master's thesis investigating the genetics of the corpus callosum in the ageing brain. The corpus callosum is an important white matter brain structure responsible for communication between the two hemispheres of the brain. Age-related changes in the corpus callosum have been associated with cognitive impairment and neurodegenerative disease. Neuroimaging data from OATS was used to extract information regarding the integrity of the microstructure of the corpus callosum. Heritability analyses were undertaken, which showed that most measures of the integrity of the corpus callosum microstructure were heritable.
- Jessica Lazarus undertook her Bachelor of Medical Science Honour's project in the emerging field of epigenetics. Epigenetics examines how expression of genes is controlled by mechanisms other than changes to the DNA code. One such epigenetic mechanism is the reversible methylation of DNA. This contributes to genes being switched on or off. In this study, DNA methylation of a particular gene was associated with memory performance in older adults (Lazarus et al, 2015, *Journal of Alzheimer's Disease*). This work is exciting as DNA methylation may be influenced by environmental factors, such as diet, and may suggest strategies to prevent or delay age-related memory decline. Jessica is progressing this work as part of her PhD.
- OATS researchers are part of the EuroDiscoTWIN consortium. This international collaboration combined resources to investigate the incidence and discordance of type 2 diabetes (T2 diabetes) in older twins. Discordance is where only one twin has developed the condition, and it is used to determine how much of the condition is influenced by genetics (Willemsen et al, 2015, *Twin Research and Human Genetics*, Dec 2015). The study examined data from nearly 35,000 twin pairs aged 45 years and older. From the OATS study, 9.6% of our participants had T2 diabetes. In other countries T2 diabetes ranged from 2.6% to 12.3%. The percentage was higher in studies with older twins, and in countries with higher national diabetes rates. Of all the twin pairs in the study, only 716 (5.1%) identical twin pairs, and 1,619 (8.0%) non-identical pairs were discordant for diabetes. Across all countries, the heritability was estimated at 72%. This study demonstrated that T2 diabetes has a high incidence in most countries, and that it has high heritability between twins.

Output:

- 6 peer-reviewed journal publications were published or accepted for publication in the journals of *Neuropsychologia*, *Twin Research and Human Genetics, Journal of Alzheimer's Disease, PLOS ONE, Nature,* and *Molecular Psychiatry.*
- 3 manuscripts submitted for publication are under review.
- End of year newsletter was produced for OATS participants, informants and collaborators.
- Professor Perminder Sachdev gave a presentation on the OATS at the opening of the NSW Node of the Australian Twin Registry at the University of Sydney in November 2015.

Benefits: Data from OATS Wave 1 and 2 has made significant contributions in relation to understanding the genetic factors underlying many aspects of cognition and brain imaging parameters. Important findings have emerged which will assist in the understanding of genetic contributions to cognitive functions such as processing speed, executive ability and episodic memory, and which support the cognitive reserve hypothesis. The heritability of brain structures, both cortical and subcortical, brain metabolites and markers of small vessel disease, such as lacunar infarction and white matter hyperintensities, have been examined and can inform future genetic investigations. Work on amyloid imaging and functional magnetic resonance imaging is proceeding and epigenetic studies are progressing. Longitudinal data from this cohort has the potential to inform research in cognitive ageing into the future, and offers an excellent resource for collaborative work.

Funding: 2013-2015 NHMRC Project Grant – Older Australian Twins Study, Wave 3; 2015-2017 NHMRC Project Grant – Amyloid Imaging OATS Sub-Study.

Date commenced:

- January 2013 - Older Australian Twins Study, Wave 3
- January 2015 - Amyloid Imaging OATS Sub-study

Expected date of completion: December 2017

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)

Project description: Prior investigations of human structural brain networks have elucidated core features of human structural brain networks. We provide the first study of structural topological organisation, particularly in reference to the crucial role of hub-regions, in the elderly brain. Here, diffusion-weighted imaging was performed on 115 cognitively normal subjects (74-96 years) from the MAS study. The second component of this project involves investigation of functional connectivity in the same participants using resting-state fMRI. Previous research has established a link between structural and functional connectivity in human brain networks. We are interested in examining how the nature of this relationship affects cognitive performance in the elderly. We identify spatio-temporal resting-state patterns of functional connectivity within our population, and examine whether structural and functional connectivity changes within these networks is predictive of age-related changes in cognitive performance.

Aims:

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

Design & method: The present study investigates a cognitively normal population drawn from the MAS study (74-96 years). High-angular probabilistic tractography was performed on the diffusion-weighted images of each subject. Structural networks were then constructed, representing connectivity between 512 predefined brain regions. We sought to investigate the architectural features of hub-regions, left-right asymmetries, and sexual dimorphisms. In a subset of these participants, functional networks were also constructed, representing the functional connectivity between the same predefined brain regions. Leveraging multivariate analysis procedures, we investigated the combined influence of demographic (i.e. age, education) and cognitive measures on functional brain networks.

Progress to date: We have discovered very interesting findings regarding the structural topology of the elderly brain, which have never been observed within the field. These findings have been published in *NeuroImage*. We observed that the topology of hub-regions is consistent with adult connectomic data and, more importantly, their architectural features reflect their ongoing vital role in network communication. We also found substantial sexual dimorphisms, and striking lateralizations in structural connectivity within this population. In terms of the second component of this project, we have identified a diffuse functional subnetwork whose expression opposes the effects of age against core cognitive processes, such as attention and processing speed. We have also demonstrated increased educational attainment possibly confers greater resilience to age-related cognitive decline by acting upon non-cognitive networks.

Benefits: We have been able to implement sophisticated technical advancements in constructing connectivity information acquired from diffusion imaging, and resting-state fMRI. In addition, this

body of work provides a systematic investigation of brain structure and function in the cognitive elderly. This is an important benchmark for the field of neurodegenerative disorders, such as AD.

Output: 1 conference presentation (*SBMT* 2014), 1 journal publication (*NeuroImage*), 1 poster presentation (OHBM 2016).

Funding: NHMRC.

Date commenced: January 2014

Expected date of completion: March 2016

The role of polyphenolic compounds in modulating AD pathology

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

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

Project description: Assess the effect of polyphenolic compounds on Aβ oligomer and aggregate formation and the effect on cells exposed to Aβ monomers and oligomer formed during "ageing" *in vitro*.

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.

Design & method: Controlled experimental design, testing the effect of presence or absence of polyphenolics on Aβ aggregate formation *in vitro* and effects on cells exposed to Aβ aggregates *in vivo*. Aggregate formation will be monitored by isothermal calorimetry, gel electrophoresis and electron microscopy. Effects on cells will be monitored using cell viability assays, microscopy, mitochondrial function and proteomics.

Progress to date: Experiments are ongoing. Some of the results have been presented at conferences and a manuscript reviewing this area has been published.

Benefits:

- Potential development of low toxicity strategies for AD prevention and/or treatment of MCI/early AD.
- Better understanding of the effects of polyphenolic compounds on Aβ aggregation.
- Identify specific, naturally occurring polyphenolic compounds which may slow or prevent Aβ aggregation.

Output: 2 conference presentations, 1 invited oral presentations, 1 publication.

Funding: NHMRC, Rebecca L. Cooper Medical Research Foundation, UPRA PhD scholarship to Tharusha Jayasena.

Date commenced: 2011

Expected date of completion: Ongoing

The Sydney Centenarian Study (SCS)

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

Project description: The SCS is studying a cohort of individuals who have successfully reached the extreme end of life in order to determine the genetic and environmental factors that contribute to successful ageing. We are taking a broad approach to elucidate all factors that may be of interest in investigating this population. The findings will shed light on which factors are particularly important for ageing well, which in turn will allow us to inform lifestyle choices in younger and middle aged Australians. The findings will also inform decisions to improve the quality of life of older Australians, and plan for future older generations. This is particularly important as we have an ageing population which will present a disproportionate burden on the health system unless we are prepared.

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".

Design & method: Individuals 95 years and older were recruited from seven electoral districts in Sydney using the electoral roll and multiple other strategies

to obtain a representative sample. Physical and mental health and cognitive status were assessed using standard instruments in multiple sessions in the participants' places of residence, with assessments adapted to each individual. An informant was interviewed, and participants invited to donate a blood sample, do an autobiographical interview, undergo an MRI scan and enrol into the brain donation program.

Progress to date: Follow-up assessments with the original SCS cohort were completed in 2015. About 55% of people 95 years and above meet criteria for dementia. Rates of heart disease and diabetes were lower than in octogenarians, but hearing and visual deficits were common in centenarians. Rates of psychological distress were low and satisfaction with life high (mean 5.91 out of a maximum of 7). Brain volumes, both of the grey and white matter, continue to decline in the very old, but the pattern of decline is different from that seen in young-old individuals (<85 years). Structural MRI can distinguish amnestic but not non-amnestic MCI in the very old, and the structural correlates of MCI were different in the very old compared to the young old. White matter lesions are very common and extensive in centenarian brains, but they do not relate to cognitive impairment.

Benefits: By understanding the neurocognitive disorders in the very old, their determinants, their pathological correlation and functional outcomes, we will be in a better position to monitor or moderate risk factors for this age group. Equally, our enhanced appreciation of protective factors may be valuable in educating younger populations in relation to healthy ageing. The information gathered in this study will assist in planning of health and social systems for the exceptionally old.

Output: 4 papers published, 1 in press, 3 in preparation.

Funding: NHMRC

Date commenced: October 2008

Expected date of completion: Data collection completed. Further papers in preparation. A second centenarian cohort to be recruited in 2016-17.

The Sydney Memory & Ageing Study (MAS)

CHeBA staff: Henry Brodaty, Perminder Sachdev, Julian Trollor, Brian Draper (conjoint), Nicola Kochan, Kristan Kang, John Crawford, Karen Mather, Wei Wen, Adam Theobald, Kate Maston

Project description: The MAS began in 2005 to examine the clinical characteristics and prevalence of mild cognitive impairment (MCI) and related syndromes, to determine the rate of change in cognitive function over time and to investigate risk and protective factors for cognitive decline and dementia. It is one of the largest longitudinal studies of this kind in Australia and has resulted in many scientific publications and several national and international collaborations. The cohort has been systematically assessed with a comprehensive range of tools. The focus is on cross-sectional neurocognitive function and its longitudinal change over time, terminating with neuropathology.

Aims:

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

Design & method: At the baseline assessment from 2005 to 2007, 1037 non-demented individuals aged 70-90 were recruited from two areas of Sydney, following a random approach to 8914 individuals on the electoral roll. They underwent detailed neuropsychological and medical assessments and donated a blood sample for clinical chemistry, proteomics and genomics. A knowledgeable informant was also interviewed. Structural MRI scans were performed on 544 of the participants, and subgroups participated in studies of falls and balance, metabolic and inflammatory markers, functional MRI and prospective memory. The group will continue to be followed up annually with the end point being dementia or death.

Progress to date:

- The longitudinal cohort has been followed up and yielded a large amount of data on many aspects of brain ageing and dementia. Acquisition of 8-year follow-up data was completed in 2015, with 9-year follow-up currently taking place and collection of 10-year data due to commence in February 2016.
- We have studied a wide range of risk factors for cognitive impairment, including genetic determinants (including white matter lesions, hippocampus, subcortical brain structures, grey matter volumes), arterial stiffness, dietary mineral intake, glucose disorders, inflammatory markers (e.g. MIC-1, IL6) and lifestyle factors.

- Collaborations include: COSMIC, PROMOTE, CHARGE, ENIGMA, PERADES, BRIDGET and EADB.

Benefits: Our research has found modifiable factors which influence neuropsychiatric disorders, in particular cognitive decline. This can be translated into effective intervention and policy for optimal treatment programs that are affordable, acceptable and practical in the Australian context. International collaborations provide opportunities for researchers to share and compare data from existing studies, allowing systematic examination of brain ageing issues on a larger scale.

Output: 104 published papers, 53 papers in preparation or submitted, several conference presentations in Berlin, Sydney and Washington DC.

Funding: NHMRC.

Date commenced: September 2005

Expected date of completion: Ongoing

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

CHeBA staff: Karen Mather, Anbupalam Thalamuthu, Perminder Sachdev

Other key investigators: Dr Nicola Armstrong (Murdoch University), Associate Professor John Kwok (NeuRA, UNSW), Professor Peter Schofield (NeuRA, UNSW)

Project description: Prior studies suggest epigenetics may play a role in late-onset Alzheimer's disease. However, few studies have examined the role of long non-coding RNAs (ncRNAs) in age-related memory loss, an early marker of Alzheimer's disease.

Aims: To identify long ncRNAs and other types of RNAs associated with age-related memory performance.

Design & method: Identical twins from the Older Australian Twins Study who were discordant for memory performance were selected for this study. RNA was extracted from donated peripheral blood samples and RNA sequencing performed. The transcriptomes of discordant twins were compared.

Progress to date: Identical twin pairs discordant for memory performance have been identified, RNA extracted and sequencing completed. Initial analyses have been performed.

Benefits: Identified long ncRNAs may be useful as biomarkers of early Alzheimer's disease. This work may also clarify their role in the aetiology of the disease. Ultimately, it may suggest clinical diagnostic, prognostic and treatment strategies for Alzheimer's disease.

Output: A manuscript and a conference presentation are planned.

Funding: This project is gratefully supported by a Yulgilbar Foundation Alzheimer's Research Program Grant. OATS is supported by the NHMRC Project Grant 1045325. Karen Mather was kindly supported by the Thomas Foundation and by the NHMRC Capacity Building Grant 568940.

Date commenced: December 2013

Expected date of completion: December 2016

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)

Project description: Transcranial Direct Current Stimulation (tDCS) has been shown to enhance cognition in psychiatric patients. A majority of Computer Cognitive Training (CCT) trials have demonstrated improvement in healthy older adults and older adults with MCI. Our trial is the first to test the ability of tDCS to bolster the effects of CCT in older adults with memory problems.

Aims: To 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)).

Design & method: Double-blind randomised controlled study. Participants are randomised to one of two conditions: active or sham (placebo) tDCS during CT across 15 sessions (1 hour a session, 3 sessions per week).

Progress to date: Data collection commenced in January 2013. So far we have had 37 study completers with 1 participant still to follow up. In 2016 we will recruit a further 12 participants who

will additionally complete neuroimaging. The trial will be completed by early 2017. Preliminary analysis suggests that both groups showed large memory improvements over the study duration.

Benefits: This research may help to develop new interventions for improving cognition and memory in people at risk for dementia.

Output: The research will be submitted for publication once completed.

Funding: Thomas Foundation, DCRC-ABC.

Date commenced: January 2013

Expected date of completion: February 2017

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

CHeBA staff: Karen Mather, Anbu Thalamuthu, Perminder Sachdev

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

Project description: Epigenetics refers to factors that influence gene expression that are independent of changes to the DNA code. Disruption of the normal epigenetic state has been associated with ageing, deficits in memory, age-related cognitive dysfunction and Alzheimer's disease (AD) and many other outcomes. Methylation of the genome is an epigenetic mechanism and can itself be influenced by genetic variation, stochastic processes and by the environment. The identical twin design controls for genetic background, age and sex and minimizes differences in early environmental experiences and thus is an ideal model to identify differentially methylated genomic regions and environmental factors associated with different traits.

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

Design & method: Genome-wide DNA methylation of identical twin pairs from the Older Australian Twins Study (OATS) will be assessed using the Illumina 450K array. Statistical analyses will be undertaken to identify differentially methylated regions and environmental factors associated with particular traits. In a separate study, as part of the EuroDiscoTWIN consortium, DNA methylation at over 3 million sites will be assayed in identical twins discordant for type 2 diabetes.

Progress to date: The 450K methylation data has been collected. Some preliminary analyses have been undertaken. Type 2 diabetes discordant MZ twin pairs are currently being assayed.

Benefits: This work will improve our knowledge regarding the epigenetic and biological processes underlying age-related phenotypes. It will also shed light on the environmental factors that may influence DNA methylation. As epigenetic changes are potentially reversible, it makes them ideal therapeutic targets for future studies. This work may also suggest new strategies to combat age-related decline and disease.

Output: Poster presentation at the GeneMappers conference, Adelaide, 2015 (Armstrong et al.).

Funding: OATS is supported by the NHMRC Project Grant 1045325.Karen Mather was kindly supported by the Thomas Foundation and by the NHMRC Capacity Building Grant 568940. Methylation work was supported by NHMRC Grants 613608 and 61302 (held by Professor Naomi Wray, administered by Queensland Brain Institute, University of Queensland)

Date commenced: January 2015

Expected date of completion: Ongoing

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

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

Other investigators: Dr Fei Song (formerly CHeBA), 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)

Project description: Quantification of vitamin binding protein levels (particularly afamin and vitamin D binding protein) in Mild Cognitive Impairment (MCI) and Alzheimer's disease (AD) plasma in a variety of population based cohorts, from Sydney and elsewhere in Australia.

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.

Design & method: Both cross-sectional and longitudinal designs are used. Cohorts include: Sydney MAS (all 4 waves), Hunter Community Study (HCS), Dominantly Inherited Alzheimer's disease Network (DIAN), Older Australian Twins Study (OATS) and Sydney Centenarian Study (SCS).

Progress to date: Experiments are based on previous screening using the iTRAQ proteomics approach with pooled plasma. Individual plasma samples are currently being assayed using ELISA and both local and international collaborators involved, with provision of additional plasma samples or assay of our samples with validated ELISA.

Benefits:

- Potential biomarker panel to assist in diagnosis of predisposition to MCI and/or AD.
- Identify robust biomarkers, which show consistent change across studies.
- Understand the effect of plasma vitamin binding protein changes on cognition and brain volumetrics.
- Determine how plasma vitamin binding protein levels change with age, particularly advanced old age.
- Understand the role of specific vitamin binding proteins (afamin and VDBP) in the ageing brain.

Output: None to date.

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.

Date commenced: 2012

Expected date of completion: Ongoing

Completed Projects

Alcohol consumption and incident dementia over 4-years: Evidence from the Sydney Memory and Ageing Study

CHeBA staff: Karen Mather, Nicole Kochan, Brian Draper (conjoint), Julian Trollor (conjoint), Perminder Sachdev, Henry Brodaty

Other investigators: Dr Megan Heffernan (DCRC, UNSW), Dr Amelia Assareh (BABS, UNSW), Dr Simone Reppermund (School of Psychiatry, UNSW), Mr Jing XU (DCRC, UNSW)

Project description Alcohol consumption is a potentially modifiable risk factor for dementia, but the literature on this is not completely consistent. It is not known whether this inconsistency is partly due to an interaction with the apolipoprotein E (*ApoE*) genotype, an established risk factor for Alzheimer's dementia.

Aims: The aim of this study was to examine whether alcohol consumption predicts cognitive decline and incident dementia over 4-years, and if this effect is moderated by *ApoE* ε4 status.

Design & method: Participants were community-dwelling older adults (70-90 years) from an ongoing longitudinal study who did not have dementia at baseline. Incident dementia was assessed at 2-years and 4-years using the DSM-IV criteria. Logistic regression models were used to test the association between recent (12-month) and past alcohol consumption and cognitive impairment at baseline. As well as cognitive decline and incident dementia over 4 years, covariates included age, years of education, sex, cerebrovascular disease and depression.

Findings: Of the 594 participants, 48 developed dementia (6.9%) during follow-up. Number of standard drinks per day was not associated with incident dementia (OR 1.0 95% CI 0.8-1.2). Carriers of the *ApoE* ε4 allele were more likely to develop dementia (OR 3.3 95% CI 1.4-7.7) but there was no interaction with alcohol consumption (OR 0.8 95% CI 0.6-1.3). Results were similar amongst participants who reported a change in past drinking habits.

No association was found between recent and previous alcohol intake and risk of dementia when examined separately and there was no interaction with *ApoE* ε4 allele status.

Benefits: This study puts into question previous findings. A more nuanced approach to effects of alcohol on risk of dementia is required.

Output: 1 paper in press, *J Alzheimer's Disease* (Heffernan M et al).

Funding: N/A

Date commenced: July 2014

Date completed: December 2015

Analysis of DNA methylation variation in the apolipoprotein-A1 gene and its relationship with episodic memory performance in older adults

CHeBA Staff: Jessica Lazarus (Hons/PhD student), Karen Mather, Anne Poljak, Perminder Sachdev, Anbupalam Thalamuthu, Teresa Lee, Nicole Kochan

Other investigators: Professor David Ames (National Ageing Research Institute; Royal Melbourne Hospital), Dr Nicola Armstrong (Murdoch University), Associate Professor John Kwok (NeuRA, UNSW), Dr Fei Song (formerly CHeBA), Dr Margaret J. Wright (QIMR Berghofer Institute, Brisbane, Australia)

Project description: Levels of plasma *apolipoprotein A* levels have been associated with age-related cognitive performance and decline. An Honours project examining DNA methylation variation in the *apolipoprotein A* gene and age-related memory performance was undertaken using participants from the Sydney Memory and Ageing Study. This work was based on preliminary data from a project examining genome-wide methylation in memory-discordant identical twins from the Older Australian Twins Study.

Aims: To examine whether DNA methylation variation in the *APOA1* gene was associated with episodic memory performance and ApoA1 protein levels.

Design & method: In the Sydney Memory and Ageing Study, methylation analysis of the apolipoprotein A gene was undertaken using pyrosequencing. Plasma apolipoprotein A1 levels had been previously assayed and memory performance assessed. Linear regression analyses were undertaken to assess the relationships between *APOA1* gene methylation and (i) plasma apolipoprotein A1 levels and (ii) memory performance.

Findings/Benefits: The results suggest that an epigenetic mechanism, DNA methylation variation, may contribute to control of *apolipoprotein A1* gene expression and memory performance.

Output: The results were written up as a successful Honours thesis by Ms Lazarus in 2014. This work has now been accepted for publication in a peer-reviewed journal and was published in 2015 (Lazarus et al., *J Alzheimer's Disease*).

Funding: Sydney MAS is supported by the NHMRC Program Grant 568969. Karen Mather was kindly supported by the Thomas Foundation and the NHMRC Capacity Building Grant 568940.

Date commenced: February 2013

Date completed: January 2015

Assigning optimal residential aged care facility parameters and resources for people with and without dementia: iHome project

CHeBA staff: Lynn Chenoweth, Henry Brodaty

Other investigators: Dr Victor Vickland (DCRC, UNSW), Duffield, C., Professor Jane Stein-Parbury (University of Technology), Professor Marion Haas (University of Technology Sydney)

Project description: The team's RCTs of the person-centred model conducted in 60 randomly assigned Australian aged care homes, showed that agitation in people with dementia reduced significantly at post-test and follow-up (p=0.01; p=0.03) compared with usual aged care models (p=0.56; p=0.48). The mean improvements for resident quality of life were also significantly improved for person-centred care (PCC) (p=0.002; p=0.001), compared with usual care (p=0.93; p=0.87 respectively). Study data were used to construct iHome (a computer model of a typical aged care home) with AnyLogic software, employing the open-source Eclipse software development platform. A three dimensional simulated layout of the virtual aged care home (iHome) was constructed, representing a set of ideas that initialises a group of virtual people (active agents) which resemble real world aged care home consumers, and managers and staff who provide different services over the 24 hour period. The RCT data and iHome specifications compare favourably with publically available Australian aged care datasets on organisational, environmental, consumer, managerial, and staff characteristics. In the simulated environment a tree of virtual objects (active agents) which encapsulate each other, run concurrently in a common environment to show the interactions, events and responses of active agents. Experimenting in the virtual environment allows modification of different active agent staff and service timeframes, so as to identify the most efficient and/or positive care activities and schedules which produce the most benefit for active agent residents.

Aim: To develop the iHome in preparation for testing iHome specifications (optimal and feasible) in real world conditions, using a mixed method, cluster RCT in 10 treatment homes and 10 control homes which aims to assess quality of life and functional outcomes for aged care residents with different abilities and needs.

Design & methods: iHome was constructed and tested through computer simulation over 12 months using mixed methods.

Findings: The iHome model assumptions were tested by: manipulating different variables in each of the three theoretical constructs in subsequent iHome experiments; activity charts were developed and expanded for resident and staff active agents being modelled for care services; individual active agent characteristics and sets of rules were allocated to the major activities of daily living, operating systems and interactions occurring between staff and residents active agents in the 24/7 cycle; computer animations with charts and graphs were developed to show relationships between different variables which could be adjusted to reflect plausible scenarios and the range of changes that may occur at different times of the day for residents with different characteristics and needs; and real-life case scenarios from the RCT extant data were extracted and subjected to experimentation in iHome model.

Benefits: Preliminary experimentation with iHome reveals that its person-centred features (socio-cultural context) and the person-centred care/lifestyle services modelled (interactional environment) produce positive outcomes for the 'virtual' aged care clients (subjective experiences). iHome's capabilities will enable researchers to respond more quickly to government and aged care sector requests to determine person-centred parameters (systems, structures and

resources) for aged care homes, that are able to produce positive care experiences and outcomes for older people.

Output: 1 journal publication (*Future Medicine Neurodegenerative Disease Management*), 1 conference presentation.

Funding: Montefiore Home funding (administered by CHeBA) supports Professor L. Chenoweth's research position with CHeBA, University of NSW Goldstar Award (administered by DCRC-ABC).

Date commenced: March 2014

Date of completion: June 2015

Biometal imaging in the Octodon degus

CHeBA staff: Nady Braidy, Anne Poljak, Perminder Sachdev

Other investigators: Professor Nibaldo Inestrosa (Pontificia Universidad Católica de Chile), Dr Chris Marjo (BMSF, Mark Wainwright Analytical Centre, UNSW), Dr Anne Rich (BMSF, Mark Wainwright Analytical Centre, UNSW), Dr Helen Rutlidge (BMSF, Mark Wainwright Analytical Centre, UNSW)

Project description: The accumulation of redox-active transition metals in the brain and metal dyshomeostasis are thought to be associated with the aetiology and pathogenesis of several neurodegenerative diseases, and Alzheimer's disease (AD) in particular. However, the mechanism by which these biometals regulate the pathogenesis and progression of AD remains unclear. We report the distribution profile of biometals in the aged brain of the endemic Chilean rodent *Octodon degus (O. degus)* – a natural model to investigate the role of metals on the onset and progression of AD.

Aims:

- To quantitatively image the anatomical distribution of Cu, Fe, Zn, Ca, and Al, in the brains of aged *O. degus* by a laser ablation inductively coupled plasma (ICP) system using mass spectrometry (LA-ICPMS).
- To delineate regions of interest and determine the biometal concentrations in the *O. degus* brain with advanced age.
- To investigate potential mechanisms for these changes by examining the expression of biometal trafficking pathways, including lysosomal function, major Fe/Cu regulatory genes, and selected ZnTs and ZIPs.

Design & method: *O. degus* were obtained from a breeding colony at the animal facility of the University of Valparaiso, Chile and maintained in a temperature controlled room (23 ± 1 °C), under a 12hr: 12hr light/dark cycle, with water and food provided *ad libitum*. At the time of this study, 32 Male *O. degus* were grouped by age: 1, 3, 5 and 7 years old (n = 8 per group). Ages were selected to represent the development of AD-like pathology (which normally starts to appear at ~ 3 years).

Findings: Using laser ablation inductively coupled plasma mass spectrometry (LA-ICPMS), our quantitative images of biometals (Fe, Ca, Zn, Cu, and Al) appear significantly elevated in the aged *O.degus* and show an age-dependent rise. The metals Fe, Ca, Zn, and Cu were specifically enriched in the cortex and hippocampus, which are the regions where amyloid plaques, tau phosphorylation and glial alterations are most commonly reported, whilst Al was enriched in the hippocampus alone. Using whole brain extracts, age-related deregulation of metal trafficking pathways was also observed in *O.degus*.

Benefits: The data demonstrates the significance of biometal modulation as an important therapeutic strategy for the treatment of AD.

Outputs: 1 publication; 1 manuscript in preparation for submission.

Funding: NHMRC, Chilean Conecyt Postdoctoral Prize

Date commenced: 2014

Date completed: December 2015

Genetics of grip strength

CHeBA Staff: Jessica Chan (Medicine student), Karen Mather, Anbupalam Thalamuthu, Perminder Sachdev

Other key investigators: Dr Nicola Armstrong (Murdoch University), Professor John Attia (University of Newcastle), Associate Professor John Kwok (NeuRA, UNSW), Professor Stephen Lord (NeuRA, UNSW), Dr Jasmine Menant (NeuRA, UNSW), Dr Chris Oldmeadow (University of Newcastle), Professor Peter Schofield (NeuRA, UNSW)

Project description: This project was an independent learning project undertaken by a 4th year Medicine student. Grip strength is an indicator of muscle strength and is a predictor of mortality and morbidity in older adults. Previous studies suggest grip strength has moderate to high heritability. Using two cohorts of middle-aged to older adults, the Sydney Memory and Ageing Study and the Hunter Community Study, this project sought to examine the genetics of muscle strength.

Aims: To identify genetic variants associated with a marker of muscle strength, grip strength, in mid to late life.

Design & method: Hand grip strength was measured using standard methods. Genome-wide genotyping data imputed to Hapmap 2 was used for analyses. A candidate gene study examining previously identified genetic variants from the literature and biologically relevant genes was undertaken using linear regression. A genome-wide association study for grip strength was also undertaken.

Findings: Although genome-wide significant results were observed in the discovery analyses, the results were not replicated in an independent cohort. Further studies using larger sample sizes are required.

Benefits: Potential benefits arising from this work include a better understanding of the contributions of genetics to muscle strength, specifically, grip strength, which is an important indicator of physical health in older adults.

Output: The results were written up as the final report for a successful Medicine Independent Learning Project by Jessica Chan. This work has now been published in the journal *AGE* (Chan et al., 2015).

Funding: Sydney MAS is supported by the NHMRC Program Grant 568969. Karen Mather was kindly supported by the Thomas Foundation and by the NHMRC Capacity Building Grant 568940

Date commenced: February 2013

Date completed: February 2015

Investigating the ageing retinal vasculature and its cerebrovascular, cardiovascular and cognitive correlates

CHeBA staff: Geraldine Koo (Medicine Independent Learning Project student), Karen Mather, John Crawford, Julian Trollor, Wei Wen, Nicole Kochan, Perminder Sachdev

Other key investigators: Center for Vision Research, Westmead Millennium Institute, University of Sydney: Victoria Cosatto, Paul Mitchell, Elena Rotchtchina, Ava Tan, Jie Jin Wang

Project description: Age-related changes in the eye can be measured non-invasively, easily and objectively and may be useful as a proxy for age-related vascular changes occurring in other tissues, particularly the brain. Age-related changes occur in most tissues of the eye including changes in the diameter of retinal blood vessels, retinal tissue thinning and loss of corneal endothelial cells. A measure that can be used to assess retinal ageing is retinal vascular calibre, which estimates the diameters of retinal arterioles and venules using retinal photography. Prior studies have associated retinal vascular calibre measures with neurological and cardiovascular/cerebrovascular measures such as hypertension, diabetes, stroke, vascular dementia, cognitive performance and cerebral small vessel disease. However, few prior studies have had the capacity to investigate baseline retinal vascular measures and longitudinal health outcomes in older adults.

Aims: To elucidate the cross-sectional and longitudinal relationships between retinal vascular calibre measures in older adults and (a) cognitive performance; (b) neuroimaging measures and (c) cardiovascular measures.

Design & method: At baseline assessment, retinal photographs were taken of Sydney Memory and Ageing Study participants. Retinal vascular caliber was measured by collaborators from the Sydney Vision Centre. Association analyses were performed with retinal caliber measurements and the traits of interest.

Findings: Using participants from the Sydney Memory and Ageing Study, retinal venular pathology was associated with age-related cognitive performance and decline, particularly for women, but was not associated with dementia. This work suggests that the retinal microvasculature may serve as an independent biomarker for age-related cognitive performance and decline.

Benefits: This research contributes to the knowledge regarding whether retinal caliber measures may be used as a model to improve our understanding of vascular ageing and age-related outcomes.

Output: This project has been written up as Geraldine's Medicine Independent Learning Project. A manuscript is in preparation for journal submission.

Funding: Sydney MAS is supported by the NHMRC Program Grant 568969. Karen Mather was kindly supported by the Thomas Foundation and by the NHMRC Capacity Building Grant 568940.

Date commenced: February 2015

Date completed: October 2015

Living with dementia in retirement villages: Investigating the experiences of retirement village residents with dementia

CHeBA staff: Lynn Chenoweth

Other investigators: Alzheimer's Australia NSW: Kylie Miskovski, Brendan Moore

Project description: Access to appropriate support in retirement villages including dementia-friendly environments, inclusive communities, and community care services might help to help delay or prevent premature entry of people with dementia having to move to residential aged care home. Knowing how well retirement villages are set up to support people with dementia and their carers will assist retirement village operators and community care providers to identify and respond to the specific structural, physical and psychosocial requirements of retirement village residents with dementia. Families/carers will, subsequently, be more able to determine at what stage the person with dementia requires assessment for possible relocation to a residential aged care home, or whether they require a dementia-specific extended aged care package to help them remain living in the village.

Aim: To investigate the experiences of people with dementia living in retirement villages and ascertain the extent to which people with dementia are well supported to age in place through the provision of community care services and informal support from other members of the village community.

Design & method: This was an exploratory research project, using mixed-methods. Stage 1 employed interviews and focus groups with people with dementia and their carers, and village managers of three retirement villages, which informed the development of research instruments used in stage 2 (focus group and interview schedules and an on-line survey). The instruments were piloted at one village before being rolled out to eight retirement villages run by different types of operators (a mix of for-profit and not-for-profit, and large and small organisations) in diverse locations with different socio-economic demographic resident populations in the Sydney metropolitan area and five retirement villages in regional NSW, including Port Macquarie, Central Coast, South Coast, Central West and Tweed Heads. The on-line survey was made accessible to all Australian retirement village managers and staff and community-based services staff who provide services to Australian retirement villages.

An expert advisory group contributed to the study design and methodology, and joined focus groups to make recommendations on how to making retirement villages more accessible and responsive to people with dementia (representatives from Retirement Village Residents Association; Aged & Community Services Association of NSW & ACT, IRT South West Sydney, and village residents).

Findings/Benefits: The study findings highlight the need for retirement village providers to create enabling environments by providing opportunities for psychological and practical support to people with dementia and their partners, facilitating social interaction with others and access to local community infrastructure. The results also strongly support the need for co-located supported care services and incorporate social and physical structures for the person with dementia, for the benefit of both themselves and their partner. The human need for social connection, sense of community and support provided by the village community, represents a major motive for retirement village selection.

Output: 1 report: Alzheimer's Australia NSW (Moore, B., Miskovski, K., **Chenoweth, L**.) *Living with dementia in retirement villages.* December, 2015. Sydney, Alzheimer's Australia NSW. Launch of Report at:

- NSW Parliament House, Member's Lounge, August 2015
- Retirement Living Summit 2015
- ACS seminars and managers courses 2015
- ACS conference in May 2016
- AlzNSW stand at retirement village expos.

Funding: Montefiore Home funding (administered by CHeBA) supports Professor L. Chenoweth's research position with CHeBA, Illawarra Retirement Trust (not administered by CHeBA).

Date commenced: January 2014

Date completed: September 2015

Metabolomics of natural and non-natural animal models for AD

CHeBA staff: Nady Braidy, Anne Poljak, Perminder Sachdev

Other investigators: Dr Sonia Bustamante (BMSF, Mark Wainwright Analytical Centre, UNSW), Professor Nibaldo Inestrosa (Pontificia Universidad Católica de Chile), Dr Chris Marjo (BMSF, Mark Wainwright Analytical Centre, UNSW), Dr Anne Rich (BMSF, Mark Wainwright Analytical Centre, UNSW), Dr Helen Rutlidge (BMSF, Mark Wainwright Analytical Centre, UNSW)

Project description: Numerous studies have shown an association between the levels of the N-methyl-D-aspartate (NMDA) receptor co-agonist, D-serine, and neurological disorders, including Alzheimer's disease (AD) in particular. However, the mechanism by which D-serine regulates the pathogenesis and progression of AD remains unclear.

Aims:

- To measure D- and L-Serine levels in hippocampal samples from the aged brain of the endemic Chilean rodent *Octodon degus (O. degus)* – a natural AD model - to investigate their role in the onset and progression of AD.
- To evaluate using immunofluorescent and western blotting analysis, of serine racemase (SR), an enzyme that converts L-serine to its dextrarotatory enantiomer, and TUNEL assay for apoptosis.
- To quantify the levels of the essential amino acids, L-alanine, L-threonine, and glycine were also assessed using gas chromatography mass spectrometry (GC-MS).

Design & method: *O. degus* were obtained from a breeding colony at the animal facility of the University of Valparaiso, Chile and maintained in a temperature controlled room (23 ± 1 °C), under a 12hr: 12hr light/dark cycle, with water and food provided *ad libitum*. At the time of this study, 32 Male *O. degus* were grouped by age: 1, 3, 5 and 7 years old (n = 8 per group). Ages were selected to represent the development of AD-like pathology (which normally starts to appear at ~ 3 years).

Findings:

- 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 SR and TUNEL expression.
- 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.
- Deregulation of amino acid levels may be associated with the development and progression of AD.

Benefits: Deregulation of amino acid levels is likely to contribute to the pathological changes reported in AD, including excitotoxicity, oxidative stress, and neuronal cell death.

Outputs: 1 publication, with a further manuscript submission underway.

Funding: NHMRC, Chilean Conecyt Postdoctoral Prize

Date commenced: 2014

Date completed: December 2015

Rhythm of Life project (phase 1)

CHeBA staff: Lynn Chenoweth

Other investigators: Anglican Retirement Villages: Kristine Rice, Rob Freeman, Burke.

Project description: In its Pilot Charter, the aged care provider organisation planned

to realise a continuous improvement program to develop, identify and articulate a new model of care which is underpinned by evidence and best practice within the concepts of Person Centred Care (PCC). The project was incorporated within the organisation's continuous improvement processes under the leadership of eight project teams, where each team identified three areas of improvement implemented in twelve-week cycles. These teams covered: *Change Management, Dementia Specific Unit, Clinical Practice, Recreation & Lifestyle, Staffing & HR strategy, Education, Environment and Food.* This initiative was an example of the organisation's resource investment in organisational service improvements and a culture change. There had been significant investment in personnel's time to undertake literature reviews on best practice; this preparatory work led to the development of the project's plan and model of care. The dedication of a specific Governance Committee exemplifies the significance of the project for the organisation.

Aims: At a strategic level, the aged care provider organisation aimed to implement person-centred care throughout the organisation, beginning with a trial in a pilot facility.

Design & method: The project utilised an action based research methodology over 18 months, which was incorporated within the organisation's continuous improvement processes, using mixed methods.

Findings/benefits: The first phase of the project has been completed, with the following being achieved: audit of the organisation's management structure, culture, care services and care environment in 48 of its residential care services across NSW using the Person-Centred Environment and Care Assessment Tool (PCECAT); identification of management strategies that support the implementation of person-centred care (PCC) and determine whether these strategies are reflected in the quality of care (M Nursing student study); and development of strategic processes to improve services in each of the

portfolios *Change Management, Dementia Specific Unit, Clinical Practice, Recreation & Lifestyle, Staffing & HR strategy, Education, Environment and Food,* based on the PCECAT recommendations.

The PCECAT findings provided a very good measure of quality of service quality for the aged care organisation, because it is consistent with the Australian Aged Care Standards, adheres to Tom Kitwood's principles for the implementation of a person-centred aged care service, and has been validated against tools used widely in residential aged care systems. Insight was gained into the actual management strategies that support person-centred services in a residential aged care facility. The managers' leadership and oversight of strategies to embed person-centred services have been linked with the PCECAT indicators of quality improvement, and have been found to be achievable within financial constraints. The project also confirmed that the best intentions and enthusiasm from managers and staff will face a David and Goliath battle without broader organisational (executive and board) support. Direct care staff and managers were empowered to be responsive to peoples' needs with a new organisational culture strategy described as the *'yes culture'*. Organisational leadership was exemplified with the steering committee creating a *toolkit* change process through a continuous improvement process. The second phase of the project is now underway, targeting specific areas for further improvement.

Output: 1 Masters of Nursing thesis submitted to University of Technology Sydney (Zarb, A., Stein-Parbury, J., Chenoweth, L. Management influence on development of a person-centred aged care system), 1 manuscript submitted, 1 manuscript in preparation, 1 conference presentation.

Funding: Montefiore Home funding (administered by CHeBA) supports Professor L. Chenoweth's research position with CHeBA, Anglican Retirement Villages (not administered by CHeBA).

Date commenced: February 2014

Date completed: June 2015

Sir Moses Montefiore Jewish Home (Montefiore Home) PCECAT project

CHeBA staff: Lynn Chenoweth

Other investigators: Montefiore Home: Janine Grossmann, Ann Brodie

Project description: A facility-level audit was conducted in all four of Montefiore Home's aged care facilities with the Person-Centred Environment and Care Assessment Tool (PCECAT), in order to determine the extent to which the organisational structures, physical environment, work culture and care services were person-centred. Concepts for review included quality indicators according the Residential Aged Care Standards, person-centred principles and staff empowerment and resident enablement and decision-making. Overarching this framework, Donabedian's model for evaluating health care services and quality of care was incorporated using the specific constructs of structure, process and outcomes. These two data collection methods helped to obtain systems-level data on service quality according to person-centred principles and the Australian Aged Care Standards.

Aims: To assess the extent to which Montefiore Home's organisational structures, physical environment, work culture and care services were person-centred, and to provide recommendations on areas for improvement where needed.

Design & methods: The 12 month audit was conducted over 12 months, using mixed methods in four of Montefiore Home's aged care facilities. Semi-structured interviews were undertaken with senior and middle managers and staff of all care units, and programs (catering, housekeeping, nursing, recreation, allied health, religious and pastoral care), as well as interviews with residents and their family members, observations of service delivery and residents' responses them, and document reviews such as care and recreation plans, and medical and nursing progress notes.

Findings/benefits: The PCECAT audit was completed and a detailed report of the project findings was presented first to the executive staff, and then to the Board, outlining the positive findings and areas for improvement, with recommendations presented in specific areas of the different homes.

The PCECAT findings provided a very good measure of quality of service quality for the aged care organisation, because it is consistent with the Australian Aged Care Standards, adheres to Tom Kitwood's principles for the implementation of a person-centred aged care service, and has been validated against tools used widely in residential aged care systems. Insight was gained into which services supported person-centred principles in the four Montefiore Home residential aged care facilities, and how these were being provided. This information will help Montefiore Home to continuously monitor its services against quality standards.

Output: Project Reports to Montefiore Home Board and executive staff.

Funding: Montefiore Home.

Date commenced: February 2014

Date completed: March 2015

The genetics of hippocampal volume

CHeBA staff: Karen Mather, Wei Wen, Anbu Thalamuthu, Perminder Sachdev

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

Project description: The hippocampus is a key brain structure involved in memory and learning. Hippocampal volume declines with ageing and is associated with age-related neurodegenerative disease. Clarification of the role genetics plays in determining hippocampal volume and atrophy may elucidate the mechanisms underlying hippocampal ageing and atrophy.

Aims:

- To estimate the heritability of hippocampal volume in older adults.
- To identify single nucleotide polymorphisms (SNPs) that influence hippocampal volume and atrophy.

Design & method: Heritability was estimated in the Older Australian Twins Study (OATS). Genome-wide association studies were performed on hippocampal volume and atrophy using the Sydney Memory and Ageing Study (Sydney MAS) and OATS.

Findings: Heritability of hippocampal volume was estimated to be high (62-65%). There were no genome-wide significant results for hippocampal volume or atrophy over 2 years. In candidate gene analyses, two previously identified genetic variants for hippocampal volume were nominally significant (rs6581612, rs6265).

Benefits: Identification of genetic variants associated with hippocampal volume and atrophy may lead to a greater understanding of how genetics (i) influences hippocampal volume in older adults and (ii) contributes to hippocampal atrophy over the lifespan. This work suggested that genetics plays a major role in determining hippocampal volume in older adults.

Output: A manuscript has been published in 2015 in *PLOS ONE* (Mather et al.).

Funding: Sydney MAS is supported by the NHMRC Program Grant 350833. OATS is supported by the NHMRC Project Grant 1045325. Karen Mather was kindly supported by the Thomas Foundation and by the NHMRC Capacity Building Grant 568940.

Date commenced: June 2013

Date completed: January 2015

The prevention and management of mental disorders in older Australians (Capacity Building Grant)

CHeBA staff: Perminder Sachdev, Henry Brodaty, Karen Mather, Nady Braidy, Nicole Kochan, , Wei Wen, Anne Poljak, Adith Mohan, Julia Muenchhoff, Brian Draper (conjoint), Gavin Andrews (conjoint)

Other investigators: Professor Stephen Lord (NeuRA, UNSW), Professor Helen Christensen (Black Dog Institute), Professor Jacqueline Close (NeuRA, UNSW), Prof John Piggott (CEPAR, UNSW), A/Prof Olivier Piguet (NeuRA, UNSW), Professor Felicia Huppert (Cambridge University), Professor Philip Mitchell (School of Psychiatry, UNSW), Professor Peter Schofield (NeuRA, UNSW), Prof Gilles Guillemin (Macquarie University), Professor Maree Teesson (NDARC, UNSW), Professor Michelle Moulds (School of Psychology, UNSW)

Previous team investigators (2009-2015): Dr Melissa Slavin (conjoint), Associate Professor Nick Titov (now Macquarie University), Associate Professor Michael Valenzuela (now University of Sydney), Associate Professor Lee-Fay Low (now University of Sydney), Dr Louise Mewton (now NDARC, UNSW), Dr Matthew Sunderland (now NDARC, UNSW), Dr Jasmine Menant (NeuRA, UNSW), Dr Adrienne Withall (SPHCM, UNSW), Dr Simone Reppermund (now Department of Developmental Disability Neuropsychiatry [3DN], UNSW), Dr Adith Mohan (now Senior Lecturer, School of Psychiatry, UNSW and PhD Candidate), Dr Julia Muenchhoff (CHeBA).

Project description/aims:

3. Understanding health and disease in older people living in the community, and improving their health and well-being through priority health approaches. Six streams had been identified to comprise the research agenda that team investigators (TIs) will address:
    i. Optimising the use of epidemiological mental health data in the elderly;
    ii. Identifying at-risk individuals;
    iii. Establishing risk factors for cognitive ageing;

iv. Positive and successful ageing;
v. Preventing dementia and/or delaying its onset; and
vi. New services for cognitively impaired older Australians.

2. Finding new evidence to inform policy and practice relating to the care of the elderly.
3. Developing the careers of potential future research leaders in this area through mentoring and training.

Design & method: Each TI has 1 primary mentor, 1 secondary mentor and 1 or more additional mentors. TIs undertake two reviews per year to assess performance and support/training needs, as well as attending targeted mentoring and training programs to support research and leadership skills development.

Findings/Output/Benefits: The CBG, through its term, supported 12 researchers with a range of specialities, including genetic epidemiology, proteomics, neuropsychology, classification and assessment of psychiatric disorders in the elderly, online treatment of geriatric anxiety and depression, aged care service delivery, cerebrovascular damage and cognition, successful ageing, protective factors for cognitive decline, falls, gait and dizziness. To date, they have produced over 120 publications, been awarded more than $11 million in competitive grants and supervised 33 higher degree research students. TIs have been widely recognised through promotions, prizes and awards including, in 2015, including a Dean's Rising Star Award to Dr Karen Mather, and the appointment of Dr Adith Mohan as Senior Lecturer in the School of Psychiatry, UNSW Medicine.

Funding: NHMRC.

Date commenced: January 2009

Date completed: December 2015

Transitional care for patients with dementia

CHeBA staff: Lynn Chenoweth

Other investigators: University of Newcastle: Associate Professor Ashley Kable, Professor Dimity Pond, Conjoint Professor Anne Duggan, Dr Carolyn Hullick

Project description: When people with dementia are admitted to hospital, the unfamiliar environment combined with factors such as pain, additional medication and surgery can result in exacerbations of confusion and agitation. Hospital clinicians may encounter challenges in the person's care assessment, management and discharge planning, and find it difficult to access post discharge services for people with dementia. These difficulties can give rise to interruptions in continuity of care in the post discharge period and poor outcomes for the person and their family carer. If the discharge summary provided inadequate information about treatment provided during hositalisation, pending test results and medication changes, then the person's GP is poorly positioned to maintain continuity of care after discharge from hospital and tests may be duplicated, medications changed and referrals delayed. People with dementia have problems remembering when appointments are due, when to take medications and how to follow instructions provided to them. This study investigated this process in order to provide recommendations on how to address deficits in hospital discharge and transtions from hospital for people with dementia.

Aim: To evaluate transitional care for people with dementia against expected discharge criteria.

Design & method: A cross sectional study was conducted over 18 months in one acute hospital in a regional area of New South Wales, to evaluate discharge documentation of people with dementia who were discharged home, interviews were held with the family carers of people with dementia post-discharge, and focus groups were held with hospital and community staff, including GPS, involved in the person with dementia's discharge.

Findings/Benefits: The study findings have informed recommendations on how to address deficits in hospital discharge and transtions from hospital for people with dementia, including what is required in discharge summary reporting to the patient's GP, community service providers and residentila aged care providers. The results indicate that some aspects of the discharge process were not done consistently for all patients, and some patients were potentially more vulnerable due to inadequate information being provided to their GP for ongoing management. The provision of medications, medication dose decision aids, home medicines review and risk assessment for people with dementia, were aspects of this process that present opportunities for improvement. The lack of contact information for patient support groups and advanced care planning is a clinically significant concern for people with dementia.

Output: 1 review published (*Australasian Journal on Ageing*), 1 journal publication (*BMC Health Services Research*), 1 manuscript submitted, 2 conference presentations, 1 symposium presentation.

Funding: Montefiore Home funding (administered by CHeBA) supports Professor L. Chenoweth's research position with CHeBA, Dementia Collaborative Research Centre (administered by University of Newcastle), Department of Health and Ageing (administered by University of Newcastle).

Date commenced: June, 2013

Date completed: August 2015

Understanding the genetics of white matter microstructure of the corpus callosum

CHeBA staff: Sri Chandana Kanchibhotla (Masters student), Karen Mather, Anbupalam Thalamuthu, Wei Wen, Perminder Sachdev

Other investigators: Professor David Ames (National Ageing Research Institute; Royal Melbourne Hospital), Dr Nicola Armstrong (Murdoch University), Dr Margaret J. Wright (QIMR Berghofer Institute, Brisbane, Australia), Dr Lin Zhuang (formerly CHeBA)

Project description: Age-related changes in the corpus callosum are associated with age-related cognitive and physical impairments and neurodegenerative disease. The integrity of the microstructure of the corpus callosum can be assessed using diffusion tensor imaging (DTI). This Masters project investigated the genetics of the microstructure integrity of the corpus callosum. It utilised data from the Older Australian Twins Study and the Sydney Memory and Ageing Study.

Aims: To estimate the heritability and to identify genetic variants for white matter integrity measures of the corpus callosum.

Design & method: White matter integrity measures for the corpus callosum (DTI) were estimated from neuroimaging scans. Heritability was estimated using the twin sample and structural equation modelling. A genome-wide association study (GWAS) has been undertaken using both the OATS sample and the Sydney Memory and Ageing Study.

Findings: Most DTI measures of the integrity of the corpus callosum microstructure were heritable in this sample of older adults. No genetic variants were associated with DTI corpus callosum measures, either using genome-wide or candidate gene analyses. This work suggests larger samples are required to find genetic variants associated with the microstructure integrity of the corpus callosum in older adults.

Benefits: Potential benefits from this work include a better understanding of the contributions of genetics to the integrity of the corpus callosum, an important brain structure, which facilitates communication between the two hemispheres.

Output: The heritability of the corpus callosum study has been published in the journal, *PLOS ONE* (Kanchibhotla et al., 2014). GWAS were undertaken and the results were included in Ms Kanchibhotla Master's thesis, which was successfully completed in 2015.

Funding: OATS is supported by the NHMRC Project Grant 1045325. Sri Chandana Kanchibhotla was supported by a scholarship from the Dementia Collaborative Research Centre– Assessment and Better Care, UNSW. Karen Mather was kindly supported by the Thomas Foundation and the NHMRC Capacity Building Grant 568940.

Date commenced: 2011

Date completed: September 2015

Voxel-based resting-state functional connectivity

CHeBA staff: Anbupalam Thalamuthu, Perminder Sachdev, Wei Wen

Other investigators: Professor Yong He (Beijing Normal University, China), Dr Haobo Zhang (formerly CHeBA)

Project description: The resting-state functional network reflects the intrinsic architecture of the brain network. Evidence has shown that individual variations in resting-state functional connectivity strength (rs-FCS) are related to their differences in cognitive performance, and the relationship between rs-FCS and cognition also exists in older adults. While previous studies extracted rs-FCS from coarsely pre-defined regions, this study uses voxel-based rs-FCS to correlate with neuropsychological tests in community-dwelling, cognitively healthy older adults.

Aims:

- To investigate resting-state functional connectivity using whole-brain voxel-based resting-state connectivity measures.
- To investigate the heritability of whole-brain connectivity.

Design & method: We used voxel-based rs-FCS to correlate three neuropsychological tests (episodic memory, language and executive) in 71 community-dwelling, cognitively healthy older adults aged 73-90 years.

Findings/Benefits: Two implications might be drawn from our findings. Firstly, the intrinsic functional architecture possibly reflects a functional repertoire of neural response. The co-activation of spontaneous neuronal activities at rest may represent a preparatory state of the brain for quick responses to cognitive tasks, which explains the predictive ability of rs-FCS in task-activated areas to relevant task performance. Secondly, competition might exist between distinct neural systems in the brain intrinsic network architecture. The opposite FCS-cognition relationships between task-activated and task-deactivated areas might stem from the inherent anti-phase relationship between them, which is also evident in neural activation patterns during task and rest. A pervasive competition appears to be embedded in the anti-correlated neural systems, to maximise their allocation of brain resources. The balance derived from such competition might endow an individual with a better ability in certain cognitive functions, whilst providing a disadvantage for other cognitive functions.

Output: OHBM2015 poster, a manuscript is in preparation.

Funding: NHMRC, ARC.

Date commenced: July 2013

Date completed: December 2015

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

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

Karen Mather
Research Fellow, *Leader Genetics & Genomics Group*

Adith Mohan
Research Fellow

Julia Muenchhoff
Research Fellow

Anbupalam Thalamuthu
Research Fellow

Wei Wen
Associate Professor, *Leader Neuroimaging Group, Director Neuroimaging Laboratory*

Professional & Technical Staff – Research

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

John Crawford
Research Officer (Statistician)

Catriona Daly
Research Assistant, *ICC-Dementia Consortium Coordinator*

Tanya Duckworth
Research Assistant

Ying (Niki) He
Technical Officer

Jiyang Jiang
Student Assistant (Casual)

Kristan Kang
Data Manager

Sri Chandana Kanchibotla
Research Assistant (Casual)

Darren Lipnicki
Research Officer, *COSMIC Consortium Coordinator*

Kate Maston
Research Assistant

Adam Theobald
Research Assistant

Oscar Wen
Student Assistant (Casual)

Professional & Technical Staff – Support

Kate Crosbie
Administrative Assistant (Casual)

Sophia Dean
Administrative Officer

Craig Douglass
Administrative Assistant (Casual)

Suzanne Forrester
Administrative Assistant

Heidi Mitchell
Marketing & Communications Officer

Michael Young
Administrative Assistant (Casual) (*until 27 August 2015*)

Conjoint Staff

Gavin Andrews
Professor of Psychiatry, Chief Investigator, *NHMRC Program Grant ID 568969*

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

Nicola Gates
Lecturer

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

Teresa Lee
Senior Lecturer, *Co-Leader Neuropsychology Group*

Charlene Levitan
Adjunct Associate Lecturer

Ora Lux
Senior Lecturer

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

Melissa Slavin
Senior Lecturer

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)*

Lee-Fay Low
Senior Visiting Fellow (*May 2014-May 2017)*

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)*

CHeBA Honorary Research Fellows

Dr Nicola Armstrong

Dr Tao Liu

Dr Simone Reppermund

Dr Fei Song

Dr Haobo Zhang

Dr Wanlin Zhu

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, *Analytical Cellular Pathology*

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)
- Chair, Dementia Committee, NHMRC Knowledge Translation Faculty (2013-present)
- International Advisor, Institute of Alzheimer's Education Advisory Board, Hong Kong (2013-2015)
- Member, International Advisory Committee of the National Institute of Dementia, South Korea (2013-2015)
- Honorary Professor, Kiang Wu Nursing College, Macau (2014-present)
- Member, Reference Committee, NSW Policy of Mental Health for Older People and Dementia Care, NSW Department of Health (1993-present)
- Executive Member, Australasian Consortium of Centres for Clinical Cognitive Research (AC4R) (2000-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-present)
- 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 Journal of Psychiatry in Medicine* (1996-present), *International Psychogeriatrics* (1996-present), *Neurodegenerative Disease Management* (2010-present), *The Australian Journal of Dementia Care* (2012-present)

Professor Lynn Chenoweth

- Professor of Aged & Extended Care Nursing, Faculty of Nursing, Midwifery & Health, University of Technology, Sydney (retired 31 December 2015)
- Lead, NSW Core Committee, Dementia Collaborative Research Centre
- Lead, NSW Expert Advisory Group, Dementia Collaborative Research Centre – Assessment and Better Care, UNSW
- Lead, NSW Steering Committee, Dementia Collaborative Research Centre – Assessment and Better Care, UNSW

- Member, Research Advisory Group, Parkinson's Australia
- 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
- Member, Nursing Curriculum Advisory Committee, Notre Dame University
- 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
- Approved Supervisor, College of Clinical Neuropsychologists, Australian Psychological Society

Dr Teresa Lee

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

Dr Karen Mather

- Visiting Research Fellow, Neuroscience Research Australia (NeuRA)

Dr Adith Mohan

- Consultant Neuropsychiatrist, Neuropsychiatric Institute, Prince of Wales Hospital

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 Member, Rebecca L. Cooper Medical Research Foundation

Professor Perminder Sachdev

- 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)
- 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*, *Brain and Mind Matters*, *The Open Neuroimaging Journal*, *American Journal of Geriatric Psychiatry, Journal of Alzheimer's Disease*

Hon. Associate Professor Kuldip Sidhu

- 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)
- Member, International Stem Cell Initiative, UK (2010 -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*.

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
- 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, 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, Scientific Committee for Congress 2017
- Member, International Neuropsychiatric Association

Appendix C: Postgraduate Students

CURRENT

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: Dr 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
- Supervisor: 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

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

Jiang Jiyang

- 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

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
- Masters by Research 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 Anbu 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

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

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

COMPLETED

Sri Chandana Kanchibhotla

- Investigating the genetics of the microstructure of the corpus callosum in the ageing brain
- Masters by Research student
- School of Psychiatry, Faculty of Medicine, UNSW
- Supervisors: Professor Perminder Sachdev, Dr Karen Mather, Professor Peter Schofield
- Masters conferred September 2015

Aileen Lowe

- Advanced characterisation of skin derived neuroprecursors
- PhD student
- School of Psychiatry, Faculty of Medicine, UNSW
- Supervisors: Associate Professor Michael Valenzuela, Hon. Associate Professor Kuldip Sidhu
- PhD conferred 2015

Amanda Olley

- A decision making model of Obsessive Compulsive Disorder (OCD): A neuropsychological and functional neuroimaging investigation
- PhD student
- School of Psychiatry, Faculty of Medicine, UNSW
- Supervisors: Professor Perminder Sachdev, Professor Gin Malhi
- PhD conferred May 2015

Katrin Seeher

- The psychosocial effects of becoming a carer: Predicting psychological distress and caregiver burden in family members and friends of older people with normal cognitive function, mild cognitive impairment and dementia over time
- PhD student
- School of Psychiatry, Faculty of Medicine, UNSW
- Supervisors: Professor Henry Brodaty, Associate Professor Lee-Fay Low, Dr Simone Reppermund
- PhD conferred June 2015

Appendix D: Awards

Dr Nady Braidy

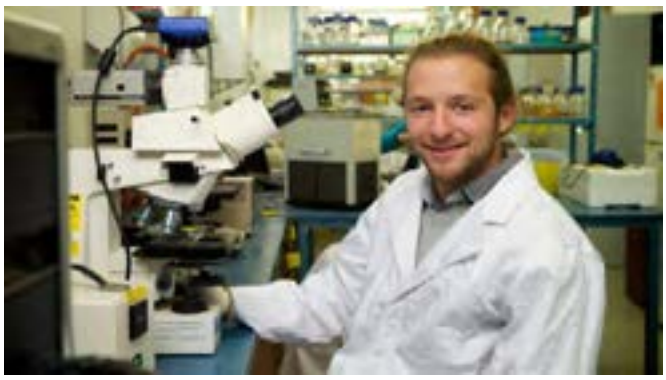
- Chilean Conecyt Postdoctoral Prize (2015-2017) to examine whether the South American rodent *Octodon degus* is a unique natural model for the study of the pathobiology of Alzheimer's disease.

Dr Karen Mather

- Dean's Rising Star Award, UNSW Medicine for significant contributions to research.

Dr Adith Mohan

- Promoted to Senior Lecturer



Dr Nady Braidy

Dr Karen Mather

Dr Adith Mohan

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

*Project began incurred expenses in November 2015

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 Permnder 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

*Extension granted to 30 November 2016

UNSW Medicine Faculty Research Support

Funding Source: UNSW Australia
Project ID: PS37942
Investigator/s: Prof Perminder Sachdev
Duration: 1 year: 2015
Total Funds: $200,000

Identifying the genetic determinants of white matter hyperintensities

Funding Source: UNSW Australia – Goldstar Award
Project ID: RG142755
Investigator/s: Dr Karen Mather, A/Prof Wei Wen, Dr Anbupalam Thalamuthu, Prof Paul Thompson, Prof Stéphanie Debette
Duration: 1 year: 2015
Total Funds: $40,000

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

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

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

Agilent 1290UHPLC Equipment Grant (Part 1)

Funding Source: NHMRC
Project ID: RG134156-B
Investigator/s: Prof Perminder Sachdev, Dr Anne Poljak, Dr Naidy Braidy, Dr Julia Muenchhoff, et al.
Duration: 1 year: 2014*
Total Funds: $109,711

*Project acquitted and closed January 2015

Agilent 1290UHPLC Equipment Grant (Part 2)

Funding Source: UNSW MREII Funds
Project ID: RG134854
Investigator/s: Prof Perminder Sachdev, Dr Anne Poljak, Dr Naidy Braidy, Dr Julia Muenchhoff, et al.
Duration: 1 year: 2014*
Total Funds: $18,039

*Project acquitted and closed January 2015

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
Amount per year: $37,445.50

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
Amount per year: $74,891

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

Funding Source: NHMRC Project Grant
Project ID: RG122225
Investigator/s: Prof Perminder Sachdev, Dr Margie Wright, Prof David Ames, A/Prof Julian Trollor, A/Prof Wei Wen, Prof Bernhard Baunes, Dr Teresa Lee, Dr John Crawford
Duration: 3 years: 2013-2015
Total Funds: $912,022

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

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

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

Brains in the oldest old (PhD Scholarship)

Funding Source: NHMRC / DCRC-ABC
Project ID: RG102939-P
Investigator/s: Prof Perminder Sachdev, Ms Zixuan Yang
Duration: 1.5 years: 2013-2014
Total Funds: $15,000

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

Living with dementia in retirement villages: investigating the experiences of retirement village residents with dementia

Funding Source: Alzheimer's Australia NSW/IRT Research Foundation Research Grant
Project ID: RG141330
Investigator/s: Prof Lynn Chenoweth
Duration: 1 year: 2013-2014*
Total Funds: $28,009

*Project closed and acquitted 25 November 2015

Genetic and epigenetic variation and early markers of late-onset Alzheimer's disease

Funding Source: Alzheimer's Australia Research / Postdoctoral Fellowship in Dementia
Project ID: RG123330
Investigator/s: Dr Karen A Mather
Duration 2 years: 2013-2014*
Total Funds: $100,000

*Project closed and acquitted 2 March 2015

Plasma protein profiles in normal brain ageing and early stages of dementia

Funding Source: Australian Research Council (ARC) Discovery Project
Project ID: RM10093
Investigator/s: Prof Perminder Sachdev, Dr Anne Poljak, Prof Mark Duncan, Prof John Attia, Prof Peter W Schofield, Dr John Crawford
Duration: 3 years: 2012-2014*
Total Funds: $330,000

*Project closed and acquitted March 2015

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

Funding Source: NHMRC Program Grant
Project ID: RM06756
Investigator/s: Prof Perminder Sachdev, Prof Henry Brodaty, Prof Gavin Andrews
Duration: 5 years: 2010-2014*
Total Funds: $6,090,000

*Project acquitted and closed March 2016

Prevention and management of mental disorders in older Australians

Funding Source: NHMRC Capacity Building Grant
Project ID: RM06714
Investigators: Prof Perminder Sachdev, Prof Henry Brodaty, Prof Gavin Andrews, Prof Stephen Lord
Duration: 5 years: 2009-2013*
Total Funds: $2,352,525
Amount per year: $407,505

*Project acquitted and closed December 2015

Philanthropic

The Dementia Momentum Initiative, (excluding Wipeout Dementia and direct donations)

Funding Source: Roth Charitable Foundation
Project ID: PS38252
Awardees: Prof Perminder Sachdev
Prof Henry Brodaty
Duration: 6 years: 2015-2020
Total Funds: $90,000
Funding Source: Sachdev Foundation
Project ID: PS38252
Awardees: Prof Perminder Sachdev
Prof Henry Brodaty
Duration: 1 year: 2015
Total Funds: $40,000
Funding Source: Vincent Fairfax Family Foundation
Project ID: PS38252
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 Healthy Brain Ageing at UNSW

Funding Source: The Sir Moses Montefiore Jewish Home
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
Awardees: Prof Perminder Sachdev
Prof Henry Brodaty
Duration: 3 years: 2015-2017
Total Funds: $335,000

The Thomas Foundation Grant

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

Appendix F: Statement of In-Kind Contributions

- The AMP Foundation
- ARIA Restaurant Sydney
- Breathe Fire Specialised Training
- Hurley
- HWL Ebsworth Lawyers
- KPMG
- Murray Fraser, Sprout Daily
- Queenscliff Surf Life Saving Club
- Rockdale City Council
- Surfing NSW

Appendix G: Statement of Financial Performance

Centre for Healthy Brain Ageing (CHEBA)

Statement of Financial Performance for the Year Ended 31 December 2015

		Notes	2015 $	2014 $
Funds				
	Research Revenue		737,838	1,876,397
	Donations		583,873	365,895
	Fees		-	-
	Faculty Funds	3	-	10,000
	UNSW Contribution - Competitive	1	229,387	52,886
	UNSW Contribution - Strategic	2	240,000	-
	Sundry Other Revenue		20,260	1,709
Total Funds		**1,811,358**	**2,306,887**	
Costs				
	People Costs		1,672,752	1,872,655
	Scholarship Stipends		71,049	50,151
	Contract & Consulting Services		106,567	222,061
	Repairs and Maintenance		120	4,086
	Consumables		52,758	35,928
	Travel		53,775	63,443
	Equipment		25,063	125,039
	Other Expenses		36,423	24,308
	Internal Expense		(61,178)	52,248
Total Costs		**1,957,329**	**2,449,919**	
Operating result		**(145,971)**	**(143,032)**	
Opening Balance		**606,309**	**749,341**	
Closing Balance		**460,338**	**606,309**	

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

Journal articles

Agar M, Beattie E, Luckett T, Phillips J, Luscombe G, Goodall D, Mitchell G, Pond D, Davidson P, Chenoweth L. Pragmatic cluster randomised controlled trial of facilitated family case conferencing compared with usual care for improving end of life care and outcomes in nursing home residents with advanced dementia and their families: the IDEAL study protocol. *BMC Palliat Care*. 2015 Nov 21; 14:63. DOI: 10.1186/s12904-015-0061-8. PMID: 26589957 / PMCID: PMC4654825

Anstey KJ, Sargent-Cox K, Cherbuin N, Sachdev PS. Self-reported history of chemotherapy and cognitive decline in adults aged 60 and older: the PATH Through Life Project. *J Gerontol A Biol Sci Med Sci*. 2015; 70(6): 729-35. PMID: 24368774. DOI: 10.1093/gerona/glt195. [Epub 2013 Dec 24].

Arcot J, Kim J, Trollor J, Brodaty H, Crawford J, Sachdev P. Anthropometric indices in a community-dwelling Australian population aged 70-90 years: The Sydney Memory and Ageing Study. *Nutrition & Dietetics*. 2015; 72(1):8-15. DOI: 10.1111/1747-0080.12140. [Epub 11 Sep 2014].

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Baldwin R, Chenoweth L, de la Rama M, Liu X. Quality failures in residential aged care in Australia: relationship between structural factors and regulation imposed sanctions. *Australas J Ageing*. 2015 Dec; 34(4):E7-E12. DOI: 10.1111/ajag.12165. PMID: 24854338 [Epub 2014 May 22].

Beattie E, O'Reilly M, Moyle W, Chenoweth L, Fetherstonhaugh D, Horner B, Robinson A, Fielding E. Multiple perspectives on quality of life for residents with dementia in long term care facilities: Protocol for a comprehensive Australian study. *Int Psychogeriatr*. 2015 Oct; 27(10):1-9. DOI: 10.1017/S1041610215000435. PMID: 25899853 [Epub 2015 Apr 22].

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Brodaty H. The practice and ethics of dementia care. *Int Psychogeriatr*. 2015; 27(10):1579-81.

Chan JP, Thalamuthu A, Oldmeadow C, Armstrong NJ, Holliday EG, McEvoy M, Kwok JB, Assareh AA, Peel R, Hancock SJ, Reppermund S, Menant J, Trollor JN, Brodaty H, Schofield PR, Attia JR, Sachdev PS, Scott RJ, Mather KA. Genetics of hand grip strength in mid to late life. *Age (Dordr)*. 2015 Feb; 37(1):9745. DOI: 10.1007/s11357-015-9745-5. PMID: 25637336 [Epub 2015 Feb 1].

Chenoweth L, Jeon Y-H, Forbes I, Stein-Parbury J, Fleming R, Cook J, Cheah S, Fletcher S, Tinslay L. PerCEN trial participant perspectives on the implementation and outcomes of person-centered dementia care and environments. *Int Psychogeriatr*. 2015; 27(12): 2045-57. DOI: 10.1017/S1041610215001350. PMID: 26307245 [Epub 2015 Aug 26].

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Appendix I: Conference Presentations

Brouwer RM, Glahn DC, Hibar DP, Hua X, Jahanshad N, Abramovic L, …, Sachdev PS, et al. Genetic influences on longitudinal changes in subcortical volumes: results of the ENIGMA Plasticity Working Group. *21st Annual Meeting of the Organization for Human Brain Mapping (OHBM)*. 14-18 June 2015; Honolulu, USA. [Poster abstract 4095].

Brouwer RM, Glahn DC, Hibar DP, Hua X, Jahanshad N, Franz CE, Koenis MMG, Mather K, Swagerman S, Thalamuthu A, Wen W, Boomsma DI, Gilmore JH, Gogtay N, Kahn RS, Kremen WS, Sachdev PS, Wright MJ, Thompson PM, Pol HEH. Genetic influences on longitudinal changes in subcortical volumes: results of the ENIGMA Plasticity Working Group. *70th Annual Scientific Convention and Meeting of the Society of Biological Psychiatry*. 14-16 May 2015; Toronto, Canada. *Biol Psychiatry*. 2015; 77(9):84S. DOI: 10.1016/j.biopsych.2015.03.006 [Abstract 223].

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Chenoweth L, Fielding E, O'Reilly M, Beattie E. Staff attitudes toward care of people with dementia in Australian residential aged care facilities. *30th International Conference Alzheimer's Disease International*. 15-18 April 2015; Perth, Australia [Abstract OC090].

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Cherbuin N, Shaw M, Sachdev P, Anstey K. Higher bodyweight is associated with lower cortical thickness in the early 60s. *21st Annual Meeting of the Organization for Human Brain Mapping (OHBM)*. 14-18 June 2015; Honolulu, USA. [Poster abstract 3556].

Cherbuin N, Shaw M, Salat DH, Sachdev PS, Anstey KJ. Integrity of the grey/white matter border is associated with cognitive performance in ageing: The PATH Through Life Project. *XII International Conference on Cognitive Neuroscience (ICON-XII)*. 7-31 July 2014; Brisbane, Australia. *Frontiers* 2015. DOI: 10.3389/conf.fnhum.2015.217.00110. [Abstract MCE013].

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Jahanshad N, Kochunov P, Armstrong N, Bastin M, Bearden C, Brouwer R, …, Sachdev PS, et al. Meta-analyzing genome-wide associations with white matter microstructure - the ENIGMA-DTI group. *21st Annual Meeting of the Organization for Human Brain Mapping (OHBM)*. 14-18 June 2015; Honolulu, USA. [Poster abstract 3407].

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Kable A, Pond D, Chenoweth L. Health Professional Perspectives on the Discharge Process and Transitional Care for Patients with Dementia and their Carers – a qualitative study. *30th International Conference Alzheimer's Disease International*. 15-19 April 2015; Perth, Australia [Abstract OC120].

Kochan N, Pont S, Brodaty H, Woolf C, Crawford J, Sachdev P. A brief computerised cognitive test battery for detecting mild neurocognitive disorders and early dementia. *2015 DCRC 9th Annual Forum*. Sep 2015; Sydney, Australia. *Australian Journal of Dementia Care*. 2015; 4(4):33-4 [Abstract A23].

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Ireland D, Liddle J, Harrison F, Sachdev P, Brodaty H. Low-Energy Bluetooth Beacons for Lifespace Assessment of People with Neurological Conditions [Paper #1570196221]. *International Symposium on Antennas and Propagation (ISAP2015)*. 9-12 Nov 2015; Hobart, Australia. *IEEE* 2015; in press.

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Kochan NA, Pont S, Brodaty H, Woolf C, Crawford J, Sachdev PS. A brief computerized test battery for detecting mild neurocognitive disorders and early dementia. Dementia Collaborative Research Centre, Dementia Research Forum 2015, Sydney.

Lupton MK, Strike L, Wen W, Mather KA, Armstrong NJ, Thalamuthu A, McMahon KL, de Zubicaray GI, Assareh AA, Simmons A, Proitsi P, Powell JF, Montgomery GW, Hibar DP, Westman E, Tsolaki M, Kloszewska I, Soininen H, Mecocci P, Velas B, Lovestone S, Brodaty H, Ames D, Trollor JN, Martin NG, Thompson PM, Sachdev PS,Wright MJ, Alzheimer's Disease Neuroimaging

Initiative. The use of genetic risk factors to assess prodromal brain changes in Alzheimer's disease. *American Society Human Genetics Annual Meeting*; 6-10 October 2015; Baltimore, USA [Poster abstract PgmNr 1229].

Mather KA, Thalamuthu A, Chen BJ, Janitz M, Armstrong NJ, Sachdev PS, Sydney Centenarian Study and the Sydney Memory and Ageing Study Teams. Longevity and the transcriptome: Identifying gene expression changes in long-lived individuals. *American Society Human Genetics Annual Meeting*; 6-10 October 2015; Baltimore, USA [Poster abstract PgmNr 3082].

Thalamuthu A. Multivariate statistical methods based on genetic similarity for gene mapping. *International Conference on New Horizons in Statistical Modeling and Applications 2015*. Chennai, India.

Appendix J: Workshops & Invited Lectures

Agar MA, Luckett T, Phillips J, Chenoweth L, Cook J, Brooks D, Mitchell G, Beattie E, Pond D, Luscombe G, Goodall S, Davidson PM. Implementing facilitated case conferencing for aged care residents with advanced dementia – development of a Palliative Care Planning Coordinator role. *Australian Palliative Care Conference*. Sep 2015; Sydney, Australia.

Brodaty H [Keynote Speaker]. What's new in dementia? *OT Practise in Dementia Forum*. 1 May 2015; Ultimo, Sydney, Australia.

Brodaty H. What's New in the Prevention and Treatment of Alzheimer's? 4 May 2015; War Memorial Hospital, Sydney.

Brodaty H. Better Brain Better life. *Neuropsychiatry Training Weekend 2015: Neuropsychiatry Narratives*. 17-18 April 2015; Sydney, Australia.

Brodaty H. Preventing AD. 25 Aug 2015; Watsons Bay PROBUS Club.

Brodaty H. Depression, dementia, pseudodementia, pseudo-pseudodementia and pseudodepression. *CHeBA-RANCP Forums – Prevention of Depression & Depression in Late Life*. 17-18 Sept 2015; Sydney, Australia.

Brodaty H [Keynote speaker]. Psychosocial research consortium to advance mental health of older people in the Asia Pacific Region. *Asia-Pacific Research Symposium 2015*. 29 Sep 2015; Sydney, Australia.

Brodaty H. Trials conducting dementia trials. *NICM Symposium*. 1 Dec 2015; Sydney, Australia.

Brodaty H. Don't worry, have fun. Humour and Happiness for Healthy Ageing Forum. 18 Nov 2015; Sydney, Australia.

Brodaty H [Panel Member]. In Conversation with the DCRC Directors: "Thinking about answers to the Big Questions". *National Dementia Research and Knowledge Translation Forum*. 7-8 Sep 2015; The Wesley Conference Centre, Sydney.

Brodaty H. Better Brain Better Life. *Better Brain Better Life Public Forum*. 19 Aug 2015; Mounties Community Club, Sydney.

Brodaty H. Researching Positive Ageing. *Better Brain Better Life Public Forum*. 4 Mar 2015; Rockdale, Sydney.

Chenoweth L. Effective strategies in implementing person-centred residential care. *Annual Better Practice Conference*. 29 May 2015; Melbourne, Australia.

Chenoweth L. Person-centred palliative care of the person with dementia. *Alzheimer's Disease Association Taiwan Annual Research Conference*. 11-15 October 2015; Taipei, Taiwan.

Chenoweth L. Overcoming barriers to person-centred care in dementia services. *Alzheimer's Disease Association Taiwan Annual Research Conference*. 11-15 October 2015; Taipei, Taiwan.

Chenoweth L. Person-centred dementia care audit for residential care and day care. International Dementia Conference in Taiwan-Developing Best Practice in Continuum of Dementia Care. 10 Oct 2015; Taipei, Taiwan.

Chenoweth L. Competencies for aged care nursing. *NSW Nurses and Midwifery Board Annual Better Practice Conference*. 16 Oct 2015; Sydney, Australia. Podcast access: http://www.nswnma.asn.au/education/podcasts/

Chenoweth L, Fielding E, O'Reilly M, Beattie E. Staff attitudes toward care of people with dementia in Australian residential aged care facilities. *30th International Conference Alzheimer's Disease International*. 15-18 April 2015; Perth, Australia [Abstract OC090].

Chenoweth L, Sankaran S, Baghbanian A. Instituting team cognition as a culture change process for effecting residential aged care staff well-being and reciprocity. *18th Cognition in the Rough Conference*. Academy of Management. 15-18 Aug 2015; Vancouver, Canada,

Draper B, Withall A, White F, Cations M, Brodaty H, Demirkol A, Sachdev P, Trollor J, Gonski P, Loy C. Time to diagnosis for young-onset dementia – what factors contribute to delay? Findings from INSPIRED study. *30th International Conference Alzheimer's Disease International*. 15-18 April 2015; Perth, Australia [Abstract P152].

Fry M, Arendt G, Chenoweth L. Nurse initiated analgesia could reduce cognitive impairment as a risk factor for delayed analgesia in older people: a multicentre study. *3rd Annual Worldwide Nursing Conference*. 29-30 June 2015; Singapore.

Fry M, Chenoweth L, Arendt G. Emergency nurses perceptions of the role of family/carers in pain management practices for cognitively impaired older persons: A qualitative study. *3rd Annual Worldwide Nursing Conference*. 29-30 June 2015; Singapore.

Fry M, Arendt G, Chenoweth L, MacGregor C. Do observational pain assessment tools improve the timeliness of analgesia for cognitively impaired older persons. *ASEM International Conference*. 9-10 Dec 2015; Victoria.

Fry M, Chenoweth L, Arendt G. Assessing and managing pain in the older person: a qualitative study. *Australian Nursing and Midwifery Conference*. 15-16 Oct 2015; Newcastle, Australia.

Jeon Y-H, Brodaty H, Low L-F, …, Chenoweth L. et al. Development and validation of the four item Cornell Scale for Depression in Dementia (CSDD-4) for screening depression in nursing homes. *International Psychogeriatric Association Conference (IPA)*. 13-16 Oct 2015; Berlin, Germany.

Kable A, Chenoweth L, Pond D. Health professional perspectives on the discharge process and transitional care for patients with dementia and their carers – a qualitative study. *SAHRT (Sydney Alliance for Healthcare, Research and Training) Symposium. Toward Best Practice in Integrated Care: Celebrating Cuccesses, Confronting Challenges*. 20 Nov 2015; Sydney, Australia.

Kable A, Pond D, Chenoweth L. Health Professional Perspectives on the Discharge Process and Transitional Care for Patients with Dementia and their Carers – a qualitative study. *30th International Conference Alzheimer's Disease International*. 15-19 April 2015; Perth, Australia [Abstract OC120].

Kable A, Pond D, Hullick C, Duggan A, Chenoweth L. Evaluating transitional care for people with dementia discharged home from hospital. *HRAANZ Conference*. 10 Dec 2015; Sydney, Australia.

Kochan NA. [Invited speaker]. Cognitive impairment in late-life depression. *Neuropsychiatry Narratives, Training Weekend* presented by Neuropsychiatric Institute, POWH and CHeBA, UNSW. April 2015; Sydney, Australia.

Kochan NA. Maximising your Memory. *Better Brain Better Life Public Forum*. 19 August 2015; Mounties Community Club, Sydney.

Kochan NA Can an old dog learn new tricks? Neuroplasticity and improving your memory in older adulthood. Montefiore Life Newsletter, March 2015.

Kochan N [Chair]. Causes, Correlates, and Risks. *National Dementia Research and Knowledge Translation Forum*. 7-8 Sep 2015; The Wesley Conference Centre, Sydney.

Lapkin S, Levett-Jones T, Chenoweth L, Johnson M. The effectiveness of interventions designed to reduce nurse medication administration errors. Synthesis of findings from nine systematic reviews. *Quality and Safety Summit – Leveraging Nursing Leadership*. 23-24 November 2015; Toronto, Canada.

Mather KA. Longevity and the Transcriptome: Identifying gene expression changes in long-lived individuals. Poster at the *American Society Human Genetics Annual Meeting*. 6-10 October 2015; Baltimore, USA.

Mohan A. Stimulating the brain. *Better Brain Better Life Public Forum*. 4 Mar 2015; Rockdale, Sydney.

Sachdev P. [Invited speaker]. *56th Annual meeting of the Japanese Society of Neurology*. 20-23 May 2015; Nigata, Japan.

Sachdev P. ICC-Dementia. June 2015; Sardina, Italy.

Sachdev P. [Invited Speaker]. *57th Annual Meeting of the Japanese Geriatric Society*. 12-14 June 2015; Japan.

Sachdev P. AAIC. Washington, USA; 18-23 July 2015. [not presenting, just attending].

Sachdev P. A new approach to diagnosing vascular cognitive disorders: the VASCOG criteria. *VasCOG*. Sept 2015; Japan.

Sachdev P. [Invited Speaker]. *International Conference of Neuroepidemiology*. 18-20 Nov 2015; Gold Coast, Australia.

Sachdev P. [Invited Speaker]. *Mental Health Forum organised by AASHA [an initiative of the Australian Hindi Indian Association (AHIA)]*. 10 Oct 2015; Sydney, Australia.

Sachdev P. [Invited Panel Member]. Q & A on the topic "Let's talk dementia". *Wolper Wellbeing Program*. 2 Sep 2015; Bondi Junction, Sydney.

Sachdev P. Understanding the interaction between vascular and Alzhiemer pathologies. *NICM Symposium*. 1 Dec 2015; Sydney, Australia.

Sachdev P. [Invited Panel Member]. Dementia Q&A seminar, sponsored by Group Homes Australia. 22 Oct 2015; Warringah Mall, Sydney.

Sachdev P. The Heart & The Brain. *Better Brain Better Life Public Forum*. 19 August 2015; Mounties Community Club, Sydney.

Thalamuthu A. Multivariate Statistical Methods Based on Genetic Similarity for Gene Mapping. *International Conference on New Horizons in Statistical Modeling and Applications*. 2015; Chennai, India.

Thalamuthu A. Conducted two-day workshop on R and SAS. 2-3 Mar 2015; SDNB Vaishnav College for Women, Chennai, India.

Wong L, Stein-Parbury J, Chenoweth L. Community Carer Support Program for Chinese Dementia Carers in Northern Sydney Local Health District, New South Wales, Australia. *3rd International Conference on Alzheimer's Disease and Dementia*. 31 Aug – 2 Sept 2015; Toronto, Canada.