UNSW AUSTRALIA

Annual Report
Centre for Healthy Brain Ageing (CHeBA)

Never Stand Still | Medicine | School of Psychiatry

OCT 2012 – DEC 2013

CONTENTS

CHAIRMAN'S REPORT

ROGER CORBETT AO

I am pleased to present the annual report of the Centre for Healthy Brain Ageing (CHeBA) in my inaugural year as Chairman of the Advisory Committee.

I would like to begin by congratulating the Co-Directors of CHeBA, Professors Henry Brodaty and Perminder Sachdev, for their significant contributions to dementia research and their relentless drive for people to achieve a full life span unaffected by loss of cognitive ability. I would also like to express my gratitude to the Deputy Chair, Dagmar Schmidmaier AM, and my remaining fellow Committee members, Richard Matthews AM, Roger Layton AM, Richard Grellman, Dr Sudarshan Sachdev, John Gray and John Thomas (who are outlined on the following pages), for their involvement in the Centre's development since its inception in October 2012. I would also like to acknowledge John Porter who was originally a Committee member but had to stand down to take an overseas position.

Early in 2013, I was privileged to act as MC at a fundraising event generously hosted by ARIA Restaurant, which connected significant members of the corporate community to CHeBA. I extend my thanks to Richard Grellman for his involvement as speaker at this lunch, and express my sincere thanks to the corporate attendees who became key players in the expansion of CHeBA's campaigns.

Alzheimer's disease will be one of the big burdens on our country's health and aged care systems. With an ever-increasing ageing population, the numbers of people who will need a significant amount of care at the end of their life is growing. This will have a substantial impact on the public purse. Anything that can be done to prolong healthy ageing, particularly brain health, is going to be invaluable.

One of the strengths of CHeBA is its multi-disciplinary research approach, addressing ageing-related brain diseases through the latest work in epidemiology, clinical research, neuroimaging, genetics, proteomics, metabolomics and other innovative approaches. The complexities of managing a multi-disciplinary research centre have been showcased to the Committee, and as the intricacy of brain research increases, we collectively agree that CHeBA is well placed for the challenge. Another positive feature of CHeBA is that the Co-Directors regard research as an international endeavour and are actively building consortia to bring the power of collaborative research to bear upon these challenges facing our society.

With significant developments in neuroscience over the last decade, there is considerable hope that researchers may be in a position to prevent and treat age-related disorders like Alzheimer's.

If the group has any major limitation, it is due to the fact that researchers and staff members are spread out over a number of sites, hampering effective communication between researchers. The Committee is hopeful that 2014-2015 will see an integration of the group on one site, further enhancing its capacity for cutting-edge research.

I agree with the key findings of the Strategic Review of Health and Medical Research led by Simon McKeon, of which Professor Brodaty was a panel member, which recommended more investment, advancing clinical trials, establishing research hubs and providing incentives for philanthropists.

Overall, the Committee has been exceptionally impressed with what CHeBA has been able to achieve throughout 2013 and is inspired by the focus of everyone involved. The problems dementia brings society are enormous, but we are privileged to have the experts devoted to the cause of this research.

The emphasis is not only on new discovery, but on translating new findings into real health outcomes for the community.

DIRECTORS' REPORT

The establishment of the Centre for Healthy Brain Ageing (CHeBA) on 22 October 2012 marked the realisation of a longstanding ambition that both of us harboured to bring together researchers from a diverse set of disciplines under one collaborative research umbrella with a focus on the ageing brain and dementing disorders. We are grateful to the Thomas Foundation and the Montefiore Homes for their generous donations which helped make this goal a reality.

CHeBA hopes to meet a major need in the health research environment in Australia. Our population is ageing, and with it come the challenges of increasing dependence, reduced workforce participation and increasing burden of disease. The greatest burden on this population, and thereby on society, is imposed by brain diseases, in particular dementia. Not only is dementia a huge economic burden, its human costs on the individual and the family are incalculable. Recent findings from Alzheimer's disease International (ADI) state that the number of people living with dementia worldwide in 2013 is estimated at 44.35 million, and projected to reach 75.62 million in 2030 and 135.46 million in 2050. In Australia, there are currently over 300,000 people with dementia, and the number is increasing rapidly. The challenge is indeed great!

If we are to improve the health of older Australians and postpone or prevent dementia, centres like CHeBA are critical. The research being conducted at CHeBA spans the spectrum from molecules and genomic science right through to enhancing cognition and developing health policy. The emphasis is not only on new discovery, but on translating new findings into real health outcomes for the community. As laboratory scientists rub shoulders with clinicians, health care workers and policy makers, we hope that the excitement of bench research will be felt at the bedside and in the boardroom.

It is our ambition to make CHeBA a leading brain ageing research centre in the world. As this report shows, much has been achieved in the short time since CHeBA was established. We are grateful to the dedicated CHeBA staff for all their hard work. There are many challenges, one of the foremost being finding a new home for CHeBA such that all the researchers can be brought together to interact with

each other. Obtaining research funding to continue and indeed expand our research programs will always remain a challenge in our competitive society. We feel that the CHeBA staff have the skill to meet this challenge head-on.

We are grateful for the wonderful support received from so many quarters. Our Advisory Committee, led by Mr Roger Corbett, has inspired and guided us through the year with amazing generosity. UNSW Australia (The University of New South Wales) has supported the establishment of CHeBA with great alacrity, and we are grateful to the Chancellor, Mr David Gonski, the Vice-Chancellor, Prof Fred Hilmer, and the Dean of Medicine, Prof Peter Smith for their advice and encouragement. The Steering Committee, comprising Professors Terry Campbell and Philip Mitchell, has also been unwavering in its support. Many other supporters and benefactors, too numerous to name individually, have donated time and money to CHeBA, and we greatly appreciate their contributions.

This report highlights the many achievements of the youthful CHeBA in 2013. We hope it will impress upon you the hope and the promise that CHeBA wishes to bring to all people with age-related brain diseases and to society in general. We commend this report to you.

Sincerely,

Perminder Sachdev

Henry Brodaty

ABOUT THE CENTRE

The Centre for Healthy Brain Ageing (CHeBA) is a premier research institution in Sydney, 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, Professor Henry Brodaty and Professor Perminder Sachdev.

OUR PURPOSE

The Centre is positioned as a leader in multidisciplinary research into the ageing brain, and an international hub for collaborative engagement. Its work extends from molecular work in the genetics and proteomics laboratories, to tissue culture and cell-related work in the Stem Cell Lab, to neuronal systems and networks in the Neuroimaging Lab, to clinical, epidemiological and sociological research, to research on ageing health policy using its strong links with teaching hospitals, aged care providers, state and federal governments and its established ageing cohort studies. Its work strongly emphasises implementation, capacity building and translational research.

OUR VISION

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

OUR MISSION

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

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's objectives are to:

- Determine the pathway of normal and abnormal brain ageing in the community.
- Identify risk and protective factors for 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 other strategies.
- Conduct educational activities for a workforce involved in the care of the elderly, especially those with dementia.
- Design models of assessment and care using the latest research evidence.
- Develop research programs in special populations, e.g. young-onset dementia, dementia in intellectual disability.

OUR FUNCTIONS AND GOALS

The functions of the Centre are to:

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

This will be achieved through:

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

- Development of specialised research facilities and laboratories that give the Centre a clear competitive advantage over competitors nationally and internationally, both in the quality and nature of research that can be conducted, and in the attractiveness of working at UNSW for new staff.
- Extensive linkages with practitioners and policy makers at local, state and national levels to improve relevance and impact of research.
- Increased numbers of skilled researchers undertaking research and evaluation activities in this field.
- Enhancing numbers of postgraduate research students.
- Exercising enhanced influence via dissemination and transfer of research findings through publications, presentations and forums with a focus on academic, practitioner and policy maker audiences.

GOVERNING STRUCTURE

Centre Steering Committee

The Centre Steering Committee is the major decision making body 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, Senior Associate Dean, Chair of CHeBA Steering Committee
- Professor Philip Mitchell, Head of School of Psychiatry, UNSW
- Professor Henry Brodaty (Co-Director)
- Professor Perminder Sachdev (Co-Director)

CHeBA ADVISORY COMMITTEE

The CHeBA Advisory Committee is a group of senior academic and business leaders with an interest in furthering brain ageing research.

The role of the CHeBA Advisory Committee is to assist and guide the Directors and the Centre's Steering Committee on matters of strategy, fund-raising, policy, marketing and media, specifically to:

Professor Terry Campbell

Professor Philip Mitchell

- Enhance the profile and community awareness of the Centre and of 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:

- Mr Roger Campbell Corbett AO
  Chair of the CHeBA Advisory Committee
  Director, Walmart/Fairfax Media/Reserve Bank of Australia
- Mr John Gray
  Partner, HWL Ebsworth Lawyers
- Mr Richard J Grellman AM
  Director, FCA
- Professor Roger Layton AM MeC FAIM
  UNSW Emeritus Professor of Marketing
- Associate Professor Richard Matthews MBBS AM
  Director, Neuroscience Research Australia (NeuRA)
- Dr Sudarshan Sachdev
  Opthalmologist
- Ms Dagmar Schmidmaier AM FALIA
  Deputy Chair of the CHeBA Advisory Committee
  Co-ordinator, Chief Executive Women Leaders' Program

"Our Advisory Committee's wisdom, experience, knowledge of different fields and skills has added enormous value to CHeBA and enhanced our capacity to reach others, spread our message and raise awareness and support."

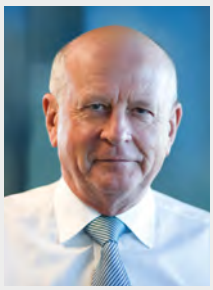
Professor Henry Brodaty

- Mr John M. Thomas KSS FAICD FIFS JP
  Principal, JT Consultancy
- Scientia Professor Perminder Sachdev
  AM MD PhD FRANZCP
  Co-Director, CHeBA
  Clinical Director, Neuropsychiatric Institute
  Professor of Neuropsychiatry, UNSW
- Scientia Professor Henry Brodaty
  AO MB BS FRACP FRANZCP
  Co-Director, CHeBA
  Director, Aged Care Psychiatry and Head of Memory Disorders Clinic, Prince of Wales Hospital
  Professor of Psychogeriatrics, UNSW

2013 MEETING DATES: 27 February 2013, 9 October 2013

ADVISORY COMMITTEE

L to R: Professor Perminder Sachdev AM, John Gray, John Thomas, John Porter, Associate Professor Richard Matthews AM, Dr Sudarshan Sachdev, Dagmar Schmidmaier AM, Professor Henry Brodaty AO (not in attendance: Roger Corbett AO, Richard Grellman AM, Professor Roger Layton AM)



ROGER CORBETT AO

Director, Walmart / Fairfax Media / Reserve Bank of Australia

From January 1999 to September 2006, Roger served as CEO of Woolworths Limited. He is now a director of Wal-Mart, the Reserve Bank of Australia and Fairfax Media. Roger was appointed a Member of the Order of Australia (AM) in the 2003 Queen's Birthday Honours, for service to the retail industry, particularly as a contributor to the development of industry policy and standards, and to the community. In 2008, he was promoted to an Officer of the Order of Australia (AO) for service to business, particularly through leadership and executive roles in the retail sector and a range of allied organisations, and to the community.

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.

RICHARD J GRELLMAN AM

Director / FCA

Richard is Chairman of WHK Ltd, Genworth Mortgage Insurance, AMP Insurance, Association of Surfing Professionals (Int) Ltd and Director of Bisalloy Steel Group Ltd. Richard worked with accounting firm KPMG for 32 years. The majority of this time was spent in the Corporate Recovery Division, with the last 10 years more specifically focused on the provision of strategic advice and services to the Financial Services sector.

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
MBBS AM

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.

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

SCIENTIA PROFESSOR PERMINDER SACHDEV
AM MD PhD FRANZCP

Co-Director, CHeBA

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

SCIENTIA PROFESSOR HENRY BRODATY
AO MB BS FRACP FRANZCP

Co-Director, CHeBA

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

SIGNIFICANT HIGHLIGHTS

"While ageing is inevitable, losing our mental capacity is not."

Professor Perminder Sachdev

LAUNCH OF CHeBA

On 22 October 2012, a new direction in positive ageing was initiated when the Centre for Healthy Brain Ageing was launched to help tackle an illness that affects over 300,000 people in Australia and is the nation's third leading cause of death, dementia.

CHeBA's Co-Directors Scientia Professors Henry Brodaty AO and Perminder Sachdev AM were dubbed the "dynamic duo" by UNSW Chancellor David Gonski AC at the launch, who also said that the Centre brought together a number of visionaries.

Originally joining forces back in 1992 with an NHMRC grant to fund their research into late-onset schizophrenia, Professors Henry Brodaty and Perminder Sachdev's collective vision with the Centre is to change the future face of age-related brain disorders.

The strength of CHeBA is in its multi-disciplinary approach, as it addresses ageing-related brain diseases through the latest work in epidemiology, clinical research, neuroimaging, genetics, proteomics, metabolomics and other innovative approaches. It also regards research as an international endeavour and is building consortia to bring the power of collaborative research to bear upon these challenging problems facing our society.

Funding for the Centre came from the Thomas Foundation, Montefiore Jewish Home, other philanthropic sources and donations, as well as grants from the Australian National Health & Medical Research Council and the Australian Research Council.

UNSW Medicine Dean, Professor Peter Smith, said the funds provided a solid foundation for the Faculty's critical research into ageing.

"By investigating strategies to understand the mechanisms underpinning cognitive decline associated with the ageing brain, how to prevent this occurring and how best to help people with dementia and their families, CHeBA's ultimate goal is for people to achieve their full life span and enjoy a good quality of life unaffected by loss of cognitive abilities."

Professor Henry Brodaty

"These very generous donations from the Thomas Foundation and the Montefiore Home will enable us to research important issues to tackle one of the most critical global public health challenges," he says.

CHeBA was officially launched 123 years to the day since the first Montefiore home opened and on the third anniversary of the death of Don Lane, who had Alzheimer's disease and whose son PJ Lane is the Centre's official Ambassador.

David Freeman AM, President of Montefiore Home delivered his support for the Centre, and David Thomas OAM of the Thomas Foundation and PJ Lane both made heartfelt speeches that touched everyone in the audience. CHeBA was officially launched by Hon Susan Ryan AO who congratulated Henry Brodaty and Perminder Sachdev for their persistent and enduring dedication to healthy ageing.

Since the launch in October 2012, CHeBA has established itself firmly as a pre-eminent centre in brain ageing research, and has increased its focus on strong collaborations internationally to create broader and better outcomes through research.

APPOINTMENTS

CHeBA has celebrated a number of appointments since its launch in October 2012, including significant appointments of the Co-Directors, Professor Henry Brodaty and Professor Perminder Sachdev.

Professor Perminder Sachdev

Professor Lynn Chenoweth

The American Psychiatric Association elected Scientia Professor Perminder Sachdev to International Distinguished Fellowship in December 2012. This action was taken on the recommendation of the Membership Committee of the American Psychiatric Association and with the approval of the Board of Trustees. This Fellowship is in recognition of Professor Sachdev's significant contributions to the psychiatry profession. Professor Sachdev was also appointed Chief Medical Advisor to Alzheimer's Australia in March 2014.

"When I started my training in Psychiatry in the early 1980s, my family and friends were surprised at my choice of specialty. Psychiatry was a low status medical discipline, stigma against mental illness was rife, and research funding for psychiatric disorders was meagre. We have come a long way since then. Psychiatry has now established a proud place alongside other disciplines in medicine and is developing a strong empirical basis. Mental illness has come out of the closet and governments and funding agencies no longer ignore it. However, we have a long distance yet to travel, and our successes in the last three decades are tempered by slow progress on many fronts."

"Professor Chenoweth is an eminent academic nursing researcher who has brought complementary knowledge and expertise in aged care nursing, care models and healthy ageing to CHeBA."

Professor Henry Brodaty

Professor Henry Brodaty with outgoing President of the International Psychogeriatric Association, Professor Jacobo Mintzer

Co-Director Scientia Professor Henry Brodaty was appointed Montefiore Chair of Healthy Brain Ageing in October 2012, and at its biannual Congress in Seoul on 4th October 2013 became President of the International Psychogeriatric Association after two years as President-Elect. His goals over his two year term centre on membership and impact.

"I would like to increase the reach of IPA to professionals globally" he said, "with special emphasis on those in low and middle income countries where mental health services in general and those for older people in particular are underdeveloped". Professor Brodaty emphasised the importance of educational programs for health professionals and the opportunities for internet based programs.

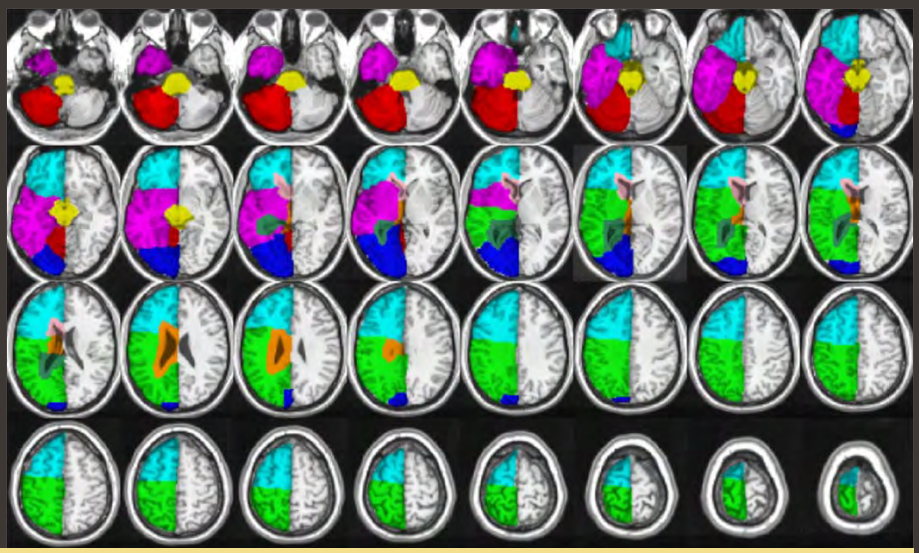
The mission of IPA is to improve the mental health of older people everywhere through education, research, professional development, advocacy, health promotion, and service development. IPA's vision is better mental health for older people worldwide through its member geriatric psychiatrists, geriatricians, neurologists, nurses, social workers, psychologists, primary care physicians and occupational therapists.

In 2013 Professor Lynn Chenoweth took up a half time appointment with CHeBA, while retaining her current UTS role half time as Professor of Aged and Extended Care Nursing.

Professor Chenoweth has an international reputation as a leading dementia care researcher, scholar and advocate.

NEW CRITERIA FOR VASCULAR DEMENTIA

A highlight of research from CHeBA this year is the publication of new diagnostic criteria for Vascular Cognitive Disorders, including vascular cognitive impairment and vascular dementia (VaD).



The new criteria that emerged have been greatly influenced by the research carried out at CHeBA through the Sydney Stroke Study and Sydney Memory and Ageing Study.

Vascular disease is the second most common cause of dementia after Alzheimer's disease (AD), and since its mechanisms and risk factors are better understood, it may be more preventable than AD. It is however a very heterogeneous disorder and its research diagnosis has been bedevilled by inconsistency between the different sets of criteria currently available, and in fact the definition of dementia which is more reflective of AD than VaD.

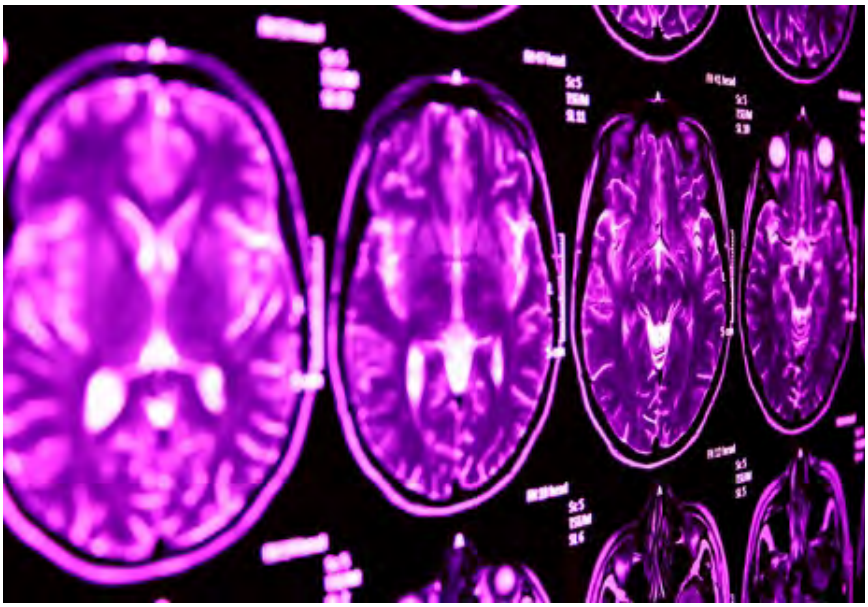
The International Society for Vascular Behavioural and Cognitive Disorders (VASCOG) wanted to change this, and a group led by CHeBA Co-Director Perminder Sachdev met in 2009 to critique the current criteria, and draft a proposal for a new set of criteria. This was later reviewed through multiple drafts by the group, including additional experts and members of the Neurocognitive Disorders Work Group of the DSM-5 Task Force. The new criteria that emerged have been greatly influenced by the research carried out at CHeBA through the Sydney Stroke Study and Memory and Ageing Study. The term Vascular Cognitive Disorders (VCD) is used to broadly categorise this group. It is recognised that the cognitive impairment in VCD is somewhat different from that seen in AD, and this is reflected in the criteria. The criteria also recognise that vascular cognitive impairment is on a continuum, and waiting for dementia to manifest may be very late in the process. It is also recognised that VCD and AD often co-occur, and in fact vascular disease may promote AD pathology.

The proposed criteria for VCD provide a coherent approach to the diagnosis of this diverse group of disorders, with a view to stimulating clinical and pathological validation studies. Their application may lead to a fundamental change in the way vascular dementia is conceptualised.

Ref: Sachdev P, Kalaria R, O'Brien J, Skoog I, Alladi S, Black SE, Blacker D, Blazer DG, Chen C, Chui H, Ganguli M, Jellinger K, Jeste DV, Pasquier F, Paulsen J, Prins N, Rockwood K, Roman G, Scheltens P. Diagnostic Criteria for Vascular Cognitive Disorders: a VASCOG Statement. Alzheimer Dis Assoc Disord. 2014 Mar 13. [Epub ahead of print] PMID: 24632990.

MCI REVERSAL FINDINGS

A significant highlight of our research this year used data from CHeBA's prospective, population-based Sydney Memory & Ageing Study to show that one in four elderly people with Mild Cognitive Impairment – a precursor to dementia – naturally 'reverts' to normal cognition.



The findings of the CHeBA study led by Professor Perminder Sachdev challenge a popular belief that older people with Mild Cognitive Impairment (MCI) are inevitably on the path to dementia. The study, published in *PLoS One*, investigated factors predicting or associated with reversion from MCI to normal cognition and showed that some people, in fact, get better.

The study had 223 participants (48.9% male) aged 71-89 years, all with MCI at baseline who were reassessed two years later. While 11 participants had progressed to dementia, the majority (n=157) continued to manifest MCI. Surprisingly, 66 (29.6%) were judged to have reverted to 'normal' cognition.

People who reverted from MCI to normal cognition were generally more resilient and seemed to be ageing "better". They were more likely to have controlled their high blood pressure, and were generally more physically and mentally active. Personality also appeared to play as role, and the reverters tended to show greater openness to experience. Higher complex mental activity was also of significant benefit. Importantly, 'reverters' also had better ability to smell and had better vision.

While the research gives hope to people with mild cognitive problems, Professor Sachdev cautioned that any benefits could be limited over time. "Some people may still go on to develop dementia eventually. It's a matter of how long they can keep it at bay.

"For this reason it's important for people to know that they can improve the quality of their life for some time through exercise and good health care," he said.

The study was supported through a Program Grant from the National Health & Medical Research Council of Australia (NHMRC). DNA samples for the study were extracted by Genetic Repositories Australia, an Enabling Facility supported by the NHMRC. *APOE* genotyping was performed at Neuroscience Research Australia (NeuRA). Neuroimaging was performed at the NeuRA Imaging Centre. Blood samples were collected by South Eastern Area Laboratory Service.

Professor Sachdev said both mental and physical exercise give direct benefits to the brain. Exercise also offers many indirect effects, correcting other risk factors associated with cognitive decline, such as reducing obesity and blood pressure, and controlling diabetes.

ENHANCING MEMORY FUNCTIONING IN MCI

Currently, there is no effective intervention available for people at risk for dementia, with pharmacological approaches having so far proven ineffective.

However, behavioural interventions, such as cognitive training have shown promise for improving cognition, particularly memory. Improving memory is especially important for people who are at risk and have objectively measured memory impairment, i.e., diagnosed with amnestic Mild Cognitive Impairment (aMCI). aMCI is considered the symptomatic pre-dementia phase of Alzheimer's disease (AD), the most common form of dementia.

This double-blind randomized controlled study led by Dr Adith Mohan and Dr Donel Martin aims to investigate an exciting novel approach we have developed for improving memory in people diagnosed with aMCI; cognitive training (CT) combined with mild non-invasive brain stimulation (transcranial direct current stimulation (tDCS)). Based on our prior work in healthy participants, we expect that this combined approach (i.e., tDCS + CT) will be more effective in improving memory and cognition than CT alone.

In the study, participants are randomized to one of two conditions: active or sham (placebo) tDCS during CT across 15 sessions (1 hour a session, 3 sessions per week). Data collection commenced in January 2013. So far we have had 21 study completers and currently have 4 participants enrolled and receiving treatment. Results so far indicate that there is a difference favouring the active tDCS + CT condition on the primary outcome measure assessing learning and memory and on a secondary outcome measure assessing speed of information processing.

The hope is that through brain stimulation using tDCS we will achieve sustained improvement in people's cognitive abilities providing benefit to people with MCI, and delaying the onset of dementia in those affected, and in doing so, provide a longer period of good quality life.

HUMOUR THERAPY IN NURSING HOMES

We designed a program of humour therapy to counter the distressing scene of older people in nursing homes sitting apathetically, disengaged and demonstrating little reactivity.

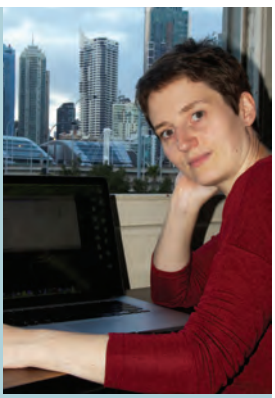
Mr Jean-Paul Bell with SMILE study participant

We piloted and then conducted a cluster randomised controlled trial of humour therapy in 35 nursing homes across Sydney – about half the nursing homes received the intervention and the other half continued to provide care as usual. The humour therapy was provided for 2 hours per week to all individual residents of sections of participating nursing homes by a trained therapist and during the week by a staff member who had volunteered to receive training. After 3 months and at follow-up at 6 months, residents who had received the humour therapy were less agitated and, after adjusting for dose of therapy and support of staff and management, were less depressed and had better quality of life ratings. An award-winning film of the therapy was screened on ABC TV. Subsequently, over 70 nursing homes have now signed up for humour therapy for which they are paying themselves.

*this program is administered by the Dementia Collaborative Research Centre – Assessment & Better Care

1. Low LF, Goodenough B, Bell JP, Spitzer P, Fling R, Casey AN, Chenoweth L, Liu Z, Brodaty H. The Sydney Multisite Intervention of LaughterBosses and ElderClowns (SMILE) study: A cluster randomised trial of humour therapy in nursing homes. BMJ Open. 2013 3(1) doi: 10.1136/bmjopen-2012-002072
2. Brodaty H, , Low, LF, Liu Z, Fletcher J, Roast J, Goodenough B, Chenoweth L. Successful ingredients in the SMILE Study: Resident, staff and management factors influence the effects of humor therapy in residential aged care. American Journal of Geriatric Psychiatry (8 October 2013) doi: 10.1016/j.jagp.2013.08.005

Predictors and outcomes for caregivers of people with mild cognitive impairment: A systematic literature review



Katrin Seeher is a PhD student supervised by Professor Henry Brodaty.

Research on the impact of mild cognitive impairment (MCI) on family members is relatively new. In a recent systematic literature review we summarised the current evidence for negative outcomes for MCI carers and established predictors for these negative outcomes.

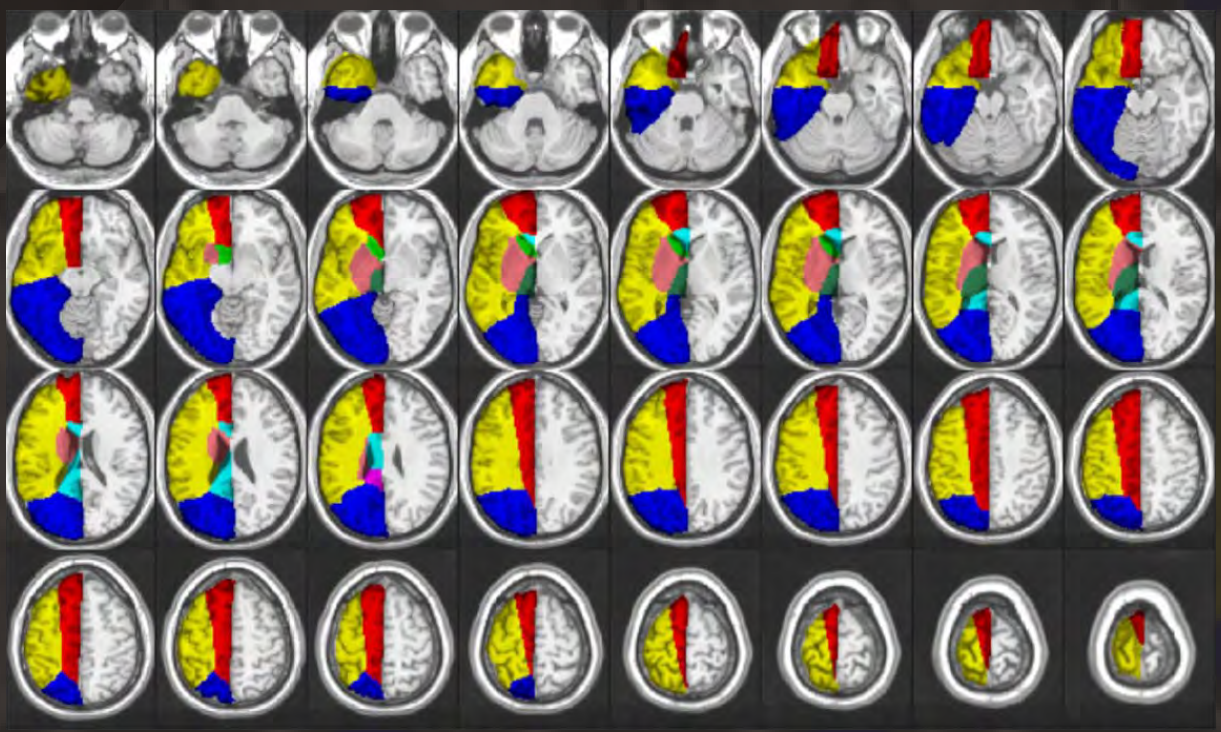
The strongest evidence currently exists for depression. Across six studies, almost a quarter of MCI carers reported clinically elevated levels of depression. While their symptoms were not as pronounced as in dementia carers they exceeded what is usually reported for the general population. The same was found for caregiver burden, stress and anxiety although the evidence was based on single studies only.

Studies varied drastically with respect to the predictors and outcomes investigated. Individual studies linked longer symptom duration, younger carer age and lower carer education to increased levels of stress, depression or burden, although not consistently. Patients' behavioural or functional symptoms and carers' appraisals of these symptoms also predicted depression and burden.

The findings of our review, which were limited entirely to cross-sectional and clinical data, may not be generalizable to the broader community. Also, the long-term trajectory of these negative carer outcomes remains uncertain at this stage. Katrin's PhD project aims to close some of these gaps.

Ref: Seeher K, Low LF, Reppermund S and Brodaty H: Predictors and outcomes for caregivers of people with mild cognitive impairment – A systematic literature review. Alzheimer's and Dementia 2013, 9(3): 346-355; doi:10.1016/j.jalz.2012.01.012

PHD COMPLETIONS



PHD COMPLETIONS

11 students received their PhD, showcasing the quality, breadth and depth of brain ageing research undertaken at CHeBA. PhD theses encompassed a diverse range of topics and techniques, including neuroimaging, proteomics, neuropsychology, brain stimulation, genetics and cognition. We congratulate Drs Seyed Amir Hossein Batouli, Yue Cui, Nicola Gates, Jaemin Kim, Teresa Lee, Tao Liu, Michael Player, Im Quah-Smith, Chao Suo, Haobo Zhang and Lin Zhuang. Dr Teresa Lee was awarded the UNSW Dean's Rising Star Award and Drs Haobo Zhang and Lin Zhuang have been appointed as post-doctoral fellows in the Neuroimaging group at CHeBA.

DR SEYED AMIR HOSSEIN BATOULI

Genetic and environmental influences on brain structure and biochemistry in the elderly: data from the Older Australian Twins Study

Healthy brain functioning is an important part of healthy ageing. Several brain features have shown links with healthy ageing; including brain size, brain white matter hyperintensity (WMH) and brain metabolites. Age-related changes are influenced by both genetic and environmental factors, and this study looked at how they influence the structure and biochemistry of the brain. Participants were recruited from the Older Australian Twin Study (average age 72 years). Firstly structural equation modeling was performed to compare MRI brain scan data from identical and fraternal twins. The influences of age and sex on the heritability of these parameters were examined, as well as identifying any common genetic factors. Estimations showed significant heritability of the brain size, WMH volume and brain biochemistry in the elderly. Brain size heritability decreased with age, but WMH volume heritability increased. There were no significant differences between males and females in the heritability of brain metabolites and WMH volumes, but the heritability of brain size was higher in males. Also, common genetic factors were observed between the volumes and WMHs of different brain regions and also between the brain metabolites. The results showed that the human brain is largely influenced by genetic factors in later life, but that this influence may diminish with increasing age, particularly for brain size. As environmental factors may become more important in later life, it is suggested that healthy ageing may be optimized by enrichment of environmental conditions.

DR NICOLA GATES

Psychological wellbeing and quality of life in Mild Cognitive Impairment

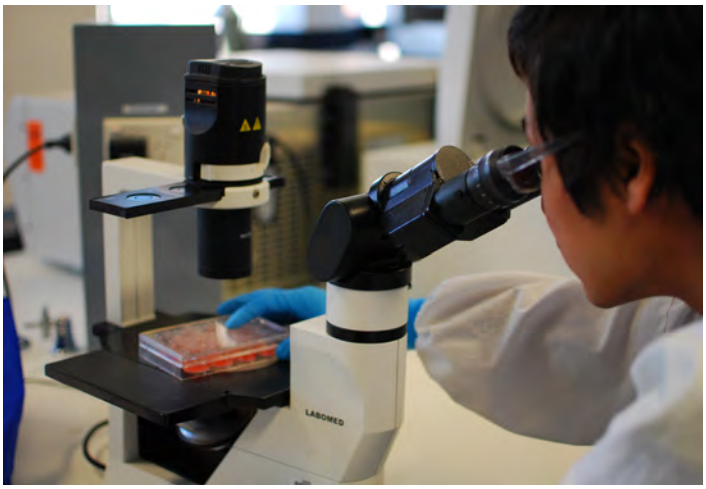
Psychological wellbeing (PWB) and a high Quality of Life (QoL) are indicators of successful ageing. With increasing numbers of older adults and their desire for positive ageing, along with projections of dementia prevalence and policy interest to reduce health expenditure, interest in PWB and QOL has risen significantly. Coupled with this has been the advancement of lifestyle interventions as a means to preserve independence, improve cognition, and promote PWB. Evidence from epidemiological studies and clinical trials suggests that cognitive training (CT) and physical exercise (PE) interventions in adults with Mild Cognitive Impairment (MCI) may improve cognition. However, to date there has been limited investigation of QoL and PWB outcomes in these studies. Therefore, the first investigation was an empirical analysis of a theoretical 3-tiered model of PWB using cross sectional baseline data from the SMART trial. The final model predicted 61% of the variance of PWB in MCI with memory concern and cognitive deficits identified as significant predictors of PWB, along with negative affect and QoL. Following 26 weeks of SMART CT and PE intervention, linear mixed model analyses revealed that mental health-related QoL and Purpose in Life subscale within PWB improved following combined intervention, and CT in isolation resulted in improved levels of Autonomy, and Self- Acceptance, both aspects of PWB. By contrast, isolated PE had no significant benefit on any component of QoL or PWB. Lastly, regression analyses indicated that improved cognitive performance following intervention was not associated with a reduction in memory concern or improvement in QoL or PWB. The three investigations of this thesis demonstrated overall that PWB and QoL in MCI have multiple influences, that complex inter-relationships exist between negative affect, cognition and memory concern, and that interventions designed to improve cognition do not necessarily improve PWB. Clinical implications from this research include recognising the importance of memory concern for PWB and QoL in MCI, the implementation of early intervention programmes in MCI, potential role of CT to improve aspects of PWB, and the development of PWB and QoL outcomes in future research studies.

As part of the Capacity Building Grant, CHeBA has established a strong mentorship program for our junior researchers

CAPACITY BUILDING GRANT

CHeBA's NHMRC-funded Capacity Building Grant (CBG) supports promising junior researchers to develop into international leaders in their fields.

Since 2009, the CBG has supported 12 researchers in 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 and protective factors for cognitive decline. To date, they have produced over 100 publications and been awarded more than $11 million in competitive grants. Our researchers have supervised 28 higher degree research students and established international collaborations with researchers in the UK, USA, France, Germany, the Netherlands, Norway, Chile, Iran and Oman. As part of the Capacity Building Grant, CHeBA has established a strong mentorship program for our junior researchers. Mentors are drawn from within CHeBA as well as collaborative partners, such the Black Dog Institute, Neuroscience Research Australia (NeuRA), the Australian School of Business, the Schools of Psychiatry, Psychology and Medical Sciences (UNSW), the Prince of Wales Hospital, St Vincent's Hospital and the National Drug and Alcohol Research Centre (NDARC) as well international collaborators in UK, Europe, USA, Canada and Asia.



"Globally dementia costs $600 billion a year and if it were a country it would be the world's 18th largest economy. If it were a business, a company, it would be the biggest." Professor Henry Brodaty

MEET A CAPACITY BUILDING GRANT RESEARCHER

Dr Nady Braidy

Dr Braidy is an NHMRC Early Career Research Fellow (2013-2016) at UNSW (UNSW, Sydney, Australia). He was the sole recipient of the Alzheimer's Australia Viertel Foundation Postdoctoral Research Fellowship in 2012. Dr Braidy has 39 peer reviewed publications, 5 book chapters and 1 international patent, and has presented orally at over 20 national and international conferences. In 2012, he was awarded the International Junior Investigator of the Year Award in Geriatric Psychoneuropharmacology for his contribution to ageing and neurodegenerative diseases. Dr Braidy believes that maintaining cellular energy anabolism will lead to improved protection against age-associated pathologies in humans, including neurodegeneration and cognitive decline. Dealing with an ageing population is a significant challenge for health systems and economies around the world, and strategies to delay or reverse individual age-associated disorders are the subject of intense interest. Dr Braidy's work proposes a single strategy that will broadly treat age-related disorders. He presents small molecule candidates that can be used to pharmacologically modulate nicotinamide adenine dinucleotide levels and gene silencing by histone deacetylases, which might be used to treat ageing.

KEY STUDIES

"If previous centuries were all about infectious diseases, and the twentieth century about cancer and heart disease, the twenty-first century will be about neurodegenerative disease, the failure of the brain."

Professor Brodaty

KEY STUDIES

The composition of Australia's population is projected to change considerably as a result of population ageing.

Research is needed to assist the public health system better plan for the future and may assist younger people make better lifestyle choices to improve their quality of life as they grow older. CHeBA runs a number of longitudinal studies which are investigating factors associated with healthy brain ageing and cognitive decline. Our research is intended to inform national health policy and service delivery, as well as brain ageing research and treatment in Australia and internationally.

Prior to the launch of CHeBA, our research was conducted under the banner of the Brain & Ageing Research Program which was consolidated in 2005 with an NHMRC program grant. This grant enabled the establishment of large longitudinal cohorts to examine risk and protective factors in ageing.

The value of a longitudinal study increases exponentially with each subsequent wave of data until the objectives have been met.

MAS – Research Assistant Ruby Tsang and study participant Yvonne Sharah

SYDNEY MEMORY & AGEING STUDY (MAS)

The Sydney Memory & Ageing Study (MAS) investigates neurocognitive function and its change over time (cohort age range 70-90 years at baseline). This research enables us to compare normative cognitive ageing with pathological cognitive decline, including Alzheimer's disease, vascular dementia and frontotemporal dementia. We aim to develop and refine measures for early diagnosis and prognosis of brain ageing disorders, and examine risk factors and biomarkers (such as blood tests and MRI scans) for cognitive decline. We are also interested in identifying and testing novel treatment strategies.

To date, our research has yielded a large amount of data on many aspects of brain ageing and dementia. We have studied a wide range of risk factors for cognitive impairment, including genetic determinants, arterial stiffness, dietary mineral intake, glucose disorders, inflammatory markers and lifestyle factors. The study has been very productive (71 papers published, and 77 in preparation or submitted)

MAS is also a participant in a number of international research consortia, including COSMIC (determinants of cognitive ageing and neurocognitive disorders), ICC-Dementia (dementia and genetics of longevity), BrainInflame (neuroinflammation), PROMOTE (psychosocial aspects of ageing) and CHARGE, ENIGMA, EuroDISCOTWINS and PERADES (all genetics).

OATS participants David & Denis Lynch

OLDER AUSTRALIAN TWINS STUDY (OATS)

The Older Australian Twins Study (OATS) investigates healthy brain ageing in elderly twins. Healthy ageing is characterised by low level of disability, high cognitive and functional capacity, and an active engagement in life. Brain ageing and brain diseases are determined by multiple genetic factors that interact with environmental influences. Since identical twins share 100% of their genes, whereas non-identical twins share half the genetic information, detailed comparisons of these two groups have the potential to discover new genes involved in cognitive decline or resilience. OATS investigates environmental influences such as lifetime physical and mental activity, socioeconomic environment, and nutrition. It also investigates how biological factors, such as hypertension and antioxidant levels, interact with genes to influence brain ageing. OATS has recruited twins (N=623) aged ≥ 65 years from the three eastern states of Australia with longitudinal follow-up similar to MAS above. Eight papers have been published, >20 are in preparation and key findings were recently published.

SCS participant Major Cyril Bunny (100 years old)

SYDNEY CENTENARIAN STUDY (SCS)

The Sydney Centenarian Study (SCS) investigates the physical, psychological and cognitive health of people aged 95 years and above. To date the SCS has been important because it provides evidence that dementia is not inevitable at this age and independent living is common. The study provides an excellent resource to determine the genetic and environmental contributions to long and successful cognitive aging.

The strength of CHeBA is in its multidisciplinary approach as it addresses ageing-related diseases through the latest work in epidemiology, clinical research, neuroimaging, genetics and other innovative approaches.


CHeBA'S RESEARCH
RESEARCH
EXPERIMENT
ANALYSIS
INFORMATION
SCIENCE
EDUCATION
EXPLOR

GROUPS

GENETICS & GENOMICS

GROUP LEADER: Dr Karen Mather

Dr Karen Mather is the leader of the Genetics & Genomics group, a research fellow with CHeBA, an Alzheimer's Australia Dementia Research Foundation Postdoctoral Fellow and visiting research fellow at Neuroscience Research Australia (NeuRA). Dr Mather's major research objective is to gain a better understanding of the genetic and environmental factors involved in ageing and age-related disease using human population studies. Dr Mather is also interested in the field of epigenetics and its relationship to ageing and age-related disease. Exciting work is being undertaken in her group examining DNA methylation and non-coding RNA variation and its relationship to ageing and age-related phenotypes, such as memory performance. In 2013, Dr Mather was awarded a Postdoctoral Fellowship by the Alzheimer's Australia Dementia Research Foundation for two years, which has allowed her to focus on research related to early markers of dementia, such as age-related memory performance and decline. Dr Mather was presented with an Early Career Award at the College of Geriatric Psychoneuropharmacology Annual Conference in Pittsburgh, USA in 2013.

Aims

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

Achievements

- A significant and valued addition to our group occurred in late 2012, with the appointment of a statistical geneticist, Dr Anbu Thalamuthu. His appointment has resulted in increased capacity and ability to undertake genetics-related work and to contribute to national and international collaborative projects.
- We continue to collaborate on several genome-wide association study (GWAS) meta-analyses examining age-related and neuroimaging phenotypes with the international consortia, CHARGE and ENIGMA. This has been a fruitful collaboration with several manuscripts currently under review.
- As part of a successful Group of Eight Australia-Germany Joint Research Co-operation Scheme application, Drs Mather and Reppermund visited the Max Planck Institute of Psychiatry, Munich, for two weeks in 2013 to undertake joint genetics-based research on cognitive performance and depression using our Australian and German cohorts.
- Formation of a new collaboration with the Hunter Community Study, Newcastle, on several genetics projects, including GWAS meta-analyses examining grip strength and apolipoprotein levels. In an exciting finding, genome-wide significant results were found for a specific apolipoprotein. These results are being currently being prepared for publication.
- Our DNA methylation –cognitive ageing work was presented at the College of Geriatric Psychoneuropharmacology Annual Conference in Pittsburgh, 2013, where Dr Mather was presented with an Early Career Award.
- In 2013, Jessica Lazarus successfully completed her Honours in Medical Sciences using DNA samples and data from the Sydney Memory and Ageing study. Her thesis was entitled 'Examination of DNA methylation in the apolipoprotein A1 gene in the Sydney Memory and Ageing Study'. This work is now being written up for publication and Jessica has enrolled as a PhD student.

- A Medicine Independent Learning Project was successfully completed in 2013 by Jess Chan on the genetics of grip strength in older adults, which is currently being prepared for publication. Her work used data from the Sydney Memory and Ageing Study and the Hunter Community Study.

MOLECULAR BIOLOGY & STEM CELLS

GROUP LEADERS: Dr Nady Braidy & Honorary Associate Professor Kuldip Sidhu

Dr Nady Braidy

Dr Braidy is the co-leader of the Molecular Biology & Stem Cells group, a research fellow at CHeBA, adjunct lecturer with the School of Biotechnology and Biomolecular Sciences at UNSW, an NHMRC Early Career Research Fellow (2013-2016) and an Alzheimer's Australia Viertel Foundation Postdoctoral Research Fellow (2012). Dr Braidy's research focuses on sirtuins, a family of seven mammalian enzymes that control cellular energy and protect against numerous age-related diseases. He has also studied small molecules which indirectly activate SIRT1 and recently identified a common mechanism by which these molecules allosterically activate an NAD+-synthetic enzyme leading to increased NAD+ levels and higher SIRT1 activity.

Honorary Associate Professor Kuldip Sidhu

Hon. Associate Professor Kuldip Sidhu is the co-leader of the Molecular Biology & Stem Cells group, stem cell expert at CHeBA, and CEO & Founding Director of Cell Therapeutics Pty Ltd. He is currently President of the Society for Brain Mapping & Therapeutics. Hon. Associate Professor Sidhu's research focus is

on neural stem cells derived from both embryonic and non-embryonic sources for developing future cell therapies for various neurodegenerative diseases, like Alzheimer's, Parkinson's and other neuronal diseases. His lab was the first to produce two hESC lines, Endeavour (E) 1&2 from Australia, and have produced over 100 iPSC clones from Alzheimer's patients for studying disease progression and possible therapeutic applications.

Aims

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

Achievements

- Dr Jaemin Kim was awarded his PhD in 2013 for his thesis 'Directed differentiation of human embryonic stem cells into dopamine neurons'.
- A major project, Stem Cell Initiative for study of Alzheimer's disease, was completed resulting in more than 80 iPSC clones derived and about 11 fully characterised. These clones are available for distribution to relevant laboratories for R&D purposes and have already been distributed to 3 academic and 1 commercial institute.

RISING STAR - DR NADY BRAIDY

Dr Braidy believes that maintaining cellular energy anabolism will lead to improved protection against age-associated pathologies in humans, including neurodegeneration and cognitive decline. Dealing with an ageing population is a significant challenge for health systems and economies around the world, and strategies to delay or reverse individual age-associated disorders are the subject of intense interest. Dr Braidy's work proposes a single strategy that will broadly treat age-related disorders. He presents small molecule candidates that can be used to pharmacologically modulate nicotinamide adenine dinucleotide levels and gene silencing by histone deacetylases, which might be used to treat ageing.

In 2012, he was awarded the International Investigator of the Year Award in Geriatric Psychoneuropharmacology for his contribution to ageing and neurodegenerative diseases and the UNSW Australia Dean's Rising Star Award.

NEUROIMAGING

GROUP LEADER: Associate Professor Wei Wen

Associate Professor Wei Wen is the leader of the Neuroimaging group and director of the NeuroImaging Laboratory (NiL) in CHeBA. The NiL is a very important and successful component of CHeBA, hosting several research students and post-doctoral fellows. Associate Professor Wen's main research interest is neuroimaging with a focus on brain ageing, including structural and functional neuroimaging, brain network analysis and imaging genetics.

Aims

The Neuroimaging group is dedicated to researching the ageing of the human brain. By studying structural and functional magnetic resonance imaging and other neuroimaging modalities, we aim to improve understanding of brain ageing pathways, which in turn will lead to clinical advances in prediction, diagnosis and treatment. Our neuroimaging studies address normal ageing, Mild Cognitive Impairment (MCI), and dementia.

Achievements

- Two new PhD candidates commenced in 2013, Alistair Perry and Jiyang Jiang.
- Two new post-doctoral fellows, former PhD candidates with CHeBA, were appointed, Dr Lin Zhuang and Dr Haobo Zhang.
- From June 2013, we established a strong collaboration with visiting Professor Pierre Lafaye de Micheaux investigating heritability and genetic influence of brain structures in older individuals using Older Australian Twins Study data. We mapped heritability for both cortex and subcortical structures, including extracting three dimensional surface information for subcortical structures for the first time. 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.
- Our research into voxel-based resting-state functional connectivity is the first study to investigate the heritability of whole-brain connectivity. This approach has also exhibited a more robust, scale-free network organisation than previous region-wise approaches.
- Our research is the first to reveal the potential of white matter DTI measures as a non-invasive biomarker in early diagnosis of Alzheimer's disease. The results will have immediate and direct clinical implications, as DTI is less expensive, more readily available and less invasive than conventionally accepted biomarkers. It also opens up white matter degeneration as an independent field of enquiry in Alzheimer's disease, the mechanisms for which remain to be understood.
- We commenced the first study to investigate the relationship between the blood level of MIC-1/GDF15 and brain grey matter volume, in both cross-sectional and longitudinal settings.
- A stream of high quality publications have emanated from the Neuroimaging group in 2013 (see appendix, page 85).

NEUROINFLAMMATION

GROUP LEADER: Associate Professor Julian Trollor

Association Professor Julian Trollor is the leader of the Neuroinflammation group, inaugural Chair of Intellectual Disability Mental Health and heads the Department of Developmental Disability Neuropsychiatry within the School of Psychiatry at UNSW. Associate Professor Trollor is involved in diverse research programs including general population ageing studies, ageing and cognitive decline in intellectual disability, intellectual disability in the criminal justice system, and human rights and healthcare in intellectual disability. His research into brain ageing includes determinants and correlates of brain ageing; metabolic, cardiovascular and inflammatory factors in brain ageing; and nutrition and brain ageing.

Aims

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

Achievements

- The Neuroinflammation group produced a number of key publications, including an examination of the role of systemic inflammation on cognitive function and cognitive decline and the role of inflammatory cytokines in depression.
- We collaborated with the Neuroinflammation group from the Garvan Institute to undertake a novel examination of the association between MIC 1 and cognition and cognitive decline.
- We were successful in obtaining an NHMRC grant to undertake further research on the links between depression and inflammation. This grant will have a particular focus on the relationship between inflammatory genes and depression.

NEUROPSYCHOLOGY

GROUP LEADERS: Dr Nicole Kochan & Dr Teresa Lee

Dr Nicole Kochan

Dr Nicole Kochan is the co-leader of the Neuropsychology group. Dr Kochan is a research fellow at CHeBA and leader of the neuropsychology arm of the Sydney Memory and Ageing Study (MAS). In 2013 she was awarded an NHMRC Early Career Research Fellowship and concurrently works as a clinical neuropsychologist at the Neuropsychiatric Institute, Prince of Wales Hospital, a position she has held since 2001. Dr Kochan's PhD studies examined the efficacy of functional MRI together with a "memory stress test" to identify older adults at risk of developing dementia. Her current research work aims to develop effective methods for early identification of Alzheimer's disease and other dementias through sensitive neuropsychological measures, computerised tests of cognition and by establishing a comprehensive neuropsychological normative database for older Australian adults. Another focus of her research addresses the challenge of diagnosing cognitive impairment in individuals from cultural and linguistic diverse minorities (CALD). Her aim is to improve diagnostic accuracy in persons of CALD backgrounds by examining the cultural, linguistic and educational factors that may influence cognitive performance. In 2012-2013, Nicole received a Travel Fellowship Award from Alzheimer's Association International to present her work at the annual conference which was held in Boston, USA; she received the Gordon Parker award for Best Publication for PhD in the School of Psychiatry, UNSW; she presented her work at national and international conferences; and she was co-author on approximately 15 publications.

Dr Teresa Lee

Dr Teresa Lee is the co-leader of the Neuropsychology group. Dr Lee is a research fellow at CheBA, a senior clinical neuropsychologist at the Prince of Wales Hospital, and conjoint senior lecturer at the School of Psychiatry, UNSW. Dr Lee is a chief investigator on the Older Australian Twins Study (OATS) and has primary responsibility for the neuropsychological component, including enhancing the assessment protocol (which is based on the MAS), training and supervision of research assistants, management of data, and consultations to doctoral students and post-doctoral researchers. She is also the neuropsychologist on a panel of experts in consensus meetings in OATS, contributing to diagnostic decisions. In 2013, Dr Lee received the UNSW Australia Dean's Rising Star Award for her PhD thesis *"Genetic and environmental influences on neuropsychological functioning in later life: the Older Australian Twins Study"*.

Aims

Our research aims to advance scientific knowledge in relation to the cognitive changes occurring in the brain in normal ageing, mild neurocognitive syndromes and dementia, using neuropsychological methods and functional neuroimaging techniques. We have established strong collaborative links with other researchers in CHeBA, and are actively involved in research investigating associations between memory and cognition, as well as brain structure, metabolic disorders, inflammatory markers and falls in the older adult population.

Achievements

- In November 2013, Dr Teresa Lee was awarded a PhD for her thesis and received the UNSW Australia Dean's Rising Star Award, which acknowledges outstanding achievements of post doctoral staff and early career researchers recognised as part of the Faculty's talent management program to be outstanding in their respective fields of activity. Her thesis comprised a review of cognition in elderly twins and four published papers on the genetic and environmental influences on neuropsychological functioning in later life, using data from OATS.

RISING STAR – DR TERESA LEE, PHD

Dr Teresa Lee

Genetic and environmental influences on neuropsychological functioning in later life: the Older Australian Twins Study

Ageing is associated with cognitive decline. While many areas of cognitive functioning are affected, there is relatively limited knowledge about the contributions of genetic (G) and environmental (E) factors to cognition. This thesis looked at two specific areas of cognition: processing speed (PS) and executive functions (EF). PS is how long it takes to process information and to do a test. EF are thinking processes which include complex attention and task planning. Using data from OATS and genetic modeling, the first study looked at the extent of G influence (heritability) and E influences on multiple measures of PS and EF, and how they relate to General Cognitive Ability (GCA). PS performances in several measures and GCA were explained by one common genetic factor, suggesting that they shared the same genes. The results for EF in the second study, however, suggested it has both G and E influences. Differences in PS and EF were also both found to be related to differences in the memory of older people, but more so for PS. These findings suggest PS can be assessed to investigate declines in general cognition as people age. The last study in the thesis looked at the associations between three leisure activities (cognitive, physical and social) and various health/medical factors with cognitive performance. A number of cardiovascular, frailty and sensory factors were identified that explained differences in cognitive function between identical twins. Taken together, this research has identified important G influences and E factors that promote our understanding of mechanisms related to cognitive ageing. The results also have practical implications for the development of targeted interventions to slow age-associated cognitive decline.

- In 2013, Dr Kochan undertook collaborative work with Professor David Bunce, Leadership Chair in Cognitive Psychology at the University of Leeds. Their study investigated individual performance variability over the trials of a reaction time task in older adults, and found that greater variability and slower reaction time on a computerised test predicted the development of dementia in a group of 70-90 year-olds who participated in the MAS. The work was presented by Dr Kochan at the Alzheimer's Association International Conference in Boston, USA.
- Dr Kochan has also been collaborating with Professor John R Crawford from the School of Psychology at the University of Aberdeen to produce a neuropsychological normative data calculator that can be used by psychologists to comprehensively analyse the test performance of their older clients. It is expected that this on-line normative data tool will facilitate more accurate diagnoses of neurodegenerative disorders in older adults and will be particularly relevant to Australian clinicians who have had scant Australian data available to date. This collaborative work was presented by Dr Kochan at the College of Clinical Neuropsychologists Conference in Hobart in 2013 and was received with enormous interest from the predominantly clinical audience.
- The Neuropsychology group received a Dementia Collaborative Research Centre (DCRC) project grant for an investigation of computerised neuropsychological testing for early diagnosis of Mild Cognitive Impairment and dementia. Computerised test performance using reaction time, memory and executive tasks will be investigated in volunteers from the MAS and in a group of hospital patients presenting with memory difficulties. The study aims to facilitate the early detection of neurocognitive disorders in older adults using a computerised neuropsychological test battery and to evaluate its potential as a more culture-fair instrument than traditional methods to measure cognition in older adults from culturally and linguistically diverse backgrounds.

PROTEOMICS

GROUP LEADER: Dr Anne Poljak

Dr Anne Poljak is leader of the Proteomics group at CHeBA, a senior research scientist in the Bioanalytical Mass Spectometry Facility (BMSF), a post-doctoral fellow in the School of Psychiatry, and lecturer (conjoint) Faculty of Medicine, UNSW. Dr Poljak's research focus over the last 10 years has been on neurochemistry and age-related changes in mammalian biology, most recently on changes to brain and plasma protein profiles during ageing. Dr Poljak's work on the chemistry of nervous system diseases

has included (1) etiology of the Alzheimer's brain and delirium, (2) plasma biomarkers for ageing and age related conditions including Mild Cognitive Impairment (MCI), dementia and delirium, (3) characterisation of peptides in pheochromocytoma, and (4) the role of oxidative stress in amyotrophic lateral sclerosis. Dr Poljak has more than 25 years of experience in protein chemistry and mass spectrometry, with expertise in areas such as post-translational modifications, sequencing peptides using LCMSMS, quantitative techniques in mass spectrometry, as well as ELISA multiplex quantification of proteins. Her published work includes more than 50 research papers in international peer reviewed journals and her 1995 publication in the journal *Electrophoresis* heralded the word "Proteomics" into common usage. Dr Poljak is a reviewer for more than 20 international peer reviewed scientific journals.

Aims

The Proteomics group is a collaborative group composed of staff and students from CHeBA, the Neuropsychiatric Institute (NPI) and the MW Analytical Centre Bioanalytical Mass Spectrometry Facility (BMSF) at UNSW. The group was formed to apply state-of-the-art analytical techniques to the advancement of biomarker and pathophysiology research in the areas of normal ageing, Mild Cognitive Impairment (MCI), Alzheimer's disease and other age-related neurodegenerative conditions.

Achievements

- Dr Nady Braidy was the sole recipient of the Alzheimer's Australia Viertel Foundation Postdoctoral Research Fellowship in 2012 and was also awarded an NHMRC Early Career Research Fellowship (2013-2016). In 2012, he was awarded the International Investigator of the Year Award in Geriatric Psychoneuropharmacology for his contribution to ageing and neurodegenerative diseases and the UNSW Australia Dean's Rising Star Award.

- Dr Julia Müenchhoff was appointed as research associate on the ARC-funded project *"Plasma protein profiles in normal brain ageing and early stages of dementia"* and commenced investigating proteomics expression changes between two population based cohorts of similar design: MAS and the Hunter Community Study. Dr Müenchhoff was the recipient of two travel awards: a HUPO travel award to Yokohama Japan, 2013 and a Travel Award to the Alzheimer's Association International Conference (AAIC), Boston, USA, 2013, presenting research results of the plasma proteomics project.

CONSORTIA

CHeBA is positioned as a leader in multidisciplinary research into the ageing brain, and an international hub for collaborative engagement.

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.

CHeBA leads a number of international consortia: COSMIC, ICC-DEMENTIA and BrainInflame. 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) and PROMOTE (Psychosocial Research Consortium to Advance Mental Health for Older People in the Asia Pacific region).

COSMIC (COHORT STUDIES OF MEMORY IN AN INTERNATIONAL CONSORTIUM)

Founded in 2012, COSMIC aims to better understand the determinants of cognitive ageing and neurocognitive disorders by harmonising and pooling data from across numerous international longitudinal studies of cognitive ageing. Currently, COSMIC includes studies from Australia, Canada, USA, Brazil, China, South Korea, Hong Kong, Japan, Singapore, Spain, France and Italy.

Progress

1. A website was established to promote COSMIC and facilitate communication among member studies (**cheba.unsw.edu.au/group/cosmic**).
2. Ethics approval for the study was granted by the Human Research Committee of UNSW.
3. Studies involved in the planning of COSMIC were officially invited and enrolled as members.
4. Questionnaires were developed that sought information on the data obtained and held by member studies. These were circulated and the information returned used to develop a data request for the first project.
5. Progress was reported at AAIC 2013, with the abstract published in *Alzheimer's and Dementia*.
6. A meeting of member study leaders and representatives was held on July 15, 2013 in Boston.
7. A paper describing the rationale and methodology of COSMIC was approved by the member studies and published in *BMC Neurology*. This quickly led to contact from further studies interested in joining COSMIC.
8. By December 2013, there were 15 fully enrolled studies representing 4 continents: North America, Europe, Asia, and Australia. There were also 3 provisional members, and further studies in negotiation.
9. The first COSMIC project, titled "The prevalence of Mild Cognitive Impairment in diverse geographical and ethnocultural regions: the COSMIC collaboration", was well under way as of December 2013. Data had been requested, and usable data received from 10 studies. Strategies for harmonising data relating to education, functional ability, subjective cognitive complaints, and neuropsychological test scores were developed and implemented. For each contributing member study, the harmonised variables were used to make classifications of Mild Cognitive Impairment based on different approaches for quantifying objective cognitive impairment (cognitive domain scores derived from neuropsychological test results, Mini-Mental State Examination scores, and Clinical Dementia Ratings). As of December 2013, results obtained from the pooled, harmonised data were beginning to be supplemented by two studies in the form of their own results derived using the COSMIC protocols.

ICC-DEMENTIA

Formulated 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, Japan, South Korea, Germany, Sweden, Sardinia, Italy, Denmark and USA.

Progress

1. Data have been obtained from the participating centenarian studies for the initial harmonisation process.
2. An initial meeting of the consortium was held at the ICC meeting in South Korea in July 2013.
3. Two applications have been made for funding for phenotypic and genetic collaborations.

BRAININFLAME

Founded in January 2013, the BrainInflame during Ageing Consortium is the first of its kind to focus on inflammation related to brain function, and aims to attract international participation to further research understanding. Ageing is associated with enhanced systemic and brain inflammation, which may be linked to vascular damage, metabolic derangement and neuronal dysfunction, resulting in cognitive decline and depression. The study of risk and protective factors for inflammation, and the underlying molecular and neuronal mechanisms in relation to brain health, is an important objective of neuroscience research internationally. BrainInflame's research strategy entails both human and animal research, applying a forward and backward translation process. Current members of BrainInflame include the University of Adelaide, the University of Melbourne, the Queensland Brain Institute, the University of Groningen (the Netherlands), the University of Marburg (Germany) and the Royal College of Surgeons in Ireland (Ireland).

The objectives of *BrainInflame* are:

1. To examine the relationship between systemic inflammatory markers and brain dysfunction (cognitive impairment, cognitive decline and depression).
2. To examine the genetic basis of inflammatory markers and brain dysfunction.
3. To identify new inflammation-related genes and protein markers associated with neuropsychiatric disorders.
4. To relate systemic inflammatory markers with changes in grey and white matter.
5. To analyse gene expression profiles of inflammatory genes over time and relate to the development of brain dysfunction.
6. To pool and harmonise larger-scale studies for further systematic examination.
7. To conduct meta-analyses.

Progress

1. An NHMRC project grant was awarded to investigate the molecular underpinnings of brain ageing. At present three PhD students have been attracted to this research.
2. New staff were recruited to BrainInflame, with expertise in proteomics and gene expression studies (Dr David Stacey, University of Adelaide).
3. International collaborations have been established to work jointly on the proteomics components of inflammation during brain ageing, cognitive decline and depression in particular (Prof. David Cotter, Ireland). BrainInflame has entered a world-wide effort to discover the biological relationship between gene expression and genetic predisposition to peripheral inflammation (University of Groningen, Netherlands).
4. Professor Baune presented on the role of inflammation in brain disorders at international conferences, such as the European College of Neuropsychopharmacology meeting in Barcelona 2013.

PROMOTE

Founded in 2013, PROMOTE stands for Psychosocial Research Consortium to advance mental health of older people in the Asia Pacific region. Psychosocial research is an umbrella term that covers: causes and risk factors, mediating factors and contexts and outcomes. In psychogeriatrics it applies to mental disorders and behaviours occurring in older people, to their family carers, to professional carers, to systems of care, and to interactions with the environment. Approaches to psychosocial research derive from diverse sociological, psychological and social epidemiological paradigms, and from different theoretical frameworks.

Often the poor cousin to biological and clinical research, psychosocial research struggles to gain publication in high ranking journals, compete for research grants or to gain academic kudos. Yet many major advances in psychogeriatrics have been psychosocial and these have led to improvements in quality of life for older people with mental disorders and their families and cost savings for the community.

Despite their rapidly ageing populations and the projections that Asia-Pacific countries will account for half the world's older population with mental disorders within a generation, psychosocial research is poorly developed in this region. Furthermore, as local research conducted in many of the countries in the region is often published in their own language little

is known about their research outside their countries. By bringing together prominent investigators from six Asia-Pacific countries to describe local psychosocial research initiatives in psychogeriatrics, PROMOTE proposes to lay the foundations for the establishment of a regional consortium to advance psychosocial research and to enable collaboration, joint research programs, mentoring, training and dissemination of findings, and to facilitate cross-cultural knowledge translation. A/Professor Yun-Hee Jeon at the University of Sydney co-leads PROMOTE.

Progress

1. A joint research program has commenced to assess indicators of quality of care in nursing homes in four Asia-pacific countries. Ethics submissions are being prepared.
2. The second meeting of PROMOTE will take place at the International Psychogeriatric Association Conference in Beijing 23-26 October, 2014.

AUSTRALIAN BRAIN BANK NETWORK

The CHeBA Brain Donation Program collaborates with a number of other brain bank networks, including the NSW and Australian Brain Bank Networks. The CHeBA Brain Donation Program collects brain tissue from donors sourced from the Sydney 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 undertake detailed research into multiple aspects of ageing including healthy ageing, dementia and cognitive decline, as well as the role of genetics in ageing.

Progress

1. In 2013, 8 new brains were donated to the CHeBA Brain Donation Program.
2. 99 additional research participants have signed up to donate to the program.

COLLABORATORS

CHeBA is pleased to host two visiting fellows:
Professor Bernhard Baune in the Neuroinflammation group and
Associate Professor Pierre Lafaye de Micheaux in the Neuroimaging group.

VISITING FELLOWS

Professor Bernhard Baune is a specialist psychiatrist, clinician and researcher who is the Chair of Psychiatry and Head of the Discipline of Psychiatry, University of Adelaide, Australia. He leads the international consortium BrainInflame, is editor for the neuroscience and psychiatry section of *PLoS One* and on the editorial boards of the *International Journal of Neuropsychopharmacology, Stroke, Translational Psychiatry, Journal of Molecular Psychiatry* and *Depression Research and Treatment*. Professor Baune's research approach in psychiatry is at the interface between clinical research, psychiatric neuroscience and molecular psychiatry, stimulating forward and backward translational research in psychiatry. Areas of major research activity and internationally recognised expertise include the neurobiology of mood disorders, cognitive dysfunction and medical comorbidities. Currently, major research activities of his lab focus on the role of the immune system in the etiology and pathophysiology of psychiatric disorders. Additional research interests include the neurobiology of brain regeneration and functional trajectories in the long-term course of mental illness.

Associate Professor Pierre Lafaye de Micheaux is a researcher with degrees in physics, biostatistics, mathematical statistics and cognitive neuroscience. He is Associate Professor in the Department of Mathematics and Statistics at the University of Montreal, Canada and Assistant Professor at the Pierre Mendes France University, Grenoble. He is a member of the editorial committee of the PratiqueR collection (French). Professor Lafaye de Micheaux's research interests include asymptotics, biostatistics, Bootstrap, complex random fields, developing R packages, hypothesis testing theory, independent component analysis, linear regression methods, model selection, multiple testing, multivariate statistics, neuroscience, reproducible research, sample size determination, stochastic processes and time series analysis.

SOCIETIES/PROFESSIONAL ASSOCIATIONS

- International Neuropsychiatric Association (INA)
- International Society of Vascular Behavioural and Cognitive Disorders (VASCOG)
- International Psychogeriatric Association (IPA)
- International College of Geriatric Psychoneuropharmacology (ICGP)
- Royal Australian & New Zealand College of Psychiatrists (RANZCP)
- Australasian Society for Psychiatric Research (ASPR)

NATIONAL

Commonwealth

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

Western Australia

- Edith Cowan University, Perth

Tasmania

- University of Tasmania, Hobart

ACT

- Australian National University, Canberra

New South Wales

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

Sydney

- Academic Department for Old Age Psychiatry (ADFOAP)
- Neuropsychiatric Institute (NPI)
- Black Dog Institute
- Clinical Research Unit for Anxiety and Depression (CRUfAD)
- School of Medical Sciences, UNSW
- School of Psychology, UNSW
- School of Optometry, UNSW
- School of Biotechnology and Biomolecular Sciences, UNSW
- National Drug & Alcohol Research Centre (NDARC)
- Brain Sciences UNSW
- Neuroscience Research Australia (NeuRA)
- University of Western Sydney
- Prince of Wales Hospital
- Macquarie University
- Garvan Institute
- Australasian Research Institute, Sydney Adventist Hospital
- University of Sydney
- Bankstown-Lidcombe Hospital
- St Vincent's Hospital

South Australia

Adelaide

- Flinders University
- University of Adelaide

Victoria

Melbourne

- Monash University
- University of Melbourne
- National Ageing Research Institute
- Royal Melbourne Hospital

QUEENSLAND

Brisbane

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

INTERNATIONAL

Europe

- Innsbruck Medical University, Austria
- French National Institute of Health and Medical Research (Inserm), France
- University Aix-Marseille, France
- Max Planck Institute of Psychiatry, Germany
- Neuroscience Network Düsseldorf, Heinrich Heine University, Germany
- University of Marburg, Germany
- Golgi-Cenci Foundation, Italy
- University of Gothenburg, Sweden
- University of Zaragoza, Spain
- Lund University, Sweden
- University of Groningen, The Netherlands
- Masstricht University, The Netherlands

UK

- University of Aberdeen, Scotland
- University of Edinburgh, Scotland
- Cambridge University, England
- Cognitive Function & Ageing Studies, England
- University College London, England
- University of Leeds, England
- Royal College of Surgeons in Ireland, Ireland

North America

- Dalhousie University, Canada
- Université de Montréal, Canada
- University of California, California, USA
- Stanford University, California, USA
- University of Colorado, Colorado, USA

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

South America

- University of São Paulo, Brazil
- Universidad Católica de Chile, Chile

Asia

- Beijing Normal University, China
- Peking University, China
- Shanghai Jiaotong University, China
- Chinese University of Hong Kong, Hong Kong
- Hong Kong Polytechnic University, Hong Kong
- Keio University, Japan
- National Center for Geriatrics and Gerontology, Japan
- Tohoku University, Japan
- National University of Singapore, Singapore
- Seoul National University, South Korea

Middle East

- Sultan Qaboos University, Oman

Pacific

- Institut de Recherche pour le Développement (IRD), Tahiti, French Polynesia
- Institut Louis Malardé, Tahiti, French Polynesia

CURRENT PROJECTS

ABETA PEPTIDES IN PLASMA

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

Other investigators: Associate Professor George A Smythe (SOMS, UNSW), Dr Amelia Assareh (University of New England)

Project description: Correlation of plasma Aβ with cognition and brain volumetrics in Mild Cognitive Impairment.

Aims:

- Determine if plasma Aβ peptides 1-40 and 1-42 may be potential peripheral markers to assist in diagnosis of MCI and/or 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.

Progress to date: Data analysis completed, manuscripts in preparation.

Benefits: Identification of potential biomarkers to assist in diagnosis of predisposition to MCI and/or AD. Research into the possibility that plasma Aβ peptide levels are correlated with brain volumetric and cognitive changes.

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

Funding: NHMRC, Rebecca Cooper Foundation, Alzheimer's Australia Rosemary Foundation

Date commenced: 2007

Expected date of completion: ongoing project

ANALYSIS OF DNA METHYLATION VARIATION IN THE *APOLIPOPROTEIN-A1* GENE AND ITS RELATIONSHIP WITH EPISODIC MEMORY PERFORMANCE IN OLDER ADULTS

CHeBA staff: Karen Mather, Fei Song, Anne Poljak, Anbupalam Thalamuthu, Teresa Lee, Nicole Kochan, Perminder Sachdev

Other investigators: Ms Jessica Lazarus (Honours student, NeuRA), Associate Professor John Kwok (NeuRA), Associate Professor Margaret J. Wright (QIMR Berghofer Institute, Brisbane, Australia), Professor David Ames (National Ageing Research Institute), Dr Nicola Armstrong (Garvan Institute)

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.

Progress to date: Analyses are complete and the results are being prepared for publication.

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. Currently, she is writing this work up for publication.

Funding: NHMRC, Commonwealth Scientific and Industrial Research Organisation Flagship Collaboration Fund Grant, Alzheimer's Australia Dementia Research Foundation

Date commenced: February 2013

Expected date of completion: June 2014

ARCHIVING DATASETS OF THE BRAIN & AGEING RESEARCH PROGRAM

CHeBA staff: Perminder Sachdev, Henry Brodaty, Kristan Kang

Project description: To archive, and thereby make publicly available, the longitudinal datasets collected by the Brain and Ageing Research Program, School of Psychiatry, UNSW. Each of these datasets contains longitudinal data collected on older people ranging from healthy individuals to those with Mild Cognitive Impairment and dementia. These datasets contain the following types of data:

- cognitive phenotype
- neurocognitive assessment
- psychosocial questionnaires
- medical history + exam
- medication use
- neuroimaging
- blood chemistry
- proteomics
- genetics/genomics.

Aims:

- To facilitate the use of these datasets by researchers internationally, either by themselves or in combination with other comparable datasets, for novel enquiry and/or replication of findings from other cohorts.
- To facilitate collaborative research with and between international research groups studying brain ageing and age-related brain diseases.
- To archive the following datasets: the MAS, the OATS, the SCS and the Sydney Stroke Study (SSS).

Design & method: Archiving of data for access to international researchers requires that the data be stored in ASCIII format (de-limited text), and additional setup files be supplied to users for importing data, labels and other metadata into SPSS, SAS and STATA software environments. It also requires a 'codebook' or data-guide document (i.e. data definition statements) to aid and support analysis of archived data. The data will initially be hosted on a UNSW website, and procedures for access by external groups will be developed. Approval from the institutional ethics review board is being sought for this. Eventually, the data will be made available on the NACDA website or an alternative site such as the Alzheimer's Disease Neuroimaging Initiative (ADNI) after appropriate local approvals have been obtained.

Progress to date: The data has been fully archived. A "CHeBA Data" website, which acts as a data directory and portal whereby interested researchers can apply for and access data from the Brain & Ageing Research Program undertaken at the Centre for Healthy Brain Ageing is currently under construction.

Benefits: These datasets provide a significant opportunity to the research community because of the depth and breadth of the data collected. The databases invite inquiry from many fields, as well as providing a simple means for multidisciplinary research and projects. Potential fields of inquiry include: Psychology, Psychiatry, Gerontology, Epidemiology, Neuroimaging, Social Science, Genetics, Proteomics, etc. The datasets permit the replication of findings from other studies of ageing. These contain longitudinal cohort data which allow for the investigation into progression of diseases and neurocognitive disorders. Incidence rates of disorders can be determined, and normal ageing can also be studied. In addition to uni- and bi-variate analyses, the kinds of statistical analyses that could be conducted on these data include: mixed effects models, heritability analysis, structural equation modelling and other multivariate analyses.

Output: This project resulted in the production of the "CHeBA Data" website (above).. The website will be launched later in 2014.

Funding: National Institute of Health (USA)

Date commenced: January 2013

Expected date of completion: January 2014

ASSOCIATION BETWEEN SIRTUIN SINGLE NUCLEOTIDE POLYMORPHISMS AND FUNCTIONAL MARKERS OF BRAIN HEALTH IN AGEING

CHEBA staff: Nady Braidy, Anne Poljak, Perminder Sachdev

Project description: Emotional and cognitive decline represent major determinants to the quality of life during old age and in elderly patients with

dementia. Examining the genetic components of the ageing human brain by investigating the incidence and clinical implications of single nucleotide polymorphisms (SNPs) in sirtuin genes would help to:

1. identify individuals at risk, and
2. promote public health programs aimed at establishing healthy ageing.

Aims:

- Identify SNPs in seven sirtuin genes (SIRT1-7) in the plasma protein that occur with healthy brain ageing by examining cohorts ranging from 40-100+ years using cross-sectional data from multiple cohorts, as well as longitudinal analyses based on multiple waves of data collection within two cohorts.
- Investigate the associations between these SNPs and four functional markers of brain health and applicable tests to measure cognitive function, motor function and depressed mood.

Design & method:

Subject groups: Blood samples are available from the MAS (N=1037).

Genomic analysis: Following evaluation of the mass spectrometric data against protein databases, proteomic changes will be compared against changes in gene expression of the candidate proteins. Samples were assessed for yield using a spectrophotometer and quality using the RNA 6000 Pico Chip on the Agilent Bioanalyser. Samples with an RNA integrity number greater than 7.0 were used for polymerase chain reaction (PCR) assays.

Markers for brain health: The data from the MAS will be used to find associations between a SIRT5 SNP and functional markers of brain health. These variables of interest will be based on the results of seven standardised tests: *cognitive tests*, Digit Symbol Substitution Test (DSST), the Mini-Mental State Examination (MMSE); *motor function test*, Gait speed measure; *the mood or depressive symptoms tests*, Geriatric Depression Scale, and Goldberg Anxiety Scale; *clinical and functional status*, the Alzheimer's disease Assessment Scale-Cognitive subscale (ADAS-Cog), and clinical dementia rating (CDR-psychiatrist rating); *biochemical tests*, oxidative stress markers such as *o*- and *m*- tyrosine, malondialdehyde, apolipoprotein panels, inflammatory markers, and Aβ1-40 and Aβ1-42. These measures are highly appropriate for epidemiologic settings, and are useful in studying older populations.

HAP-MAP project: The International Hap-Map Project was used to compare the allele frequency of the sirtuin SNPs versus the genotypes obtained in the MAS. In addition, through the sirtuin SNP information from the Hap-map project, we aim to identify the respective genotype (C/C, C/T, T/T) for the MAS genotype coded in numbers (0,1,2).

Hardy-Weinberg equilibrium: This test can indicate if there are data-acquisition flaws or violations of assumptions of no mutation, selection, population substructure, etc.

Statistical analysis for associations between variables: Associations between variables within our data set will be analysed using appropriate statistical methods: Normaly tests will be performed for all continuous variables. When the normality of the variables is confirmed, ANOVA will be used to test the equality of the means for each selected category. If the variables are not normally distributed, then the nonparametric equivalent of ANOVA, Kruskal-Wallis test, will be used to analyse those variables. For comparisons of the categorical variables, chi-square tests will be performed. The statistical significance level will be reported as significant at the 5% ($p<0.05$), 1% ($p<0.01$), 0.1% ($p<0.001$) and highly significant as $p<0.000$ levels. Statistical analyses will be performed using SPSS 16.0 for Windows.

Progress to date: The patients have been recruited and the SNPs have been identified. The current data is under statistical analysis.

Benefits: The biological mechanisms that regulate the age-of-onset for neurological diseases remains unclear. However, the link between transcriptome changes and normal brain ageing has been identified. Sirtuins are proteins that have been reported to influence ageing, stress and metabolism. Since sirtuins are responsible for the regulation of energy output and maintenance of normal cellular function, scientific research has been involved in the process of illnesses such as diabetes, ageing, neurodegenerative disorders and cancer associated with mitochondrial dysfunctions and cellular dishomeostasis. The proposition to be addressed is that a relation between sirtuins and cellular repair is due to the acetylating process factor. Because of their role to preserve the proper cellular function, sirtuins are related in different disease processes (i.e. chronic and degenerative diseases). This research associates the low-expressing polymorphism of sirtuins with older brain molecular age. Previous research about the relationship between genes and neurological diseases has suggested that their

expression promotes positively the progression of the disease. Some studies have been focused on finding a relationship between the sirtuin mechanism and different pathways to address preventive methods and treatments for neurological diseases. The purpose of the current study is to identify and investigate the association between single nucleotide polymorphisms in sirtuin protein and functional markers of brain health in the MAS. These associations may clarify the role of the risk mutant sirtuin alleles and the low expressions of functional markers of brain health and assist in early protection from the detrimental age-dependent effects.

Output: Manuscript in preparation.
Funding: NHMRC
Date commenced: January 2013
Expected date of completion: December 2016

BRAIN PROTEOMICS: DIFFERENTIAL EXPRESSION OF THE PROTEOME IN AD

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

Other investigators: Professor Catriona MacLean (Monash University, Melbourne) Associate Professor George A Smythe (SOMS, UNSW), Associate Professor Mark Raftery (BMSF, UNSW Analytical Centre), Professor Glenda Halliday (NeURA), Dr Claire Shepherd (NeURA)

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 five 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 Cooper Foundation
Date commenced: 2007
Expected date of completion: ongoing

DEFINING THE ROLE OF INFLAMMATION IN DEPRESSION DURING AGEING

CHeBA staff: Bernhard Baune (visiting professorial fellow), Julian Trollor, Simone Reppermund, Perminder Sachdev

Other investigators: Dr Sarah Cohen-Woods (University of Adelaide)

Project description: The relationship between inflammation and geriatric depression is well-established, and offers the potential for the development of novel therapeutic strategies based on inflammatory targets. However, the relationship between depression and inflammation is complicated by age-associated factors (e.g. cardiovascular diseases, metabolic changes, morphological brain changes) which may contribute to both inflammation and depressive symptoms. It is therefore not yet known if inflammation is a cause or consequence, or both, of geriatric depression. Central to the unravelling of this complex relationship is the determination of whether inflammation causes depression onset in old-age, or if depression itself causes increased inflammation. However, research addressing the question of bi-directionality between inflammation and geriatric depression has not been undertaken. The potential in this area has been recently demonstrated by Baune's publication showing evidence of specific inflammatory markers predicting various states of depression (remitted, current, new onset) in old-age. The development of a more sophisticated biological model of inflammation in depression during ageing is required, and this proposal will incorporate rich

data including genome-wide genetic variants, transcriptomics, and inflammatory protein data to build a model with substantial predictive power. The project will therefore enable a rapid development of knowledge of the links between depression and inflammation. Our approach is critical and necessary in order to identify novel and improved therapeutic targets and if targeted intervention and prevention is to match the rapidly growing needs of the ageing population.

Aims:

- To understand the relationship between inflammation and depression during ageing, through the investigation of the bidirectional relationship between inflammatory biomarkers in the MAS.
- To investigate the molecular underpinnings of inflammation during ageing by analysing genetic, gene expression, and protein biomarkers.
- To develop an inflammation-based prediction model of depression (consisting of clinical, genetic, gene expression and protein biomarkers in the context of inflammation) during ageing in the MAS (discovery sample) and to replicate in a second ageing sample, the OATS.

Design & method: Our study builds on two well-characterised ageing cohorts, with the aim to assay blood-based inflammatory biomarkers (proteins and gene-expression) to determine their correlation with depression. Samples were collected at the time of in-depth assessments including a psychiatric assessment of later waves. These assessments collect data on 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. Then, in order to capitalise on the rich resources available in the fourth wave of the MAS (DNA, RNA, serum), we will take a cross-sectional approach with the aim to identify gene expression that predicts these 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 demographic, clinical, confounders, 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. Through the prospective study of genotype, inflammatory signalling proteins, gene expression and depression diagnosis, we will clarify the biological role of inflammation in these mood states, and identify potential markers that could predict first onset of depressive symptoms in the elderly, as well as identify markers of remitted and current conditions and identify new targets for the treatment of depression.

Progress to date: Gene expression and serum analyses are in preparation. 1 PhD student has been appointed to the project, with another to be recruited. International collaborations have been commenced to support the project.

Benefits: This study is the first of its kind to address the question of bidirectionality between inflammation and depression in ageing. Through discovery, replication, and optimisation of a predictive model based on proteins, genes and gene expression, we will determine the potential utility of our discoveries in predicting inflammation related depression. An improved understanding of the biological and molecular underpinnings of inflammation and depression, and also directionality between the inflammation-geriatric-depression associations could lead to early identification of risk factors, and to novel and improved pharmacotherapies. This proposal will provide novel data of significant impact for prevention and interventions.

Output: None to date.

Funding: NHMRC (administered by University of Adelaide)

Date commenced: July 2013

Expected date of completion: December 2015

DIAGNOSING MAJOR DEPRESSION IN OLDER AUSTRALIAN ADULTS: IS THERE EVIDENCE FOR AGE-RELATED BIAS?

CHeBA staff: Dr Louise Mewton, Gavin Andrews, Perminder Sachdev

Other investigators: Dr Matthew Sunderland (UNSW), Dr Natacha Carragher (UNSW), Dr Phillip Batterham (UNSW)

Project description: Nationally representative surveys provide valuable information regarding the pervasiveness, risk factors, and service use associated with major depressive disorder (MDD) in

the community. This information is utilised by mental health policy makers to direct limited funding towards subgroups of the population that would benefit from targeted prevention and treatment programs (Jenkins, 2001). It is crucial that epidemiologic surveys, research studies, and policy makers assess MDD and accurately estimate prevalence and incidence rates using methods that are valid for different age groups. Likewise, it is essential that clinicians accurately determine a suitable diagnosis for patients of all ages to facilitate a positive treatment outcome. However, there is significant controversy in the literature regarding the accuracy of the diagnostic criteria for MDD in older adults. The current project aims to address the pressing need to clarify the validity of mental health assessment methods used to diagnose DSM-IV MDD in older individuals (aged 65+) within the Australian population.

Aims:

- Investigate the extent of age-related bias in the endorsement of DSM-IV MDD criteria used to estimate prevalence rates in the 2007 Australian National Survey of Mental Health and Wellbeing.
- Examine the sources of bias in older adults' interpretation of, and their capacity to respond to, self-reported questions that operationalise the diagnostic criteria for MDD.
- Propose recommendations to revise the way MDD is assessed in older adults.

Design & method: To achieve these objectives this study will utilise a complementary two-step procedure that first makes use of sophisticated statistical techniques in large epidemiological datasets followed by a series of cognitive interviews in a small target sample of older Australian adults.

Progress to date: Expert review of diagnostic symptoms completed, cognitive interview designed, recruitment commenced.

Benefits: The outcomes of the proposed research project include:

- A comprehensive understanding of the potential presence of age-related bias in prevalence estimates of MDD in old age Australian adults.
- A reliable and statistically-driven estimate of the relative impact of age-related bias on the current Australian MDD prevalence estimates in the old age population. The prevalence will be revised taking into account the impact of age-related bias.
- A greater understanding of the potential factors associated with old age that contributes to age-related bias in the assessment of MDD.
- A set of practical recommendations, based on empirical results, to revise the way MDD is assessed in the old age population for future epidemiological and clinical studies conducted in Australia and internationally.

Output: 3 journal articles, 1 conference presentation.
Funding: NHMRC
Date commenced: January 2013
Expected date of completion: December 2014

THE GENETIC AND ENVIRONMENTAL DETERMINANTS OF AMYLOID DEPOSITION IN OLDER INDIVIDUALS: AN AMYLOID IMAGING STUDY USING THE TWIN DESIGN (PIB/PET PILOT STUDY)

CHeBA staff: Melissa Slavin, Wei Wen, Anbupalam Thalamuthu, Julian Trollor, Henry Brodaty, John Crawford, Teresa Lee, Karen Mather, Perminder Sachdev

Other investigators: Professor Christopher Rowe (University of Melbourne)

Project description: β-amyloid (Aβ) plaques are one of the hallmark neuropathologies of Alzheimer's disease (AD), but many aspects of their role in the disease are unclear. Until recently amyloid plaque burden could only be determined post-mortem. Recent developments in neuroimaging allow amyloid burden to be assessed *in vivo* using positron emission tomography (PET), making it possible to examine the relationship between amyloid load and cognitive function in temporal proximity, and to design studies to examine its risk and protective factors. Here we use the power of the twin design to examine the relative contributions of heritable and other risk factors to amyloid deposition in the brains of older individuals, and further investigate its possible contribution to cognitive impairment, in one of the first large studies of its kind. To date, only one small twin study internationally has examined Aβ burden among MZ and DZ twins discordant for cognitive impairment.

Aims:

- To examine genetic and environmental factors and their interactions associated with β-amyloid (Aβ) deposition in the brains of older individuals.
- To determine the heritability of Aβ deposition in the brain as an endophenotype of Alzheimer's disease (AD).
- To determine the shared genetic and environmental variance between amyloid load and i) cognition, ii) cardiovascular disease, and iii) cerebral atrophy.

- To investigate the genetic and environmental risk (and protective) factors associated with amyloid load in older individuals. These factors include:
  - Genetic factors such as the apolipoprotein E (*APOE*) gene, the brain-derived neurotrophic factor (*BDNF*) gene, amyloid pathway genes, and other genetic polymorphisms with possible roles in amyloid deposition.
  - Environmental factors such as cognitive reserve (education, complex cognitive activity and exercise), vascular risk factors, traumatic brain injury and depression.
- To investigate the relationship between amyloid load and memory function cross-sectionally, and decline in memory longitudinally, and possible moderation of this relationship by cognitive reserve and cerebral vascular disease.

Design & method: Twin pairs will be recruited from the OATS and invited to undertake a PiB-PET scan. *Inclusion criteria*: aged 65 years or older, ability to consent, having a consenting MZ or DZ co-twin, having completed some education in English, and a minimum of at least low average estimated premorbid IQ. *Exclusion criteria*: history of epilepsy, other neurological disorder or a systemic disease impacting on cognitive functioning; current diagnosis of an acute psychotic disorder or major depression.

Progress to date: PiB-PET scans of 60 participants (17 MZ, 13 DZ pairs) were performed at Austin Hospital, Melbourne as part of the OATS. The moderate correlation of SUVR in MZ twins and the lack of correlation in DZ twins are noteworthy. However, heritability estimates are moderate, suggesting significant environmental contributions to amyloid deposition. Using 1.5 SUVR as the cut-off for a +ve scan, 6/60 (10%) (2 MZ and 4 DZ) were positive; all were discordant, with their co-twins being –ve. Among the discordant MZ twins, the greatest differences in amyloid deposition were seen in the orbitofrontal area, striatum and the anterior and posterior cingulate gyri. Among the DZ twin pair, similar regional differences in amyloid deposition were seen, with differences also seen in the ventro-lateral prefrontal area and temporal lobe. The amyloid load was not significantly associated with global cognition, memory or any of the other cognitive domains examined in this small sample. The genetic correlations of Global SUVR with memory domain and white matter hyperintensities were low and non-significant.

Benefits: Greater understanding into the role of amyloid deposition in the brains of older individuals and its possible contribution to cognitive impairment.

Output: None to date.

Funding: NHMRC

Date commenced: January 2013

Expected date of completion: December 2014

GENETICS OF APOLIPOPROTEINS

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

Other investigators: Dr Chris Oldmeadow (University of Newcastle), Professor John Attia (University of Newcastle), Associate Professor Margaret J. Wright (QIMR Berghofer Institute, Brisbane), Professor David Ames (National Ageing Research Institute), Dr Nicola Armstrong (Garvan Institute)

Project description: Apolipoproteins are important transporters of cholesterol. Previous studies implicate apolipoproteins with cognitive performance and decline. Heritability of seven plasma apolipoproteins was assessed using the Older Australian Twins Study. The majority of apolipoproteins showed a significant genetic component. 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.

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

Design & method: Plasma apolipoproteins were measured using an immunoassay method. Genome-wide genotyping data imputed to Hapmap 2 was used for analyses. Genome-wide association studies for plasma apolipoproteins were undertaken and meta-analyses performed.

Progress to date: Analyses are complete and the results are being prepared for publication.

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

Output: This work is currently being analysed for publication and conference presentation.

Funding: NHMRC, ARC, Commonwealth Scientific and Industrial Research Organisation Flagship Collaboration Fund, Alzheimer's Australia Dementia Research Foundation

Date commenced: February 2013

Expected date of completion: June 2014

GENETICS OF GRIP STRENGTH

CHeBA staff: Jessica Chan (Medicine student), Karen Mather, Anbupalam Thalamuthu, Jasmine Menant, Perminder Sachdev

Other investigators: Dr Nicola Armstrong (Garvan Institute), Dr Chris Oldmeadow (University of Newcastle), Professor John Attia (University of Newcastle), Professor Stephen Lord (NeuRA), Associate Professor John Kwok (NeuRA), Professor Peter Schofield (NeuRA)

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.

Progress to date: Analyses are complete and the results are being prepared for publication.

Benefits: Potential benefits from this work include a better understanding of the contributions of genetics to muscle strength, specifically, grip strength.

Output: The results were written up as the final report for a successful Medicine Independent Learning Project by Jessica Chan. Currently, Jessica is writing this work up for publication.

Funding: NHMRC, Alzheimer's Australia Dementia Research Foundation

Date commenced: February 2013

Expected date of completion: June 2014

GENETICS OF WHITE MATTER HYPERINTENSITIES

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

Other investigators: Dr Amelia Assareh (University of New England), Dr Nicola Armstrong (Garvan Institute), Professor Peter Schofield (NeuRA), Associate Professor John Kwok (NeuRA), Professor Simon Easteal (Australian National University), Associate Professor Margaret J. Wright (QIMR Berghofer Institute, Brisbane, Australia), Professor David Ames (National Ageing Research Institute)

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 etiology of white matter hyperintensities is unclear but is thought to be ischemic in origin. Heritability studies suggest WMHs have a genetic component.

Aims: To identify genetic variants associated with white matter hyperintensities.

Design & method: WMH burden was estimated from neuroimaging scans of participants from the MAS, the OATS and the PATH Through Life Study (administered by the Australian National University). Genome-wide genotyping data imputed to Hapmap 2 was used for analyses in the MAS and the OATS. In PATH, specific genetic variants were genotyped using standard methods. Candidate gene analyses were undertaken for WMHs in PATH. Genome-wide association studies for WMH measures were undertaken in the MAS and the OATS and meta-analyses performed.

Progress to date: Analyses are complete for the candidate gene studies and a manuscript has been written and submitted for peer-review. The results of the GWAS are still being assessed.

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

Output: A manuscript has been prepared and submitted for review.

Funding: NHMRC, Commonwealth Scientific and Industrial Research Organisation Flagship Collaboration Fund, DCRC, Alzheimer's Australia Dementia Research Foundation

Date commenced: 2012

Expected date of completion: December 2014

GENOME-WIDE ASSOCIATION STUDIES OF COGNITIVE PERFORMANCE IN COLLABORATION WITH THE CHARGE CONSORTIUM (COHORTS FOR HEART AND AGING RESEARCH IN GENOMIC EPIDEMIOLOGY CONSORTIUM)

CHeBA staff: Perminder Sachdev, Karen Mather, Anbupalam Thalamuthu, Nicole Kochan, Teresa Lee

Other key investigators: Associate Professor John Kwok (NeuRA), Professor Peter Schofield (NeuRA), Associate Professor Margaret J. Wright (QIMR Berghofer Institute, Brisbane, Australia), Professor David Ames (National Ageing Research Institute), Dr Amelia Assareh (University of New England), Dr Nicola Armstrong (Garvan Institute)

Project description: Heritability studies suggest genetic variation plays a major role in age-related 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.

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

Design & method: A genome-wide association study (GWAS) was performed on various cognitive measures using the Sydney Memory and Ageing Study and the Older Australian Twins Study. Our GWAS data contributed to a meta-analysis 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. For others, CHARGE is still assessing the results.

Benefits: Identification of genetic variants associated with age-related performance may lead to clarification of the biological underpinnings of age-related cognitive performance. Potentially, these results may lead to targeting those at risk of age-related cognitive decline and preventative or therapeutic strategies.

Output: Currently, papers are under review and include GWAS of verbal memory, executive functioning and processing speed.

Funding: NHMRC, ARC, CSIRO Flagship Collaboration Fund, Alzheimer's Australia Dementia Research Foundation

Date commenced: 2012

Expected date of completion: Ongoing

GENOME-WIDE ASSOCIATION STUDIES OF SUBCORTICAL STRUCTURES IN COLLABORATION WITH THE ENIGMA CONSORTIUM (ENHANCING NEUROIMAGING GENETICS THROUGH META-ANALYSES CONSORTIUM)

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

Other key investigators: Associate Professor John Kwok (NeuRA), Professor Peter Schofield (NeuRA), Associate Professor Margaret J. Wright (QIMR Berghofer Institute, Brisbane), Professor David Ames (National Ageing Research Institute), Dr Nicola Armstrong (Garvan Institute)

Project description: Genetics plays an important role in brain structures, as shown by heritability studies. The ENIGMA consortium, comprised of a number of international studies, seeks to find genetic variants associated with different subcortical structures such as the putamen and nucleus accumbens.

Aims: To identify single nucleotide polymorphisms (SNPs) for subcortical structures.

Design & method: A genome-wide association study was performed on subcortical structures 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.

Progress to date: Analyses are currently being completed.

Benefits: Identification of genetic variants associated with subcortical structures may lead to a greater understanding of their biology.

Output: Currently, analyses are being completed and a manuscript is being prepared by ENIGMA.

Funding: NHMRC, ARC, Commonwealth Scientific and Industrial Research Organisation Flagship Collaboration Fund, Alzheimer's Australia Dementia Research Foundation

Date commenced: 2012

Expected date of completion: Ongoing

HERITABILITY AND GENETIC INFLUENCE OF BRAIN STRUCTURES IN OLDER INDIVIDUALS USING OLDER AUSTRALIAN TWINS DATA

CHeBA staff: Wei Wen, Anbupalam Thalamuthu, Karen Mather, Jiyang Jiang, Pierre Lafaye de Micheaux (visiting research fellow), Perminder Sachdev

Other investigators: Dr Wanlin Zhu (Beijing Normal University, Beijing, China), Associate Professor Margaret J. Wright (QIMR Berghofer Institute, Brisbane, Australia), Professor David Ames (National Ageing Research Institute, Royal Melbourne Hospital)

Project description: As the population is ageing, a greater understanding of the genetic contributions to human brain structure 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. Here we plan to do comprehensive heritability and genetic correlation analysis of cortical and sub-cortical structures of 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 and sub-cortical structures of the human brain.

Design & method: We are studying over 400 twins aged 65 years and over (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. Shapes and volumes of cortical structures and volumes of 7 subcortical structures were obtained from neuroimaging scans of the MAS and the OATS. Heritability at voxel level and at 34 regions of interest (ROIs) were obtained for cortical regions. For the 7 subcortical regions, voxel level heritability estimates were obtained. Genetic correlation among the ROIs of cortical and subcortical regions was also obtained.

Progress to date: We have mapped heritability for both cortex and subcortical structures. This is the first large study of older twins of both sexes. Both the cortex and subcortical structures are examined. For the latter, three dimensional surface information was extracted for the first time. Bilateral symmetry for genetic influences was examined. Shared genetics between cortical areas and subcortical structures were investigated. The genetic architecture of the brain was also examined separately for men and women. In our preliminary results, we found that genetic patterns in the brain were generally bilaterally symmetrical. In the cortex, the superior frontal region had the greatest heritability, with an anterior-posterior gradient of genetic influence, and low genetic influence of the precuneus and the posterior cingulate. The genetic influence on the subcortical structures ranged from the lowest for the amygdala to the highest for the thalamus, with the accumbens, hippocampus, putamen, pallidum and caudate being in-between. The genetic control of the surface characteristics of the subcortical structures is not uniform, e.g. the head and the tail of the hippocampus had greater genetic mediation than the body.

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: Manuscript in preparation.

Funding: NHMRC, Alzheimer's Australia Dementia Research Foundation

Date commenced: July 2013

Expected date of completion: December 2014

IMPROVING CLINICAL DIAGNOSIS OF MILD NEUROCOGNITIVE DISORDERS USING NEUROPSYCHOLOGICAL ASSESSMENT

CHeBA staff: Nicole Kochan, Perminder Sachdev, Henry Brodaty, Melissa Slavin, John Crawford

Other investigators: Professor Kaarin Anstey (ANU), Professor David Bunce (University of Leeds, UK), Professor John R Crawford (University of Aberdeen, Scotland)

Project description: Clinical diagnosis of mild neurocognitive disorders using neuropsychological assessment is challenging in Australia because US normative data are typically used for comparison and cognitive problems are subtle and difficult to detect.

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 of non-English speaking background (NESB) 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 culturally and linguistically diverse (CALD) backgrounds.

Design & method: Data for this project will be primarily drawn from the MAS, which has a longitudinal prospective design.

Component 1: Australian normative data

This normative study will use demographic and neuropsychological data from wave 1 to construct normative data. Native English speakers (those that learned English before the age 10) (N=878) from the baseline MAS cohort will be 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. To date, 12 tests have been administered to the MAS participants from seven cognitive domains. Multiple measures are available for each test. Multiple linear regression analyses will be used to examine the influence of demographic variables (age, years of education, sex) on raw scores for each test. The proportion of variance explained by each variable will inform the relevant set of variable(s) that will be adjusted for. For the analysis of the NESB sample, education, linguistic and cultural factors will be entered into a multiple regression analysis to establish an appropriate regression equation that can be used to adjust performance for these variables in NESBs.

Component 2: Computerised neuropsychological test battery

Demographic, clinical and neuropsychological (from both paper-and-pencil and computerised tests) data and diagnostic classifications (cognitively normal, MCI and dementia) from waves 1 (baseline), 2 (2 years later) and 3 (4 years later) will be used. The clinical validation component of the study will use a cross-sectional design. The SENSUS battery will be administered to patients at the POWH Memory Disorders Clinic. Diagnostic and neuropsychological data will also be collected.

Progress to date:

Component 1:

Data analyses completed in the native English speaker sample, beta version of software program completed which will be used as a normative data calculator, main manuscript is in preparation, NESB analyses have commenced.

Component 2:

Ethics for the clinical study has been obtained and recruitment of hospital patients has commenced. Data have been cleaned for wave 1 SENSUS measures and wave 2 is underway. The first study examining the predictive value of reaction time measures is completed and manuscript preparation has commenced.

Benefits: The new data will improve practice 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.

Output: 3 conference abstracts, 1 invited presentation.

Funding: NHMRC, DCRC (for pilot study)

Date commenced: March 2012

Expected date of completion: December 2016

INFLAMMATORY MARKERS AND BRAIN STRUCTURE

CHeBA staff: Jiyang Jiang, Wei Wen, Julian Trollor, Perminder Sachdev

Other investigators: Associate Professor David Brown (St Vincent's Centre for Applied Medical Research)

Project description: Using circulating inflammatory markers and magnetic resonance imaging (MRI), recent studies have associated inflammation with brain volumetric measures.

Aims: To examine the relationship of serum levels of a divergent transforming growth factor – beta (TGF-β) superfamily cytokine, Macrophage Inhibitory Cytokine – 1 (MIC-1/GDF15), with human brain grey matter (GM) volumes, in a community-dwelling sample aged 70-90 years over two years.

Design & method: We approach the possible relationship between brain structures and an emerging novel inflammatory biomarker, Macrophage Inhibitory Cytokine-1 (MIC-1/GDF15), which is a member of the transforming growth factor-β (TGF-β) superfamily. The serum MIC-1/GDF15 concentration for both wave 1 and wave 2 was determined using an enzyme-linked immunosorbent assay (ELISA). We used T1-weighted MRI scans which were obtained by the MAS at both wave 1 and wave 2. We analysed the scans using the FMRIB Software Library and FreeSurfer.

Progress to date: Our preliminary results showed a significantly negative association between MIC-1/GDF15 serum levels and both subcortical and cortical GM volumes. Increases in MIC-1/GDF15 serum levels were associated with decreases in cortical GM volume over two years. MIC-1/GDF15 serum levels were inversely associated with GM volumes both cross-sectionally and longitudinally.

Benefits: This is the first study that has investigated the relationship between the blood level of MIC-1/GDF15 and brain GM volume, in both cross-sectional and longitudinal settings.

Output: 1 paper submitted for review.
Funding: NHMRC
Date commenced: January 2013
Expected date of completion: December 2015

IS WHITE MATTER AN EARLIER BIOMARKER THAN GREY MATTER FOR ALZHEIMER'S DISEASE?

CHeBA staff: Lin Zhuang, Wei Wen, Perminder Sachdev

Project description: White matter (WM) loss is a common finding in Alzheimer's disease (AD), but it is unclear whether WM damage is linked to amyloid pathology in AD.

Aims:

- To investigate whether microstructural white matter changes similar to those identified in AD patients can be detected in cognitively normal non-demented individuals destined to develop amnestic Mild Cognitive Impairment (aMCI).
- To examine the relationships between brain amyloid burden as measured by cerebrospinal fluid (CSF) $A\beta_{42}$ levels and white matter degeneration at different stages of the AD process.

Design & method: Data was obtained from the MAS and the Alzheimer's Disease Neuroimaging Initiative (ADNI) database. We studied cognitively normal individuals at baseline (wave 1) of the MAS. The majority remained cognitively stable (CN-stable) in the next few years (wave 2 and wave 3) and some were diagnosed with aMCI (CN-aMCI converter) some years later. Structural magnetic resonance imaging and diffusion tensor imaging were acquired at baseline to assess grey matter atrophy and microstructural white matter changes respectively. We also examined CSF $A\beta_{42}$ levels in cognitively normal individuals, early Mild Cognitive Impairment (EMCI), late Mild Cognitive Impairment (LMCI), and AD using ADNI data. Fractional anisotropy (FA) index measuring WM integrity was derived from diffusion tensor imaging (DTI), while grey matter (GM) structural measures including cortical thickness and hippocampal volume were obtained on concurrently acquired MRI structural images.

Progress to date: Near completion.

Benefits: This work will be the first to reveal the potential of white matter DTI measures as a non-invasive biomarker in early diagnosis of AD. The results will have immediate and direct clinical implications, as DTI is less expensive and more readily available (vs. fluorodeoxyglucose positron emission tomography - FDG-PET, amyloid imaging using Pittsburgh compound B PET - PiB-PET) and less invasive (vs. CSF) than conventionally accepted biomarkers. It also opens up WM degeneration as an independent field of enquiry in AD, the mechanisms for which remain to be understood.

Output: 4 peer-reviewed publications (including *Neurology*), 2 further papers have been submitted for review.

Funding: NHMRC

Date commenced: July 2012

Expected date of completion: December 2014

THE OLDER AUSTRALIAN TWINS STUDY

CHeBA staff: Perminder Sachdev, Henry Brodaty, Julian Trollor, Wei Wen, Bernhard Baune (visiting professorial fellow), Teresa Lee, John Crawford, Karen Mather, Melissa Slavin, Anbupalam Thalamuthu, Gavin Andrews, Andrea Lammel (to April 2013), Jocelyn Bowden (from July 2013), Kristan Kang

Other investigators: Associate Professor Margaret J. Wright (QIMR Berghofer Medical Research Institute), Professor David Ames (NARI, University of Melbourne), Professor Nick Martin (QIMR Berghofer Medical Research Institute), Professor Peter Schofield (NeuRA), Professor Katherine Samaras (Garvan Institute)

Project description: The OATS is the largest and most comprehensive ageing study with elderly twins ever undertaken in Australia. It is a multi-centre, longitudinal study that commenced in New South Wales in 2007 and in Queensland and Victoria in 2008. Two-year and four-year follow-up tests are carried out to measure change. Study participants are identical and non-identical twin pairs aged 65 years and older, living across the eastern seaboard. Initially, 623 participants were recruited with 450 participants re-tested at their two-year follow up. Participants undergo rigorous medical and cognitive function tests, are asked to provide blood samples and have 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 the participant's memory and thinking and daily functions.

Aims:

- To maintain a well-characterised cohort of MZ and DZ twin pairs for longitudinal data.
- 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 load.
- Exploration of the genetic basis of cognitive decline and brain changes in old age, as part of international consortia.

Design & method: Participants were recruited mainly through the Australian Twins Registry, during Wave 1 of the study. The Wave 3 assessment repeats some aspects of the Waves 1 and 2 assessments, but is more focused on current state and interval history. Assessments are performed by the Research Assistant (RA) either in participants' homes or at our research facilities (duration 3-4 hours). Neuroimaging will be performed if the participant agrees to a scan. Blood is collected by an experienced phlebotomist at an established collection centre or at the participant's home, and processed using our existing collaboration with South Eastern Area Laboratory Services (SEALS). When necessary, cognitive diagnosis (normal, MCI, and Dementia by subtype) is made by two experienced clinicians (A/Prof J.Trollor, Prof P. Sachdev) and one senior neuropsychologist (Dr T. Lee) after presentation of the data at consensus case conference.

Interview, medical assessment and neuropsychological assessment include:

- Change in demographics: age, gender, 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;
- Interval medical examination including height and weight to allow BMI calculation, blood pressure and heart rate;
- Motor examination (timed walk test, lateral stability, speech, 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 will also be 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, mini-mental state examination and clock drawing;
- 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 about the Informant: 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 (60mLs) 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.

Progress to date:

- 2-year follow-up assessments (Wave 2) were completed in November 2013, with 450 participants re-tested. Blood samples were collected from 404 participants, while 292 participants agreed to have MRI scans. Data from these assessments have been compiled and cleaned, and will shortly be released for analysis.
- 4-year follow-up assessments (Wave 3) commenced in January 2013. As of December 2013, 145 participants had been re-tested. Blood samples were collected from 98 participants and MRI scans performed for 77 participants. Wave 3 data collection will continue until late 2015.
- Two PhDs were completed in 2013 (T Lee and SAH Batouli). These theses focused on cognition and brain imaging.
- Continued collaboration with the ENIGMA (Enhancing Neuroimaging through Genetic Meta-analysis) and CHARGE (Cohorts for Heart & Ageing Research Genetic Epidemiology) consortiums.
- Established a new collaboration with international consortium to investigate the genetic contribution of diabetes and other hereditable conditions in twin cohorts (EUrodiscoTwin Consortium).

Benefits: Data from the OATS Wave 1 has made significant contributions to understanding the genetic factors underlying many aspects of cognition and brain imaging parameters. Salient 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 spectroscopic 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.

Output:

- 5 peer-reviewed journal publications have been published in the *Journal of Gerontology B Series, Neurobiology of Aging, Ageing Research Reviews, International Reviews of Psychiatry and Current Opinion in Psychiatry.*
- 2 PhD (UNSW) and 1 Honours thesis (CQU).
- 5 conference proceedings from international conferences.

Funding: NHMRC
Date commenced: 2007
Expected date of Completion: December 2015

PERSONALITY AND TOTAL HEALTH THROUGH LIFE PROJECT (PATH)

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

Other investigators: Professor Kaarin Anstey (ANU), Associate Professor Peter Butterworth (ANU), Dr Nicholas Cherbuin (ANU)

Project description: The PATH Project, run by the Centre for Research on Ageing, Health and Wellbeing, Canberra, is a large, on-going, population-based, longitudinal cohort study comprising approximately 7500 participants ranging from early to late adulthood. The project aims to track and define the lifespan course of depression, anxiety, substance use and cognitive ability, identify environmental risk and protective factors within these domains, and examine the relationships between depression, anxiety and substance use with cognitive ability and dementia. PATH has resulted in over 100 publications, and is unique among cohort studies in its age range and duration of follow-up.

Aims: PATH aims 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 four broad themes

that are relevant to each of these problems: ageing vs cohort effects; social, psychological, nutritional and genetic risk factors; and co-morbidity of mental health problems.

Design & method: PATH has 3 epidemiological cohorts (20-24, 40-44 and 60-64 years) to be followed up fourth yearly for 20 years. The two older cohorts are of interest to CHeBA and comprise 2530 individuals aged 40-44 years, and 2551 individuals aged 60-64 years at Wave 1 assessment.

Progress to date: Our group has taken responsibility for the neuroimaging and clinical chemistry components of the study. The study is now in its 4th wave (12 years from baseline), and the wave 4 assessments of the 60+ cohort are due to be completed in mid-2014.

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 **crahw.anu.edu.au/research/projects/personality-total-health-path-through-life**. 5 publications with CHeBA co-authors in 2013.

Funding: NHMRC

Date commenced: 1999

Expected date of completion: ongoing

PLASMA PROTEOMICS BIOMARKERS

CHeBA staff: Julia Müenchhoff, Anne Poljak, Fei Song, Tharusha Jayasena, Nicole Kochan, Julian Trollor, Henry Brodaty, Perminder Sachdev

Other investigators: Associate Professor George Smythe (SOMS, UNSW), Professor Mark Duncan (University of Colorado), Associate Professor Mark Raftery (BMSF, UNSW), Professor John Attia (University of Newcastle), Associate Professor Peter W. Schofield (University of Newcastle), Professor Ralph Martins (Edith Cowan University, Perth)

Project description: Plasma protein profiling of Mild Cognitive Impairment and Alzheimer's disease across two independent cohorts.

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: the MAS (all 4 waves), Hunter Community Study (HCS), Dominantly Inherited Alzheimer's disease Network (DIAN), the OATS and the 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 Cooper Foundation, Alzheimer's Australia Rosemary Foundation

Date commenced: 2006

Expected date of completion: ongoing

PREVENTION AND MANAGEMENT OF MENTAL DISORDERS IN OLDER AUSTRALIANS (CAPACITY BUILDING GRANT)

CHeBA staff: Perminder Sachdev, Henry Brodaty, Lee-Fay Low, Jasmine Menant, Karen Mather, Louise Mewton, Nady Braidy, Nicole Kochan, Simone Reppermund, Wei Wen, Anne Poljak, Brian Draper, Gavin Andrews

Other investigators: Professor Stephen Lord (NeuRA), Professor Helen Christensen (Black Dog Institute), Professor Jacqueline Close (NeuRA), Dr John Piggott (UNSW), Associate Professor Olivier Piguet (NeuRA), Professor Felicia Huppert (Cambridge), Professor Philip Mitchell (UNSW), Professor Peter Schofield (NeuRA), Associate Professor Gilles Guillemin (UNSW), Professor Maree Teesson (NDARC), Professor Michelle Moulds (Psychology, UNSW)

Project description/aims:

- Understanding health and disease in older people living in the community, and improving their health and well-being through priority health approaches. Six streams have been identified to comprise the research agenda that team investigators (TIs) will address:
  - Optimising the use of epidemiological mental health data in the elderly;
  - Identifying at-risk individuals;
  - Establishing risk factors for cognitive ageing;
  - Positive and successful ageing;
  - Preventing dementia and/or delaying its onset; and
  - New services for cognitively impaired older Australians.
- Finding new evidence to inform policy and practice relating to the care of the elderly.
- 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.

Progress to date: Since 2009, the CBG has 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 been awarded more than $11 million in competitive grants and have supervised 28 higher degree research students.

Output: >100 publications.

Funding: NHMRC Capacity Building Grant
Date commenced: January 2009
Expected date of completion: December 2014

RELATIONSHIP BETWEEN VESTIBULAR FUNCTION, DIZZINESS AND FALLS IN OLDER PEOPLE COMMUNITY-DWELLERS

CHeBA staff: Jasmine Menant, Perminder Sachdev, Henry Brodaty

Other investigators: Dr Daina Sturnieks (NeuRA and UNSW), Dr Kim Delbaere (NeuRA and UNSW), Associate Professor Prof Jacqui Close (Neura and UNSW), Professor Stephen Lord (NeuRA and UNSW)

Project description: Despite evidence of the high prevalence of vestibular vertigo among people aged over 60 years and reports that a large proportion of older people who present to emergency departments due to a fall have a recent history of vestibular impairment, clinical assessments of vestibular function are seldom conducted as part of a fall risk assessment.

Aims: This study examined further the relationship between vestibular function and falls, using a range of vestibular function tests, which should allow the precise identification of the source of the vestibular impairment.

Design & method: This is a cohort study of prospective falls. Older community-dwelling people aged 70 years and over were recruited amongst participants from the Wave 4 of the Sydney Memory and Ageing Study. Participants underwent a multidisciplinary baseline assessment comprising self-report items regarding dizziness episodes and tests of vestibular, cardiovascular, neuromuscular, balance and psychological functioning. Participants were then followed up for falls incidents for a year using monthly falls calendars.

Findings: 312 participants underwent a baseline assessment; more than half have completed their one year falls follow-up and have received an end of study report detailing their performance in the various domains assessed as well as a composite risk of falls. The remainder of participants is still being followed up for falls.

Benefits: If vestibular impairment is identified as a risk factor for falls, the study will determine whether inclusion of vestibular function test(s) into an already validated fall risk screening tool (16) can improve fall risk prediction. Such knowledge will be particularly

useful to tailor falls prevention interventions to older people with various sensory impairments.

Output: None to date.
Funding: NHMRC
Date commenced: January 2012
Date completed: December 2014

ROLE OF POLYPHENOLIC COMPOUNDS IN MODULATING AD PATHOLOGY

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

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

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 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. We will 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 understand 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 Cooper Foundation, UPRA PhD scholarship to Tharusha Jayasena
Date commenced: 2011
Expected date of completion: ongoing

STRUCTURAL TOPOLOGICAL ORGANISATION OF THE ELDERLY BRAIN

CHeBA staff: Alistair Perry, Wei Wen, Anbupalam Thalamuthu, Perminder Sachdev

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

Project description: Prior investigations of human brain structural networks have primarily focused on healthy young adults and clinical samples. We study the scans of participants aged 70-90 years of the MAS, which is a longitudinal study of community-dwelling, non-demented individuals aged 70 and above.

Aims:

- To examine age-related changes in structural topological organisation of the elderly brain
- To investigate whether both hemispheric asymmetry and sex differences in structural networks are present in an older population
- To examine changes in the structural network using functional network measures

Design & method: The present study investigates a cognitively healthy sample drawn from the MAS using diffusion-weighted imaging (DWI) scans and resting-state functional MRI (rs-fMRI) scans. This work will later involve the participants who have progressed from cognitively normal (CN) to Mild Cognitive Impairment (MCI), as we will investigate the changes of brain networks. To investigate structural organisation, we derived edge-wise calculations, and also connectivity measures at the nodal, regional, lobar, core-network and global levels.

Progress to date: Recent investigations of human structural networks have primarily focused on network hubs and more recently, rich-club organisation. Regions that have been found to bi-hemispherically participate in rich-clubs of traditional parcellation methods include the precuneus, thalamus, putamen, hippocampus and superior parts of frontal and parietal cortices. Rich clubs of high-resolution networks additionally include the limbic, frontal, temporal, parietal and occipital regions. However, our study revealed that structural connectivity was primarily distributed along ventral visual pathways,

especially within the right hemisphere. Notably, there was a marked absence of highly connected sub-cortical and frontal regions in our older sample, suggesting a shift in topological organisation with age. Lobar level analysis provided further support for a topological shift, as the presence of left frontal regions in core networks was found to significantly decrease with age. In an additional analysis, we were able to demonstrate the continuation of traditional hemispheric lateralisation in older age, as well as sex differences in asymmetry in line with previous literature. We examined the correlational relationship between cognition and brain connectivity. The cognitive domains included processing speed, memory, language, visuospatial, and executive functions. We examined the association of these cognitive assessments with both the connectivity of the whole brain network and individual cortical regions. We found that the efficiency of the whole brain network of cortical fibre connections had an influence on processing speed and visuospatial and executive functions. Correlations between connectivity of specific regions and cognitive assessments were also observed, e.g. stronger connectivity in regions such as superior frontal gyrus and posterior cingulate cortex were associated with better executive function. Similar to the relationship between regional connectivity efficiency and age, greater processing speed was significantly correlated with better connectivity of nearly all the cortical regions. We have found that age has an impact on the organisation of the structural brain connectome. The presence of hemispheric asymmetry and sex differences in the older connectome are consistent with the topological organisation reported in the previous literature.

Benefits: Our data provides further evidence on the relationship between organisation of the brain network and cognition.

Output: Part of this work will be presented as an invited presentation at the 11th Annual World Congress of SBMT (The Society for Brain Mapping and Therapeutics) in May, 2014.

Funding: NHMRC

Date commenced: March 2013

Expected date of completion: December 2015

THE SYDNEY CENTENARIAN STUDY (SCS)

CHeBA staff: Perminder Sachdev, Henry Brodaty, Charlene Levitan, Karen Mather, John Crawford, Gavin Andrews, Kristan Kang

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: Wave 1 has now been completed with 345 participants aged 95+. Six monthly follow-ups at Wave 2, 3 & 4 are continuing. We have blood samples from 216 participants, which will allow us to investigate the impact of genetics on ageing, and 57 MRI scans which will help us understand the pathology of ageing.

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 health and social systems for the exceptionally old.

Output: 3 conference abstracts.
Funding: NHMRC
Date commenced: October 2008
Expected date of completion: December 2014

THE SYDNEY MEMORY AND AGEING STUDY (MAS)

CHeBA staff: Perminder Sachdev, Henry Brodaty, Simone Reppermund, Brian Draper, Julian Trollor, Nicole Kochan, Melissa Slavin, John Crawford, Kristan Kang, Wei Wen, Gavin Andrews

Project description: The MAS began in 2005 to examine the clinical characteristics and prevalence of Mild Cognitive Impairment (MCI) and related syndromes, and to determine the rate of change in cognitive function over time. It is one of the largest longitudinal studies of this kind in Australia and has resulted in more than 40 scientific publications and several national and international collaborations. At the core of our program are five longitudinal cohorts that have been systematically assessed with a comprehensive range of tools. They cover the age range from 40 to 100+ years. The focus is on cross-sectional neurocognitive function and in 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 examine risk factors and biomarkers.

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 is followed up with brief telephone reviews annually and detailed assessments biannually.

Progress to date:

- The longitudinal cohorts have been followed up and yielded a large amount of data on many aspects of brain ageing and dementia. Wave 4 (6 years) follow-up data acquisition was completed in 2013.
- 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 established with: COSMIC – COhort Studies of Memory in International Collaboration: an international collaboration of longitudinal studies of ageing (led by our group); BrainInflame: an international collaboration for the study of neuroinflammation and its impact on cognition and mood disturbance (led by our group); PROMOTE: modelled on a similar European consortium, PROMOTE aims to enhance psychosocial research into mental illness and ageing by bringing together researchers from Japan, Korea, China, Singapore, Taiwan and Australia in Seoul to increase collaboration, foster cross-country comparisons and build capacity (led by our group); a number of international genetics consortia: CHARGE, ENIGMA, PERADES.

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: submitted for review.
Funding: NHMRC
Date commenced: 2005
Expected date of completion: ongoing

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, 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 randomized controlled study. Participants are randomized 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 20 study completers and currently have 3 participants enrolled and receiving treatment. A further 3 participants are booked to commence treatment mid-2014. Results so far indicate that there is a difference favouring the active tDCS + CT condition on the primary outcome measure assessing learning and memory and on a secondary outcome measure assessing speed of information processing.

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

Date commenced: January 2013

Expected date of completion: December 2015

TREATING DIZZINESS IN OLDER PEOPLE

CHeBA staff: Jasmine Menant

Other investigators: Professor Stephen Lord (NeuRA) and UNSW), Dr Americo Migliaccio (NeuRA), Associate Professor Nick Titov (Macquarie University), Associate Professor Jacqueline Close (NeuRA and Prince of Wales Hospital), Dr Kim Delbaere (NeuRA and UNSW)

Project description: Despite the high prevalence of dizziness in the older population, the symptom is still not well understood, is rarely assessed using a comprehensive multifaceted approach, and consequently the underlying pathology/ies remain undiagnosed thus precluding potentially effective treatments to be offered. This in turn can prolong the suffering of debilitating symptoms, lead to activity restrictions and psychological distress and reduce overall quality of life. The multifactorial etiology of dizziness combined with a limited available battery of validated objective diagnostic tests leaves clinicians reliant on what is frequently a poorly described symptom.

Aims: To assess the effectiveness of a multifaceted dizziness intervention and to develop a multiple profile assessment of dizziness for use in Specialist Clinics.

Design & method: This randomised controlled trial is being conducted in older community-dwelling people aged 65+ years suffering from dizziness but not currently treated for it. Baseline assessments are multidisciplinary and include self-report items and tests of vestibular, cardiovascular, neuromuscular, balance and psychological functioning. A panel consensus meeting including at least three of the chief investigators is held fortnightly to discuss participants' inclusion into the study and suggest interventions based on objective criterion. Included participants are randomised to either a control group who follows usual care or an intervention group who receives one or several interventions. Both groups are required to report dizziness and falls episodes in monthly calendars. Interventions administered during a six-month period are targeting key underlying causes of dizziness and are based on the highest level of evidence for each subtype and condition and include: vestibular rehabilitation, medication management, cognitive-behavioural therapy and strength and balance training. The primary outcome measures are assessed at baseline and 6-month retest and capture the four crucial aspects of the trial: reported dizziness, balance control, gait variability and quality of life.

Progress to date: During 2012, Ethics approval was obtained, clinical trial registration was completed, equipment was purchased and built, databases created, staff recruited and trained. Recruitment for the randomised controlled trial began in earnest in February 2013 and throughout 2013, 109 participants were successfully recruited into the study. By end of 2013, 51 participants had completed their involvement in the study, that being a 6-month intervention. At the end of the study, each of these participants received a final report, including assessment results. We anticipate that we will be able to complete the planned recruitment sample of 300 participants in the following two years of this four year project.

Benefits: This study will improve our understanding of dizziness by identifying the main contributory causes to this prevalent and debilitating symptom and its effects on quality of life in a representative sample of older Australians. Regarding benefit to practice and the community, the success of this project will drive the development of a dizziness profile assessment based on empirical data and consisting of a battery of tests that best classify between dizziness subtypes. We anticipate that this tool will be implemented in Specialist Clinics to assist clinicians in diagnosing pathologies contributing to dizziness and thereby offering the opportunity of effective intervention. If successful in improving dizziness symptoms and quality of life, the multifaceted intervention will also lead to recommendations for practice to improve the assessment and management of older people with dizziness.

Output: None to date.
Funding: NHMRC
Date commenced: January 2012
Expected date of completion: December 2016

UNDERSTANDING OXIDATIVE STRESS IN THE BRAIN TO PREVENT NEURODEGENERATIVE DISEASES

CHEBA staff: Nady Braidy, Anne Poljak, Perminder Sachdev

Project description: Dementia is one of the top five causes of death in Australia with an increasing incidence due to an ageing population. Significant evidence points to oxidative stress (OS) as a major underlying factor in brain cell degeneration. Unfortunately, it is not known at what stage of life this OS begins in humans or what behaviours influence OS in the human brain. As OS underlies brain cell degeneration and the development of dementia, answers to these questions will contribute to the development of strategies that will help maintain brain cell function into older age.

To shed light on these questions we will use serum samples collected across a wide age range enabling us to investigate:

a. At what age OS levels begin to increase in human CSF.
b. Whether diet, lifestyle and/or psychosocial factors are associated with OS levels in human serum.

We predict that oxidative stress in the brain will increase with at least one or more risk factors including poor diet and lifestyle choices and psychosocial stress. Some level of OS will be observable at all stages of life, but most markedly after middle age.

Aims:

- Quantitate the levels of key biochemical markers of: a) psychosocial stress b) antioxidant capacity c) oxidative stress (OS) and d) inflammation; across a wide range of human age groups.
- Correlate levels of OS measured in blood/serum with: a) the age of the subject b) existing clinical condition(s) including medications c) diet and lifestyle d) depression anxiety and stress scores e) mental activity score f) current mental state.
- Determine the changes in gene expression which occur with healthy brain ageing by examining multiple waves of data collection within our cohort.

Design & method:

Recruitment

a. Serum samples will be obtained as part of routine medical assessment at the Sydney Adventist Hospital Emergency Department and Prince of Wales Hospital.
b. Diet, lifestyle and psychosocial information will be provided by eligible participants who, on admission to Sydney Adventist Hospital, have opted to receive additional information about the study and subsequently consented to participate in arm 2 of the study. Questionnaires to be used in this study include the Depression, Anxiety and Stress Score (DASS), Mini-Mental State Examination (MMSE), Lifetime of Experience Questionnaire (LEQ),Diet Habits Questionnaire, Flavonoid Consumption Questionnaire, three day diet history, The Pittsburgh Sleep Quality Index (PSQI), School Sleep Habits Survey, Children's Sleep Habits Questionnaire, International Physical Activity Questionnaire *(IPAQ)*, Physical Activity

Questionnaire for Adolescents (PAQ-A), and the Physical Activity Questionnaire for Children (PAQ-C).

Study Population

a. Arm 1 (Biomarker Analysis Only): Serum samples will be obtained from patients as part of routine medical assessment at the Sydney Adventist Hospital Emergency Department. A broad spectrum of co-morbidities and disease severities will be included in the sample population.

b. Arm 2 (Biomarker Analysis and Questionnaire): Patients will be eligible to participate in this arm of the study if:

- Blood pathology reports on WCC, RBC, protein and glucose levels within normal range.
- The patient has no clinical or biological evidence of diseases affecting the central nervous system (CNS).
- The patient had not taken any antimicrobial, steroidal, or cytotoxic medications 12 hours prior to the serum sample collected.

Biochemical Analysis

Initial screening using iTRAQ labelling and mass spectrometry to identify relative changes within a large protein group (>150), followed by absolute quantification of specific proteins using multiplex ELISA- couples a discovery based approach to rigorous validation of the candidates by precise, cost effective and high-throughput quantification.

Genomic Analysis

Following evaluation of the mass spectrometric data against protein databases, proteomic changes will be compared against changes in gene expression of the candidate proteins. Samples were assessed for yield using a spectrophotometer and quality using the RNA 6000 Pico Chip on the Agilent Bioanalyser. Samples with an RNA integrity number greater than 7.0 were used for polymerase chain reaction (PCR) assays.

Proteomics

i. 2D gel electrophoretic separation of complex mixtures of proteins

ii. Mass spectrometric characterisation of the structure of these proteins

iii. Evaluation of the mass spectrometric data against protein databases resulting from the human genome project. By "fingerprinting" the complete mixture of plasma proteins in normal and dementia blood samples patterns of change can be assessed.

Progress to date: Data has been collected and analysed. Several publications are in preparation.

Benefits: Dementia, one of the top five causes of death, is increasing due to our ageing population. Evidence indicates OS is a major underlying factor in brain cell degeneration. This health research will examine the impact of diet, lifestyle and psychosocial factors on OS levels in the human brain in different age groups. We can observe whether there is an age range where brain OS levels begin to increase and can identify factors associated with their rise. This will enable development of prevention and treatment strategies to reduce OS and brain cell degeneration in future generations and nurture healthier living, ageing and increased wellbeing. Evidence points to free radical damage oxidative stress (OS) as a major underlying factor in cell death within the brain with age. However, it is not known what factors promote this increase in free radical activity. This project will develop plasma protein profiles of healthy cognitive ageing as well as age-related brain disorders, which will inform the pathological mechanisms underlying age-related disorders, suggest biomarkers for future work in this field and have possible translational outcomes of major national benefit.

Output: Manuscript in preparation, 2 conference abstracts, presented at public forums.

Funding: Alzheimer's Australia Viertel Foundation

Date commenced: January 2012

Expected date of completion: January 2014

UNDERSTANDING THE GENETICS OF WHITE MATTER INTEGRITY OF THE CORPUS CALLOSUM

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

Other investigators: Associate Professor Margaret J. Wright (QIMR Berghofer Institute, Brisbane), Professor David Ames (National Ageing Research Institute)

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 investigates the genetics of the microstructure integrity of the corpus callosum. It utilises data from participants of 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 will be undertaken using both the twin sample and the Sydney Memory and Ageing Study.

Progress to date: Heritability analyses are completed.

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: This work is being written up for publication.

Funding: NHMRC, ARC, CSIRO Flagship Collaboration Fund, DCRC scholarship for Masters student, Alzheimer's Australia Dementia Research Foundation

Date commenced: 2011

Expected date of completion: July 2014

VOXEL-BASED RESTING-STATE FUNCTIONAL CONNECTIVITY

CHeBA staff: Haobo Zhang, Wei Wen, Anbupalam Thalamuthu, Perminder Sachdev

Other investigators: Professor Yong He and Dr Mingui Xia (IDG/McGovern Institute for Brain Research, State Key Lab of Cognitive Neuroscience & Learning, Beijing Normal University, Beijing, China)

Project description: Resting-state functional connectivity is a basic measure of brain functional network with a robust biological basis. Previous studies have extracted resting-state functional connectivity measures from prior defined regions or where boundaries are usually coarsely defined and tend to be very large with thousands of voxel-divided regions. By contrast, our study uses whole-brain voxel-based resting-state connectivity measures. We also examine the genetic influence on the degree of connectivity across the brain.

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 have used two separate datasets for this study. In the first part of the study, we used the MAS and computed resting-state functional connectivity strength (rs-FCS) data to show that individual differences in regional rs-FCS are related to inter-individual variations in cognitive performance. In the second, we investigated the heritability of whole-brain connectivity degree using the OATS data. We used resting-state fMRI data to construct the brain network based on voxel-wise functional connectivity.

Progress to date: *Part 1:* We generated a topological map of whole-brain voxel-based rs-FCS in our cognitively healthy elderly adults. We noted that the spatial distribution of the hubs was consistent with previous findings on resting-state functional networks, which were located in the medial prefrontal cortex, lateral prefrontal cortex, lateral temporal cortex, precuneus, posterior cingulate gyrus, inferior parietal lobule, and occipital cortex. We also noted that the hubs in the midline areas were largely consistent with the topology of short-range connections, while the hubs in the lateral areas were consistent with the topology of long-range connections, in accordance with previous reports. Our study demonstrated different patterns in the correlations between voxel-based rs-FCS and three neuropsychological tests (CFA, COWAT and RAVLT), which relate broadly to three cognitive domains, i.e. language, executive function and memory, respectively. Individual differences in regional rs-FCS are related to inter-individual variations in cognitive performance.

Part 2: Resting-state fMRI data to construct the brain network based on voxel-wise functional connectivity has exhibited a more robust scale-free network organisation than region-wise approach. Moreover, our sample composition is different from prior studies in that it comprised of older adults aged 65 years and over.

Benefits: This project will contribute to a comprehensive evidence base in the understanding of functional connectivity in the human brain.

Output: Two manuscripts are in preparation.

Funding: NHMRC

Date commenced: March 2013

Expected date of completion: September 2014

WE THINK YOU CAN DANCE!

CHeBA staff: Lee-Fay Low, Henry Brodaty

Other investigators: Associate Professor Dafna Merom (University of Western Sydney)

Project description: People with dementia living in residential aged care have low levels of physical activity and exercise programs tend to be poorly attended. We think you can dance! is a cognitively enriched social dance program for people with moderate to severe dementia living in residential aged care facilities.

Aims: To increase participation in physical activity by people with moderate to severe dementia, living in residential aged care facilities.

Design & method: A cognitively enriched social dance program was created with the creative input of professional dancers and academics. The program takes familiar movements and builds on these in a choreographed way to increase physical and mental complexity while being fun and engaging. It is manualised and has been designed to be scalable and potentially self-sustainable. The program is delivered by professional dancers with the help of staff volunteers.

Progress to date: A 16-week pilot of the program is currently in progress comparing We Think You Can Dance! to a control group which listens to music.

Benefits: There is growing evidence that physical activity may maintain cognitive function in people with dementia, particularly when combined with cognitive and social activity.

Output: None to date.
Funding: Thomas Foundation
Date commenced: October 2013
Expected date of completion: June 2014

COMPLETED PROJECTS

A TALE OF THREE CITIES: COMPARISON OF TWO EPIDEMIOLOGICAL STUDIES – THE SYDNEY MEMORY AND AGEING STUDY (MAS) AND AUSTRALIAN IMAGING, BIOMARKERS AND LIFESTYLE (AIBL)

CHeBA staff: Henry Brodaty, Perminder Sachdev, Simone Reppermund, Nicole Kochan, Annu Mothakunnel

Other investigators: Professor David Ames (University of Melbourne), Associate Professor Greg Savage (Macquarie University)

Project description: This project compared data of people with no cognitive impairment (NCI) and Mild Cognitive Impairment (MCI) in order to:

i. Determine population representativeness of the samples;
ii. Determine whether differences in recruitment affect findings from the two studies;
iii. Compare normal values in three Australian sites;
iv. Test robustness of findings about lifestyle factors;
v. Examine neuropsychological test performances;
vi. Compare rates of decline;
vii. Conduct collaborative work on imaging; and
viii. Conduct collaborative work on proteomics.

Aims: The aim of this project was to enhance prevention of cognitive decline by building on data from two large epidemiological studies each of which has assessed over 1000 persons to determine predictors of healthy and pathological cognitive ageing.

Design & method: We harmonised and compared data from the MAS, where participants were randomly invited from the electoral roll in defined geographic areas in Sydney and the Australian Imaging, Biomarkers and Lifestyle Study of Ageing, which recruited cognitively normal (CN) individuals via media appeals and MCI participants via referrals from clinicians in Melbourne and Perth. We applied similar diagnostic criteria to both samples retrospectively to determine if sampling methods influenced cognitive performance of cognitively normal older people, and rates and risk factors for cognitive impairment.

Findings: A convenience sample of normal controls was likely to be younger and better functioning than that of an MCI group who were likely to perform worse than a purportedly random sample. Sampling bias should be considered when interpreting findings from studies of ageing.

Benefits: This study provided evidence for the bias relating to convenience sampling in ageing studies, and informs the methodology for future studies

Output: 1 journal publication (Annals of Epidemiology 2014).
Funding: CSIRO Prevention Flagship
Date commenced: February 2012
Date completed: June 2013

GENETIC ASSOCIATIONS OF COGNITIVE AGEING AND DEPRESSION

CHeBA staff: Perminder Sachdev, Simone Reppermund, Karen Mather

Other investigators: Dr Marcus Ising, Dr Tanja Brueckl, Dr Petra Zimmerman and Ms Nina Hoehne (Max Planck Institute, Germany)

Project description/aims: To examine and compare the genetic associations of cognitive ageing and depression on samples from Australia and Germany.

Design & method: Genome wide association analyses run on Munich and Sydney (MAS) study samples.

Findings: Within genome-wide association analyses, we identified variants in the *DGS1* gene that were associated with age-related cognitive decline in information processing speed. Analyses on age-related risk for depression revealed that the personality dimension neuroticism acts as a moderator.

Benefits: Improved understanding of the underlying mechanisms of cognitive decline and cognitive impairment in depression may assist in identifying at-risk individuals and inform novel and improved preventative and treatment strategies.

Output: Manuscript in preparation; results presented at international conferences.
Funding: Group of Eight/DAAD, Max Planck Institute
Date commenced: April 2012
Date completed: December 2013

MODELLING AND TREATING INTERNALISING PSYCHOPATHOLOGY IN A CLINICAL TRIAL

CHeBA staff: Louise Mewton, Gavin Andrews

Project description: Anxiety and depression are highly comorbid. Rather than treat these disorders individually, transdiagnostic treatments for comorbid anxiety and depression have been developed. However, when evaluating these treatments, disorder-specific symptoms remain the outcome of interest. Their effect on the mechanism underlying comorbidity, internalising psychopathology, is unknown. Capitalising on data currently being collected at CRUfAD, this project sought to establish whether such treatments address the underlying cause of comorbidity by evaluating changes in internalising psychopathology over time. Beyond developing a conceptual solution to the problem of correlated disorders in clinical trials, the present study will indicate that this approach can be applied practically and effectively in an actual clinical trial.

Aims: To determine whether iCBT results in changes in internalising psychopathology

Design & method: 635 patients aged 18 years or over who were prescribed the program for anxiety and depression by their primary healthcare professional. All patients completed the Patient Health Questionnaire 9, the Generalised Anxiety Disorder 7-Item Scale, the Mini Social Phobia Inventory and the Panic Disorder Severity Self-Report Scale. Reductions in the latent internalising trait were assessed within a longitudinal factor analysis framework that compared internalising factor means at pre- and post-treatment.

Findings: There are clinically significant reductions in the latent internalising trait following iCBT.

Benefits: By shifting the focus from observable indicators to the latent internalising trait, the current study demonstrated that iCBT also modified the general unobservable process that underpins a range of disorder-specific psychopathology.

Output: 1 journal paper submitted for review; 1 conference presentation.
Funding: Faculty of Medicine, UNSW
Date commenced: October 2012
Date completed: August 2013

STEM CELL INITIATIVE FOR THE STUDY OF ALZHEIMER'S DISEASE

CHeBA staff: Kuldip Sidhu, Jaemin Kim, Perminder Sachdev

Other investigators: Professor Gerald Muench (University of Western Sydney), Dr Lezanne Ooi (University of Wollongong), Professor Ole Issacson (Harvard University, USA)

Project description/aims:

- To develop patient-derived induced pluripotent stem cells (iPSC) for pathophysiology, modeling and pharmacological appraisals of Alzheimer's disease.
- Directed differentiation of iPSC to cortical neurons for future drug discovery.

Design & method: Recruited 11 patients with early-onset Alzheimer's disease (sporadic and familial), including age and sex-matched control individuals with HREC approval and obtained skin biopsies for derivation of iPSC.

Findings:

1. More than 80 iPSC clones were derived and about 11 fully characterised. These clones are available for distribution to relevant laboratories for research & development purposes.
2. iPSC clones distributed to three academic and one commercial institute.
3. Procedures optimised to derive cholinergic and dopaminergic neurons from iPSC.
4. Comprehensive microarray analyses of transcriptomics indicated significant differences between disease and control groups.
5. Phenotypic and genetic differences identified in patient-derived iPSC.

Benefits: With no cure for Alzheimer's disease, iPSC provides a new *in vitro* technology to study disease progression in laboratory conditions and to identify new biomarkers for future drug development.

Output: Five journal publications, 2 conference abstracts accepted (one for 2014), two invited lectures for the Annual Congress of the Society for Brain Mapping & Therapeutics (one for 2014).
Funding: NHMRC
Date commenced: December 2007
Date completed: December 2013

THE SYDNEY STROKE STUDY

CHeBA staff: Perminder Sachdev, Henry Brodaty, Darren Lipnicki, John Crawford, Wei Wen, Catherine Dong

Other investigators: Syenna Schievink, Seb Köhler, Robert van Oostenbrugge, Frans Verhey (all from Masstricht University, Netherlands)

Project description: When the study began, the progression of cognitive impairment and outcome of stroke patients not diagnosed with dementia was unclear. The determinants of post-stroke dementia and cognitive decline had also not been established.

Aims:

- To characterise the neuropsychological profile of stroke patients and track the course of their cognitive impairments over time.
- To investigate determinants of, or associations of various factors with, post-stroke cognitive impairment, including dementia.

Design & method: A total of 252 patients with a recent stroke were recruited from teaching hospitals affiliated with UNSW. There were 129 age-matched healthy controls with no history of stroke also recruited. Patients and controls underwent detailed functional, medical, psychiatric and neuropsychological assessments, initially within 3-6 months of hospital admission or upon recruitment (controls). Assessments were repeated after 12 months, 3 years, and 5 years. Subgroups of patients and controls received MRI scans at the initial and 3- and 5-year assessments. Blood sampling was conducted for determining homocysteine levels and genotyping. Consensus diagnoses of dementia and vascular Mild Cognitive Impairment were made by an experienced panel.

Findings: Cognitive functioning is lower and dementia more prevalent in stroke patients than in healthy controls. Stroke patients typically exhibit a slow decline in cognitive functioning over time, similar to controls. However, patients who experience a subsequent stroke undergo far more widespread and extensive decline. Factors found to predict impairment levels and rate of decline include lower premorbid ability, stroke volume, education (protective), smaller hippocampi, white matter hyperintensities, and possession of an APOE ε4 allele.

Benefits: The findings of the Sydney Stroke Study have suggested that preventing further strokes is the best means of minimising cognitive decline in stroke patients.

Output: Papers have been published in Neurology, Dementia and Geriatric Cognitive Disorders, *Journal of the International Neuropsychological Society*, and *Journal of Neurology, Neurosurgery & Psychiatry*.

Funding: NHMRC, The Rebecca Cooper Foundation and the Fairfax Family Foundation

Date commenced: Recruitment began in 1997.

Date completed: Five-year follow-up assessments were completed in 2005 and this study finished in 2013. Further analysis of the data collected will be undertaken as part of a new study to begin in 2014.

VISUOSPATIAL TASKS AFFECT LOCOMOTOR CONTROL MORE THAN NON-SPATIAL TASKS IN OLDER PEOPLE

CHeBA staff: Jasmine Menant

Other investigators: Dr Daina Sturnieks (NeuRA and UNSW), Dr Matthew Brodie (NeuRA and UNSW), Associate Professor Stuart Smith (NeuRA and University of Tasmania), Professor Stephen Lord (NeuRA and UNSW)

Project description: Previous research had shown that visuospatial processing requiring working memory was particularly important for balance control during standing and stepping, and that limited spatial encoding contributed to increased interference in postural control dual tasks. However, visuospatial involvement during locomotion had not been directly determined.

Aim: To examine the effects of a visuospatial cognitive task versus a non-spatial arithmetic task on gait smoothness and variability in older people, while controlling for task difficulty.

Design & method: Thirty-six people aged ≥75 years performed three walking trials along a 20 m walkway under the following conditions: (i) no cognitive task, (ii) an easy non-spatial task; (iii) a difficult non-spatial task; (iv) an easy visuospatial task; (v) a difficult visuospatial task. Gait parameters were computed from a tri-axial accelerometer attached to the sacrum. The proportion of correct answers during dual task walking and seated trials was computed for each cognitive task.

Findings: Compared with non-spatial arithmetic tasks, visuospatial cognitive tasks led to a slower, more variable and less smooth gait pattern. These findings suggested that visuospatial processing might share common networks with locomotor control, which further supports the hypothesis that gait changes during dual task paradigms are not simply due to

limited attentional resources but to competition for common networks for spatial information encoding.

Benefits: Findings from this study provided insight into cognitive processing pathways utilised in the control of locomotion. Further, given that falls in older people frequently occur while walking, understanding the relative importance of secondary cognitive task types in influencing locomotor control has implications for fall risk assessments.

Output: 1 poster presentation; manuscript under review in *PLoS One*.

Funding: NHMRC

Date commenced: January 2011

Date completed: December 2013

OUR COMMUNITY

We have been overwhelmed and inspired by the support from the community since the launch of CHeBA.

Every gift, no matter the size, and every bit of volunteer time dedicated to our cause helps us in our mission to change the future of age-related cognitive disorders.

COMMUNICATIONS & COMMUNITY ENGAGEMENT

2013 was a critical year for the Centre for Healthy Brain Ageing and it was a collective effort to build CHeBA's presence within UNSW and the community. The public programs and initiatives that have been implemented would certainly not have been as successful without such a dedicated and enthusiastic group of people within, and supporting, CHeBA.

Pictured: Heidi Mitchell, Marketing & Communications Officer

"Losing my father to dementia and watching how the disease progressed has inspired me to do everything and anything I can to make a difference. Awareness and early detection is vital but it's the research by people such as Henry Brodaty and Perminder Sachdev that holds the key to a future without dementia and dementia-related illnesses." PJ Lane

OFFICIAL AMBASSADOR PJ LANE

In 2012 we were pleased to announce that respected international actor, entertainer and philanthropist, PJ Lane, was the official Ambassador of CHeBA. Being the son of charismatic and much-loved showman Don Lane, who was diagnosed with Alzheimer's disease in 2007, PJ has experienced first-hand the struggle of watching a loved one's cognitive abilities decline.

Over the past 18 months, PJ has been a powerful Ambassador for CHeBA. He has eagerly supported our media campaigns and spoken at our public forums, providing an emotive insight into his personal experience with Alzheimer's disease. He ran alongside Professors Henry Brodaty and Perminder Sachdev, CHeBA's Co-Directors, in 2013's City 2 Surf and actively raised much needed funds for CHeBA's research into the ageing brain.

According to PJ, he has always been an advocate for research into the causes and better treatments for the disease that took his father's life prematurely. It is his love for his father that inspired him to take action in the fight against Alzheimer's and other forms of age-related brain disease. With an Ambassador like PJ championing our research, we will continue to make significant impact upon the community and are able to look positively toward our lofty goal of changing the future of age-related brain disorders.

FITNESS AMBASSADORS CHAMPIONING HEALTHY BRAIN AGEING

In June 2013 the CHeBA Champion initiative was officially launched. Increasingly, evidence is suggesting that many risk factors for dementia and Alzheimer's disease are lifestyle-related, there is hope of postponing the development of dementia through lifestyle modification. Factors such as high blood pressure, diabetes, obesity, physical inactivity, smoking and high cholesterol begin to exert their harmful effects in early and mid-adult life. The message of dementia prevention should therefore be taken to the young and healthy.

To achieve this, CHeBA's Marketing & Communications Officer, Heidi Mitchell, established a group of health-aware and dynamic Fitness Ambassadors in their 20s and 30s – known as the **CHeBA Champions** – who have enthusiastically increased understanding amongst their peers and networks about the risk factors for Alzheimer's and other dementias, and specifically the impact of lifestyle upon our brain health in late life. Most of our CHeBA Champions have a personal relationship with dementia through a family member, and demonstrate an inspiring resilience and determined optimism to gain a greater understanding of the modifiable risk factors of dementia, and do what they can for themselves to prevent age-related cognitive decline.

Sponsored by Intellectual Ventures, this initiative has been extremely successful and generated extensive media and community coverage over the previous year. We are proud of all of our Fitness Ambassadors who have shown a great deal of commitment to the cause, and at the same time driven much needed funds to advance the research being done at CHeBA to prevent cognitive decline, improve cognitive functioning as we age, and devise better care for people with dementia, especially those in nursing homes. Particular thanks to the following devotees who, in the first year of this initiative, have gone over and above in their volunteer efforts as CHeBA Champions to raise community awareness, funds and interest in our research: Hailey Maxwell, Sarah Thompson, Stephanie Campbell, Caroline Joy, Craig Douglass, Courtney Owen, Nardia Norman, Nirmala Perera, Keri Kitay, Ricky Kitay, Alex Avella, Ali Cavill, Lise Lafferty and Warren King.

The year ahead will see significant advances in the CHeBA Champion initiative, and a continued drive to create a shift in the way we all think about our ageing brains.

L to R: Professor Henry Brodaty, Heidi Mitchell, Warren King, Hailey Maxwell, Craig Douglass, Professor Perminder Sachdev

CHEBA IN THE MEDIA

In 2013 there were a number of high profile media stories featuring CHeBA research. Significant highlights included coverage of the Sydney Centenarian Study in print and on television nationally. Professor Perminder Sachdev's research into reversal of Mild Cognitive Impairment was publicised nationally in many reputable media outlets. The launch of the CHeBA Champion initiative achieved noteworthy outreach in print and on television across Australia, and CHeBA's Older Australian Twins Study also achieved national coverage in print. Chairman of CHeBA's Advisory Committee, Roger Corbett AO, was highlighted in the Australian Financial Review calling for a focus on dementia.

In addition to specific study outcomes, CHeBA's researchers were sought regularly for expert comment on radio, in print and on television. Both Co-Directors were acknowledged in leading media for their support of the UK's campaign to make dementia research a priority at the G8 Summit.

THE BRAIN DIALOGUES

CHeBA launched its blog, The Brain Dialogues, in early 2013 to showcase the latest developments in the field of brain ageing and dementia. We extend our thanks to the contributors to this blog and to all those who have taken the time to read and share our articles.

ARIA HOSTED CORPORATE LUNCH

In early 2013, ARIA Restaurant generously hosted a corporate lunch fundraiser which created valuable connections in the corporate community for CHeBA. We are extremely grateful to Richard Grellman AM who was our guest speaker at this lunch, and to the corporate attendees who are now involved in the development of our public awareness initiatives.

CITY 2 SURF

A sensational 47 people ran the City 2 Surf for CHeBA, alongside Co-Directors Professor Henry Brodaty, Professor Perminder Sachdev, Ambassador PJ Lane and the CHeBA Champions. Together Team CHeBA raised a whopping $29,000 for research, placing us firmly in the Top Ten Team Fundraisers for 2013.

Professor Henry Brodaty with City 2 Surf runners from CHeBA's major partner, Montefiore Home

PUBLIC FORUMS

This year CHeBA partnered with Prince of Wales Hospital Aged Care Psychiatry to deliver a public forum to address some of the issues of the ageing brain and promote maintenance of the brain for a healthier life. With unprecedented demand from the community, we are set to increase the number and scope of these public forums over the coming year.

"Part of our goal is to increase understanding amongst seniors that it is never too early nor too late to commence preventative strategies to reduce one's risk of cognitive decline."
Professor Henry Brodaty

L to R: Professor Henry Brodaty, CHeBA Ambassador PJ Lane, Paula Goodyer, A/Prof Sharon Naismith, Dr Murray Wright, Dr Ann Hodge

Professor Sachdev presenting
Photo courtesy of Karen Mather

SYDNEY MEMORY & AGEING STUDY INFORMATION DAY

CHeBA acknowledges the value and importance of the participants in our studies, and each year presents the year's findings and developments to participants of the Sydney Memory & Ageing Study (MAS).

The Sydney Memory and Ageing Study was initiated in 2005 to examine the prevalence, longitudinal course and risk and protective factors of cognitive impairment and decline in older individuals. In 2013, the fourth wave of assessments was completed. This study has been extremely productive, with 73 papers published and nearly as many in various stages of presentation. It has supported the work of a number of doctoral and post-doctoral fellows and spawned investigations in genetics, epigenetics, proteomics, metabolomics and neuroimaging. The data from the study are publicly available for collaborative research.

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 The Montefiore Home, who have partnered with us since the launch of the Centre in 2012.

Thomas Foundation

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

MONTEFIORE

CHeBA and The 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 extremely grateful to The Montefiore Home and David Freeman AM for the ongoing support provided to CHeBA.

GOVERNMENT & GRANT FUNDING

Australian Government National Health and Medical Research Council NHMRC

UNSW AUSTRALIA

Australian Government Australian Research Council

NIH National Institutes of Health

FOUNDATIONS

AMP

Our Sponsors

Throughout 2013, CHeBA received generous sponsorships to assist in the development of our prevention campaigns and public initiatives. We extend our deepest thanks to everyone who has contributed to CHeBA's research over the last year. We are extremely grateful to all of our donors, and to the enormous in kind support we have received for various projects. Thank you for being a part of CHeBA's journey to advance research into age-related cognitive decline.

INTELLECTUAL VENTURES

Genworth

Avant mutual group

Italian Chamber of Commerce and Industry In australia Inc.

OUR PARTNERS

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.

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.

OUR IN KIND SUPPORTERS

- Breathe Fire Specialised Training
- Brooks
- BSc (Body Science)
- Chillax
- Fitness First
- Harbinger
- Icon Foods
- Joico
- Musashi
- Regent Sports
- RioLife
- Runner's World
- Slim Secrets
- Lifestream
- WNIF

APPENDICES

STAFF LIST

Leadership

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

Perminder Sachdev
Professor, Co-Director CHeBA

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

Tao Liu
Research Fellow
(until March 2013)

Lee-Fay Low
Senior Research Fellow

Ora Lux
Research Fellow
(until December 2013)

Karen Mather
Lecturer, Leader Genetics & Genomics group

Jasmine Menant
Research Fellow
(until December 2013)

Louise Mewton
Research Fellow
(until December 2013)

Adith Mohan
Research Fellow

Julia Müenchhoff
Research Fellow

Simone Reppermund
Research Fellow, Conjoint Lecturer, MAS Coordinator

Melissa Slavin
Research Fellow
(until December 2013)

Evelyn Smith
Research Fellow
(until December 2013)

Anbupalam Thalamuthu
Research Fellow

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

Haobo Zhang
Research Fellow
(until December 2013)

Liu Zhuang
Research Fellow
(until December 2013)

Professional & Technical Staff - Research

Shaily Aggarwal
Research Assistant

Caroline Arasartam
Research Assistant
(until December 2012)

Jocelyn Bowden
Research Officer, OATS Coordinator

John Crawford
Research Officer

Yun (Victor) Deng
Data Administrator
(until January 2014)

Tanya Duckworth
Research Assistant

Therese French
Research Assistant

Kristan Kang
Data Manager

Angela King
Research Assistant

Andrea Lammél
Research Officer, OATS Coordinator
(until April 2013)

Charlene Levitan
Research Officer, SCS Coordinator
(until December 2013)

Darren Lipnicki
Research Officer

Kate Maston
Research Assistant

Anna McKenzie
Research Assistant
(until December 2013)

Annu Mothakunnel
Research Assistant
(until July 2013)

Sarah Pont
Research Assistant

Carine Pose
Research Assistant
(until September 2013)

Pieter Rossouw
Research Assistant
(until July 2013)

Mamta Sidhu
Research Assistant

Jessica Smith
Research Assistant
(until December 2013)

Ruby Tsang
Research Assistant
(until December 2013)

Claudia Woolf
Research Assistant

Professional & Technical Staff - Support

Monica Connolly
Administrative Assistant
(until December 2013)

Kate Crosbie
Administrative Assistant
(until June 2013)

Michele De Permentier
Administrative Assistant

Sophia Dean
Administrative Officer

Suzanne Forrester
Administrative Assistant

Cathy Foster
Administrative Assistant
(until December 2013)

Heidi Mitchell
Marketing & Communications Officer

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

Teresa Lee
Senior Lecturer, Co-Leader Neuropsychology group

Anne Poljak
Lecturer, Leader Proteomics group

Kuldip Sidhu
Honorary Associate Professor, Co-Leader Molecular Biology & Stem Cells group

Julian Trollor
Associate Professor, Leader Neuroinflammation group
Visiting Research Fellows

Bernhard Baune
Visiting Professorial Fellow, Leader BrainInflame Consortium
(January 2013-present)

Pierre Lafaye De Micheaux
Visiting Senior Research Fellow
(July 2013 - July 2014)

EXTERNAL APPOINTMENTS

Dr Nady Braidy

- Honorary Associate, Australian School of Advanced Medicine, Macquarie University

Scientia Professor Henry Brodaty

- Director, Primary Dementia Collaborative Research Centre, UNSW (2006-2014)
- Head and Founder, Memory Disorders Clinic, Prince of Wales Hospital, Sydney (1985- present)
- Foundation Director, Academic Department for Old Age Psychiatry, Prince of Wales/Prince Henry Hospitals (1990-2012)
- Senior Clinician, Aged Care Psychiatry, Prince of Wales Hospital, Sydney (1990- present)
- President, International Psychogeriatric Association (2013-2015)
- Member, CSIRO Prevention Flagship Advisory Committee (2011-2014)
- Chair, Dementia Committee, NHMRC Knowledge Translation Faculty (2013- present)
- Member, International Advisory Committee of the National Institute of Dementia, South Korea (2013-2015)
- International Advisor, Institute of Alzheimer's Education Advisory Board, Hong Kong (2013-2015)
- Honorary Lifetime Vice-President, Alzheimer's disease International (2005- present)
- Chair, Metlife Awards for Psychosocial Research, Alzheimer's disease International (2013-2014)
- Chariman, Alzheimer's Australia Dementia Research Foundation Ltd (2002- present)
- Chair, National Quality Dementia Care Network Executive Committee, Alzheimer's Australia (2010-present)
- Chair, NSW Dementia Expert Advisory Group, NSW Department of Health (2009- present)
- Leader, Dementia Policy Team, NSW Department of Health (2009- present)
- Member, Reference Committee, NSW Policy of Mental Health for Older People and Dementia Care, NSW Department of Health (1993- present)
- Member, Reference Committee, NSW Mental Health of Older People Task Force, NSW Department of Health (2001- present)
- Member, Priority Task Force, NSW Chronic, Aged and Community Health, NSW Department of Health (2005- present)
- Member, Health Priority Task Force for Mental Health, NSW Department of Health (2008- present)
- Member, Australian Government Dementia Advisory Group (2008- present)
- Member, Australian Government Psychogeriatric Expert Reference Group (Residential Aged Care and People with Psychogeriatric Disorders) (2008-present)
- Member, Strategic Review of Health and Medical Research Australia (McKeon Review) Panel (2011-2013)
- Member, Aged Care Reform Implementation Council, Australia (2012-2014)
- Executive Member, Australasian Consortium of Centres for Clinical Cognitive Research (AC4R) (2000- present)
- Member, EU Scientific Advisory Board for the Joint Programming Initiative for Combating Neurodegenerative Diseases (JPND) (2010-2012)
- Member, WHO Consultation Group on the Classification of Behavioural and Psychological Symptoms in Neurocognitive disorders for ICD-11.
- Member, Evaluation Board for the Psychiatry, Faculty of the Faculty of 1000 Medicine (2005- present)
- Chair, Clinical Advisory Committee, Montefiore Homes (2012-present)
- Assistant Editor, Australian and New Zealand Journal of Psychiatry
- Editorial Boards for *Aging and Mental Health* (1996- present), *Alzheimer Disease and Associated Disorders* (1995- present), *Alzheimers and Dementia: Journal of the Alzheimer's Association* (2005- present), *Australian and New Zealand Journal of Psychiatry* (1981- present), *CNS Drugs* (1999- present), *Dementia and Geriatric Cognitive Disorders* (2010- present), *F1000 Research* (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 and Health, University of Technology Sydney
- Director of the Health & Ageing Research Unit for the South Eastern Sydney & Illawarra Area Health Service
- Member, Research Advisory Committees, Alzheimer's Australia
- Member, Research Advisory and Steering Committee, Parkinson's NSW
- Member, Advisory and Steering Committees, Carers Australia
- Member, Dementia Care Steering Committee, Baptist Community Services
- Editorial board for *International Journal of Older People Nursing, Japan Journal of Nursing Science* and *Nursing Older People*.

Dr Nicole Kochan

- Clinical Neuropsychologist, Neuropsychiatric Institute, Prince of Wales Hospital, Sydney (2001- present)
- Honorary Associate, Department of Psychology, Macquarie University

Dr Teresa Lee

- Senior Clinical Neuropsychologist, Neuropsychiatric Institute, Prince of Wales Hospital, Sydney

Dr Lee-Fay Low

- Member of the Expert Advisory Group for Quality Dementia Care in the Community project, Alzheimer's Australia Victoria (2012- ongoing)
- Member of Advisory Committee, Older Person Mental Health, NSW Institute of Psychiatry (2010- present)
- Foundation Director, Arts Health Institute (2011- present)
- Member, Working Group – Putting the Older Mentally Ill Person on the Agenda (2011- present)
- Member, Multicultural Dementia Network (2011- present)
- Member, NSW Dementia Expert Advisory Panel (2009- present)

Dr Jasmine Menant

- Editorial board, *Dizziness Journal*
- Visiting Postdoctoral Research Fellow, Cognitive Neuroscience Laboratory, University Aix-Marseille and National Centre for Scientific Research (CNRS), Marseille, France (2012-2013)

Dr Adith Mohan

- Consultant Neuropsychiatrist, Neuropsychiatric Institute, Prince of Wales Hospital, Sydney
- Site coordinator of Training for Psychiatry, Prince of Wales Hospital, South Eastern Sydney and Illawarra Psychiatry Training Network

Dr Anne Poljak

- Reviewer, NSW Brain Banks Scientific Review Committee (2013-2014)

Dr Simone Reppermund

- Editorial board, *Advances in Medicine*
- Member, Scientific Committee for the XIII Annual Meeting of the International College of Geriatric Psychoneuropharmacology (2013)

Scientia Professor Perminder Sachdev

- Clinical Director, Neuropsychiatric Institute, Prince of Wales Hospital (1987- present)
- Visiting Fellow, The Centre for Research on Ageing, Health and Wellbeing, Australian National University (2012-2014)
- President, International College of Geriatric Psychoneuropharmacology (2012-2014)
- International Distinguished Fellowship, American Psychiatric Association (APA) (2012)
- Member, Executive Committee, The International Society of Vascular Behavioural and Cognitive Disorders (VASCOG) (2012- present)
- Member, 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)
- Member of the Neurocognitive Disorders Work Group, DSM-5 (2007- present)
- Member, F1000 Reports Advisory Board - Neuropsychiatry panel
- Member, NHMRC Assigner's Academy (2012- present)

- Fellow of the NHMRC Academy (2011- present)
- Chair, Section of Neuropsychiatry, RANZCP, (2005- present)
- Member, Committee on Psychotropic Drugs and Other Physical Treatments, Royal Australian and New Zealand College of Psychiatrists (1996- present)
- Invited member, Task Force of the International League Against Epilepsy (ILAE) Neuropsychobiology Commission (2011- present)
- Founding Executive Committee Member of the Tourette Syndrome Association of Australia (1989- present)
- Chair, Medical Advisory Committee of the Tourette Syndrome Association of Australia (1996- present)
- Scientific Advisory Committee, Alzheimer's Association of Australia (1995- present)
- Scientific Steering Committee, Neuroscience Institute of Schizophrenia and Allied Disorders (NISAD), The Garvan Institute, Sydney (1996- present)
- Scientific Review Committee of the Division of Psychiatry, Eastern Sydney Area Health Service (Eastern Section) (1993- present; Chair since 1996)
- 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, Middle Eastern Journal of Psychiatry and Alzheimer's, American Journal of Geriatric Psychiatry*

Associate Professor Kuldip Sidhu

- CEO & Founding Director, Cell Therapeutics Pty Ltd (2012- present)
- President, Society for Brain Mapping & Therapeutics (2012- 2014)
- Member, Expert panel on iPSC research, European Union
- Editorial board, *The Open Stem Cell Journal*

Associate Professor Julian Trollor

- Senior Medical Practitioner (Academic)/ Associate Professor in Neuropsychiatry and Intellectual Disability, South Eastern Sydney Local Health District, Sydney
- Member, Board of Directors, NSW Institute of Psychiatry
- Founder, Neuropsychiatry Section, RANZCP
- Panel of Expert Advisers, NSW Ombudsman
- Current Secretary & Treasurer, International Neuropsychiatric Association
- Founding member, Australian Consortium for Clinical Cognitive Research

Associate Professor Wei Wen

- Associate Editor, *Journal of Alzheimer's disease*

POSTGRADUATE RESEARCH STUDENTS

CURRENT

Rachael Birch

- Fragile x tremor ataxia syndrome
- PhD student
- School of Psychiatry, Faculty of Medicine, UNSW
- Supervisors: Professor Julian Trollor, Professor Kim Cornish, Dr Darren Hocking

Anne-Nicole Casey

- Friendships and social structures: understanding, assessing, and improving social networks of persons living in residential aged care
- PhD student
- School of Psychiatry, Faculty of Medicine, UNSW
- Supervisors: Dr Lee-Fay Low, Associate Professor Yun-Hee Jeon, Professor Henry Brodaty

Premilla Chinnappa-Quinn

- Post-operative cognitive dysfunction
- PhD student
- Prince of Wales Clinical School, Faculty of Medicine, UNSW
- Supervisors: Associate Professor Michael Bennett, Professor Perminder Sachdev, Dr Nicole Kochan

Maria Joana Duarte Caetano

- Effects of age, neuropsychological function and step training on gait adaptability in older people with and without Mild Cognitive Impairment or Parkinson's disease
- PhD student
- School of Public Health & Community Medicine, Faculty of Medicine, UNSW
- Supervisors: Professor Stephen Lord, Dr Jasmine Menant

Yanhong (Catherine) Dong

- Cognitive outcome after stroke
- PhD student
- School of Psychiatry, Faculty of Medicine, UNSW
- Supervisors: Dr Melissa Slavin, Professor Perminder Sachdev, Dr Christopher Chen, Dr Simon Collinson

Tharusha Jayasena

- Sirtuins and the protection against oxidative stress in brain ageing and neurodegenerative disorders
- PhD student
- School of Psychiatry, Faculty of Medicine, UNSW
- Supervisors: Professor Perminder Sachdev, Dr Anne Poljak

Jiang Jiyang

- PhD student
- Automated aMCI detection using brain network related classifiers
- School of Psychiatry, Faculty of Medicine, UNSW
- Supervisors: Associate Professor Wei Wen, Professor Perminder Sachdev

Daniela Katz

- Determinants of vestibular impairments in older people
- Master by Research student
- School of Public Health & Community Medicine, Faculty of Medicine, UNSW
- Supervisors: Professor Stephen Lord, Dr Ross Black, Dr Jasmine Menant

Sri Chandana Kanchibhotla

- Genetics of the ageing brain
- Master by Research student
- School of Psychiatry, Faculty of Medicine, UNSW
- Supervisors: Professor Perminder Sachdev, Dr Karen Mather, Professor Peter Schofield

Aileen Lowe

- Advanced characterisation of skin derived neuroprecursors
- PhD student
- School of Psychiatry, Faculty of Medicine, UNSW
- Supervisors: Associate Professor Michael Valenzuela, Associate Professor Kuldip Sidhu

Amanda Olley

- PhD student
- Obsessive compulsive disorder: a decision making model
- School of Psychiatry, Faculty of Medicine, UNSW
- Supervisors: Professor Perminder Sachdev, Professor Gin Malhi

Alistair Perry

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

Michael Player

- Neuroplasticity in health, ageing and psychiatric disorders
- PhD student
- School of Psychiatry, Faculty of Medicine, UNSW
- Supervisors: Professor Colleen Loo, Professor Perminder Sachdev

Katrin Seeher

- A study on psychosocial effects of becoming a carer: predicting caregiver outcomes such as burden, psychological distress or quality of life
- PhD student
- School of Psychiatry, Faculty of Medicine, UNSW
- Supervisors: Professor Henry Brodaty, Dr Lee-Fay Low, Dr Simone Reppermund

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

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

Zixuan Yang

- Neuroimaging and cognitive reserve
- PhD student
- School of Psychiatry, Faculty of Medicine, UNSW
- Supervisors: Professor Perminder Sachdev, Associate Professor Wei Wen

COMPLETED

Seyed Amir Hossein Batouli

- Genetic and environmental influences on brain structure and biochemistry in the elderly: data from the Older Australian Twins Study
- School of Psychiatry, Faculty of Medicine, UNSW
- Supervisors: Professor Julian Trollor, Professor Perminder Sachdev, Associate Professor Wei Wen
- PhD conferred 2013

Yue Cui

- Pattern recognition in the diagnosis and prognosis of Mild Cognitive Impairment and Alzheimer's disease
- School of Design Communication and Information Technology, Faculty of Science and Information Technology, University of Newcastle
- Supervisors: Dr Suhuai Luo, Associate Professor Wen
- PhD conferred 2012

Nicola Gates

- Psychological Wellbeing and Quality of Life in Mild Cognitive Impairment
- School of Psychiatry, Faculty of Medicine, UNSW
- Supervisors: Associate Professor Michael Valenzuela, Professor Perminder Sachdev, Professor Maria Fiatarone Singh
- PhD conferred 2013

Jaemin Kim

- Directed differentiation of human embryonic stem cells into dopamine neurons
- School of Psychiatry, Faculty of Medicine, UNSW
- Supervisors: Associate Professor Kuldip Sidhu, Associate Professor Kay Double
- PhD conferred 2013

Teresa Lee

- Genetic and environmental influences on neuropsychological functioning in later life: the Older Australian Twins Study
- School of Psychiatry, Faculty of Medicine, UNSW
- Supervisors: Professor Perminder Sachdev, Associate Professor Julie Henry, Professor Julian Trollor
- PhD conferred 2013

Tao Liu

- Morphological analysis of brain volume, cortical thickness and sulci based on magnetic resonance imaging in the elderly
- Faculty of Engineering and Information Technology, University of Technology Sydney
- Supervisors: Dacheng Tao, Jesse Jin, Wei Wen
- PhD conferred 2012

Im Quah-Smith

- An experimental and clinical study on the effects of laser acupuncture in the alleviation of depressive symptoms
- School of Psychiatry, Faculty of Medicine, UNSW
- Supervisors: Professor Perminder Sachdev, Professor Gordon Parker, Associate Professor Mark Williams
- PhD conferred 2013

Chao Suo

- Brain plasticity stimulated by physical and cognitive exercise as revealed by multimodal magnetic resonance imaging
- School of Psychiatry, UNSW
- Supervisors: Associate Professor Michael Valenzuela, Associate Professor Wei Wen
- PhD conferred 2013

Haobo Zhang

- Grey matter morphological changes in late life using magnetic resonance imaging technique
- School of Psychiatry, UNSW
- Supervisors: Professor Julian Trollor, Professor Perminder Sachdev, Associate Professor Wei Wen
- PhD conferred 2012

Lin Zhuang

- Mapping of the structural human brain networks in Mild Cognitive Impairment
- School of Psychiatry, UNSW
- Supervisors: Associate Professor Wei Wen, Professor Julian Trollor
- PhD conferred 2012

AWARDS

Dr Nady Braidy

- UNSW Dean's Rising Star Award (2012)
- International Investigator of the Year Award in Geriatric Psychoneuropharmacology (2012)

Professor Henry Brodaty

- Alzheimer's Australia Lifetime Award (2013)

Dr John Crawford

- UNSW Vice-Chancellor's Excellence Award, Professional Services (2013)
- UNSW Dean's Award for Professional & Technical Staff (2013)

Ms Kate Crosbie

- UNSW Dean's Award for Professional & Technical Staff (2012)

Ms Yanhong (Catherine) Dong

- UNSW Dean's List (PhD research) (2012)

Dr Teresa Lee

- UNSW Dean's Rising Star Award (2013)

Dr Lee-Fay Low

- NSW Young Tall Poppy Science Award (2012)
- Certificate of Excellence, Free presentations. International Psychogeriatrics Association Meeting, Seoul (2013)

Dr Karen Mather

- Early Career Award, College of Geriatric Psychoneuropharmacology Annual Conference (2013)

Dr Louise Mewton

- UNSW Dean's Rising Star Award (2012)

Ms Heidi Mitchell

- UNSW Vice-Chancellor's Excellence Award, Innovation and Entrepreneurship (2013)

GRANTS

Improving clinical diagnosis of mild neurocognitive disorders

Funding Source: National Health & Medical Research Council (NHMRC) Early Career Fellowship
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
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
Investigator/s: Prof Perminder Sachdev, Dr Margaret 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

Genetic and epigenetic variation and early markers of late-onset Alzheimer's disease

Funding Source: Alzheimer's Australia Research / Postdoctoral Fellowship in Dementia
Investigator/s: Dr Karen A Mather
Duration 2 years: 2013-2014
Total Funds: $100,000

Is the loss of white matter integrity an early neuroimaging biomarker of amnestic Mild Cognitive Impairment and Alzheimer's dementia?

Funding Source: UNSW Australia Silver Star
Investigator/s: A/Prof Wei Wen
Duration: 1 year: 2013
Total Funds: $30,000

Plasma protein profiles in normal brain ageing and early stages of dementia

Funding Source: Australian Research Council (ARC) Discovery Project
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

Secondary analyses and archiving of social and behavioral databases in aging

Funding Source: National Institutes of Health (USA)
Investigator/s: Prof P Sachdev, Prof Henry Brodaty, Dr Kristan Kang
Duration: 1 year: 2012-2013
Total Funds: $52,402

A tale of three cities: comparison of the Sydney Memory and Ageing Study and ageing and Australian imaging, biomarker and lifestyle studies

Funding Source: CSIRO Flagship Project Grant
Investigator/s: Prof Henry Brodaty, Prof Perminder Sachdev, Prof David Ames
Duration: 2 years: 2012-2013
Total Funds: $123,000

Genetic associations of cognitive ageing and depression

Funding Source: UNSW Australia/Group of Eight Australia (G08)/Germany Joint Research Cooperation Scheme (DAAD)
Investigator/s: Prof Perminder Sachdev, Dr Simone Reppermund
Duration: 2 years: 2012-2013
Total Funds: $17,100

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

Funding Source: UNSW Australia Gold Star
Investigator/s: Prof Henry Brodaty, Prof David Ames, Dr Margaret Wright, A/Prof Julian Trollor, Prof Nick Martin, A/Prof Wei Wen, Prof Bernhard Baune, Dr Teresa Lee, Dr John Crawford
Duration: 1 year: 2012
Total Funds: $40,000

Genetic and environmental determinants of brain networks in ageing: a diffusion tensor imaging based study of twins

Funding Source: NHMRC Seed Funding Project Grant
Investigator/s: A/Prof Wei Wen
Duration: 1 year: 2012
Total Funds: $144,708

Genetic and environmental contributions to amyloid burden in older Australians: a Pib-PET imaging study of twins

Funding Source: NHMRC Seed Funding Project Grant
Awardee/s: Dr Melissa J Slavin
Duration: 1 year: 2012
Total Funds: $181,265

Australian neuropsychological normative study

Funding Source: DCRC Project Grant
Awardee/s: Dr Nicole Kochan
Duration: 1 year: 2012
Total Funds: $40,000

Ian Potter Cultural Trust Travel Grant

Funding Source: Ian Potter Foundation
Awardee/s: Dr Simone Reppermund
Duration: 1 year: 2012
Total Funds: $2,500

High performance computer with four opteron processors

Funding Source: UNSW Major Research Equipment & Infrastructure Scheme
Investigator/s: Mr Victor Vickland, Prof Henry Brodaty
Duration: 1 year: 2012
Total Funds: $50,000

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

Funding Source: NHMRC Program Grant
Investigator/s: Prof Perminder Sachdev, Prof Henry Brodaty, Prof Gavin Andrews
Duration: 5 years: 2010-2014
Total Funds: $6,090,000

Prevention and management of mental disorders in older Australians

Funding Source: NHMRC Capacity Building Grant
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

**Extend grant duration approved by NHMRC, 29 April 2014 - new end date of 31 December 2014*

A cognitive and neuroimaging study of exceptionally old age: Sydney Centenarian Study (SCS)

Funding Source: NHMRC Project Grant
Investigators: Prof Perminder Sachdev, Prof Robyn Richmond, Dr Nicole Kochan, Dr Wei Wen, Dr John Crawford
Duration: 3 years: 2010-2012*
Total Funds: $826,500
Amount per year: $265,500 (2010); $290,500 (2011); $270,500 (2012)

**New end date approved by NHMRC to 31 December 2013*

Gene-environment interactions in healthy ageing and age-related neurodegeneration (the Older Australian Twins Study – OATS)

Funding Source: NHMRC/ARC Strategic Award
Investigators: Prof Perminder Sachdev, Prof David Ames, Prof Peter Schofield, Prof GA (Tony) Broe, Prof Henry Brodaty, A/Prof Julian Trollor, Dr Margaret Wright, Dr Wei Wen, Dr Teresa Lee
Duration: 5 years: 2007-2011
Total Funds: $2,000,000
Amount per year: $400,000

PHILANTHROPIC

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

The Montefiore Chair of Healthy Brain Ageing at UNSW

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

Major partner & direct donations 2013:
$336,584.16

Event & sponsorship funding 2013:
$68,617

We thank the following people who made generous donations to CHeBA between October 2012 and December 2013:

- Australian Psychological Society
- Dr Ian Paterson
- Lillian Melick
- Miss Heather Garnsey
- Mr Abie Greengarten
- Mr Alan Deutsh
- Mr Brian Topper
- Mr David Eisenberg
- Mr David Itzkowics
- Mr George Rich
- Mr Jeff Newman
- Mr John Kenneth Griffith
- Mr Michael D Price
- Mr Michael Patrick Regan
- Mr Patrick Regan
- Mr Peter Halas
- Mr Peter Rosenthal
- Mr Reginald John Sherlock
- Mr Robert Kohn
- Mr Robert Schwartz
- Mr William Highfield
- Mrs Heather Irwin
- Mrs Judith Lyell
- Ms H J Willoughby
- Ms Pamela Madafiglio
- Patrica Marshall
- Peter, Chris & David Spink
- Prime Practice Pty Ltd - Mr & Mrs Philip & Eva Palmer
- Rhiannon Stack

FINANCIAL PERFORMANCE

STATEMENT OF FINANCIAL PERFORMANCE FOR THE YEAR ENDED 31 DECEMBER 2013

	Notes	2013
		$
Funds		
Research Revenue		2,503,977
Donations		170,954
Fees		-
Faculty Funds		-
UNSW Contribution - Competitive	2	78,000
UNSW Contribution - Strategic	3	15,000
Sundry Other Revenue		3,513
Total Funds		**2,771,444**
Costs		
People Costs		2,908,302
Scholarship Stipends		22,164
Contract & Consulting Services		402,298
Repairs and Maintenance		1,470
Consumables		60,036
Travel		136,364
Equipment		32,731
Other Expenses		22,196
Internal Expense		67,076
Total Costs		**3,652,637**
Operating result		(881,193)
Opening Balance	1	1,630,535
Closing Balance		**749,341**

Notes to the Statement of Financial Performance

1. CHeBA was established as a centre in October 2012. As a result, the brought forward balance into 2013 is combination of new projects created in CHEBA and existing projects associated to the co-directors, Professor Perminder Sachdev and Professor Henry Brodaty, and other academics based in CHEBA. The brought forward balance of $1.630m includes funds relating to external research projects of $1.585m.
2. UNSW Contribution - Competitive relates to funding awarded to CHEBA from UNSW through various competitive schemes supporting research activities and infrastructure.
3. UNSW Contribution - Strategic relates to funding provided to CHEBA from UNSW as a strategic investment in the centre's research activities.

PUBLICATIONS

Journal publications

Adachi N, Kanemoto K, de Toffol B, Akanuma N, Oshima T, Mohan A, Sachdev P. Basic treatment principles for psychotic disorders in patients with epilepsy. *Epilepsia* 2013; 54(Suppl 1):19-33.

Anderson TM, Sunderland M, Andrews G, Titov N, Dear BF, Sachdev PS. The 10-item Kessler psychological distress measure (K10) as a screening instrument in older individuals. *Am J Geriatr Psychiatry* 2013; 21(7):596-606.

Anstey KJ, Cherbuin N, Eramudugolla R, Sargent-Cox K, Easteal S, Kumar R, Sachdev P. Characterizing mild cognitive disorders in the young-old over 8 years: prevalence, estimated incidence, stability of diagnosis, and impact on IADLs. *Alzheimers Dement* 2013; 9(6):640-8.

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Bhardwaj AK, Trollor J, Evans E, Brodaty H, Sachdev P, Schofield P, Mowat D, Wen W, Crawford J, Iacono T, Torr J. Successful ageing in older adults with intellectual disabilities: predictors and correlates of cognitive decline. *Journal of Policy and Practice in Intellectual Disabilities* 2013; 10(2), 107-108.

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Brodaty H, Liu Z, Withall A, Sachdev PS. The longitudinal course of post-stroke apathy over five years. *J Neuropsychiatry Clin Neurosci* 2013; 25(4):283-91.

Brodaty H, Low, L-F, Liu Z, Fletcher J, Roast J, Goodenough B, Chenoweth L. Successful ingredients in the SMILE Study: resident, staff and management factors influence the effects of humor therapy in residential aged care. *Am J Geriatr Psychiatry* 2013; pii: S1064-7481(13)00336-9. doi: 10.1016/j.jagp.2013.08.005.

Brodaty H, Seeher K and Gibson L. Dementia time to death: a systematic literature review on survival time and years of life lost in people with dementia. *Int Psychogeriatr* 2012; 24(7):1034-1045.

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Draper B, Hudson C, Peut A, Karmel R, Chan N, Gibson D. The Hospital Dementia Services Project: Aged care and dementia services in NSW public hospitals. *Australas J Ageing* 2013; doi: 10.1111/ajag.12042.

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Gates N, Sachdev P, Fiatarone Singh M, Valenzuela, M. The effect of exercise training on cognitive function in older adults with Mild Cognitive Impairment: a meta-analysis of randomized controlled trials. *Am J Geriatr Psychiatry*. 2013; 21(11):1086-97. doi: 10.1016/j.jagp.2013.02.018

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Kanchibhotla SC, Mather KA, Wen W, Schofield P, Kwok JB, Sachdev PS. Genetics of ageing-related changes in brain white matter integrity – a review. *Ageing Res Rev* 2013; 12(1), 391-401.

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Fry M, Arendts G, Chenoweth L, MacGregor C. Cognitive impairment is a risk factor for delayed analgesia in older people with a long bone fracture. New Horizons 2013. *30th Combined Health Science Conference*. 18-19 November 2013; Kolling Institute, Sydney.

Gates N, Sachdev P, Fiatarone Singh M, Valenzuela M. Model of psychological wellbeing in Mild Cognitive Impairment. *Asia Pacific Regional Conference of Alzheimer's disease International,* 11-13 December 2013; Hong Kong.

Gates N et al. Memory and Cognitive Function, but not subjective memory complaint, predict quality of life and psychological wellbeing in individuals with Mild Cognitive Impairment. *Asia Pacific Geriatric Conference,* 20-22 October 2012; Hong Kong.

Jeon Y-H, Govett J, Low L-F, Chenoweth L, McNeil G, Hoolahan A, Brodaty H, O'Connor D. Utility of the Aged Care Funding Instrument in care planning. *Australian Association of Gerontology 45th National Conference-Ageing: Challenging the boundaries*. 20-23 November 2012; Brisbane, QLD. [Oral presentation]

Jeon Y-H, Low L-F, Chenoweth L, O'Connor D, Beattie E, Brodaty H. Best practice in assessing depression in nursing homes. *International Psychogeriatric Association (IPA) 16th International Congress,* 1-4 October 2013; Seoul, Republic of Korea.

Low L-F. The Sydney Multisite Intervention of Laughterbosses and Elderclowns (SMILE): an overview of results and reflection on components of the intervention. (Presented as part of symposium of nonpharmacological interventions). *International Psychogeriatrics Association 16th International Congress,* 1-4 October 2013; Seoul, Korea.

Low L-F. Does personality affect risk for dementia? A systematic review and meta-analysis. *International Psychogeriatrics Association 16th International Congress,* 1-4 October 2013; Seoul, Korea.

Low L-F, Goodenough B, Haertsch M, Bell JP, Brodaty H. And the whole world SMILEs with you… implementing the SMILE study in practice. *Dementia Research Forum*, 21-22 September 2013; Brisbane, Australia.

Mather KA et al. Epigenetics and cognitive ageing. *International college of geriatric psychoneuropharmacology conference*, 30 Oct – 2 Nov 2013; Pittsburgh, USA [poster presentation]

Menant JC, Sturnieks DL, Brodie MAD, Smith S and Lord SR. Spatial versus non-spatial cognitive task effects on walking stability in older adults. *2nd Joint World Congress of the International Society of the Society for Posture and Gait Research (ISPGR) and Gait & Mental Function*, 22-26 June 2013; Akita, Japan. [Poster presentation]

Menant JC, Wong A, Sturnieks DL, Close JCT, Delbaere K and Lord SR. Understanding the relationship between dizziness and falls in older people. *5th Biennial Australian and New-Zealand Falls Prevention Conference*, 28-30 October 2012; Adelaide, Australia. [Podium presentation].

Menant JC, Sturnieks, DL, Fitzpatrick R and Lord SR. La réponse à des perturbations d'équilibres soudaines est un prédicteur de chutes chez les personnes âgées.*1er Congres de la Societe Francophone Posture, Equilibre, Locomotion (SOFPEL)*, 30 Nov -1 Dec 2012 ; Marseille, France. [Podium presentation]

Mewton L, Hobbs M, Sunderland M, Newby J. Andrews G. Reductions in the internalizing trait following internet-delivered transdiagnostic treatment for anxiety and depression in primary care. *Australasian Society for Psychiatric Research Annual Conference*, Dec 2013; Melbourne.

Miller Amberber A, Sachdev P, Kochan NA, Low L-F, Draper B. Assessing language changes associated with dementia and cognitive impairment in older CALD bilinguals. *Alzheimer's Australia 15th National Conference 2013*; Hobart, Australia. [Keynote presentation]

Müenchhoff J, Song F, Poljak A, Kochan NA, Brodaty H, Smythe GA, Attia J, Schofield PW, Sachdev PS. iTRAQ-based Plasma protein profiling of Mild Cognitive Impairment across two independent cohorts. *Human Proteome Organisation 12th Annual World Congress*, 14-18 Sep 2013; Yokohama, Japan. [Poster presentation]

Müenchhoff J, Song F, Poljak A, Kochan NA, Brodaty H, Smythe GA, Attia J, Schofield PW, Sachdev PS. Plasma Protein Profiling of Mild Cognitive Impairment and Alzheimer's disease. *Alzheimer's Association International Conference*, 14-18 July 2013; Boston, USA. [Poster presentation]

Perls T, Barzilai, Sachdev P, Levitan C, Pess G, Hirose N, Sebastiani P, Vina J, Atzmon G, Puca A. Centenarian Studies Network: an international collection of studies – learning from our similarities and differences. *International Association of Gerontology and Geriatrics*, 23-27 June 2013; Seoul, Korea.

Poljak A. Proteomic profiling of Alzheimer's disease brain. *17th Australasian Proteomics Society Symposium*, 2-5 Feb 2012; Lorne. [Oral presentation]

Seeher K, Brodaty H, Low LF, Reppermund S, Draper B, Kang K, Slavin M, Kochan N, Trollor J, Mather K, Sachdev P. Psychological distress in carers. Who gets it? – A study on family members of people with MCI. *National Dementia Research Forum Program and Abstract,* 27-28th September 2012; Canberra, Australia.

Seeher K, Brodaty H, Draper B, Kang K, Kochan N, Low LF, Reppermund S, Sachdev P, Slavin M, Trollor J: Psychological distress in supporters of older people with MCI. *45th Australian Association of Gerontology National Conference.* 20-23 November 2012; Brisbane. [Oral presenter]

Sidhu KS. Speaker at the *10th Annual World Congress of the Society of Brain Mapping and Therapeutics*, 2013; Baltimore, USA.

Slavin M, Giskes K, Levitan C, Kochan N, Brodaty H, Sachdev PS. Deriving normative values for the MMSE and ACE-R for the oldest-old. *International Association of Gerontology and Geriatrics*, 23-27 June 2013; Seoul, Korea.

Stein-Parbury J, Chenoweth L, Jeon Y-H, Brodaty H. The feeling world of dementia: learning person-centered care. *Dementia Care @ AAIC*, 17 July 2013; Boston, USA.

Vickland V, Brodaty H, Sadsad R, Morris T. Virtual experiments in a multi-agent model of dementia management. *Proceedings of the grand challenges in modelling and simulation* 2012; Genoa, Italy.

Yang Z, Wen W, Slavin M, Crawford J, Sachdev PS, Levitan C, Brodaty H. Accelerated ageing of the brain from 70 to 101 years old. *20th* World Congress of *International Association of Gerontology and Geriatrics*, 23-27 June 2013; Seoul, Korea.

WORKSHOPS & INVITED LECTURES

Braidy N. In vitro and In vivo models for investigating the pathogenesis of psychiatric disorder. *13th Annual International College of Geriatric Psychoneuropharmacology Meeting* 2013; Pittsburg, USA. [Invited Speaker]

Braidy N. Oxidative stress in Alzheimer's disease and ageing: revisiting the ancient phenomenon. *12th Annual International College of Geriatric Psychoneuropharmacology Meeting* 2012; Seville, Spain. [Invited Speaker]

Braidy N. NAD+: the new Achilles heel? *12th Annual International College of Geriatric Psychoneuropharmacology Meeting* 2012; Seville, Spain. [Invited Speaker]

Brodaty H. Update on diagnosis and treatment of dementia. *16th Asia Pacific Regional Conference of Alzheimer's disease in association with Macau Alzheimer's disease Association*. 14 December 2013; Macau [Invited presentation]

Brodaty H. Acute hospital care for patients with dementia in Australia. *28th International Conference of Alzheimer's disease International*. 18-20 April 2013; Taipei. [Invited presentation]

Brodaty H. Keynote presentation: improving dementia care in Australia. *Geriatric Clinical Colloquium*. 22 March 2013; Orange, Australia. [Invited presentation]

Brodaty H. Prevention and treatment of Alzheimer's disease. *Australian Disease Management Association 9th Annual National Conference*. August 2013; Sydney, Australia. [Invited presentation]

Brodaty H. Insights into the McKeon Review of health and medical research. *AAMRI 2012 National Convention Annual Dinner*. 31 October 2012; Canberra, Australia

Brodaty H. Supporting people with mental health issues who are ageing. *The mental health of older people: Connection sectors, Wesley Conference Centre*. 2 November 2012.

Brodaty H. Dementia update. *Eastern Suburbs Medicare Local*. 29 November 2012.

Brodaty H. Benefits of early detection and long-term management in dementias. *Medichem Neurosciences Summit Experts' Learning Program*. 16 May 2013; Sydney, Australia.

Brodaty H. 14 essential steps to diagnosis and management of dementia. *Brisbane General Practitioners Conference and Exhibition and Brisbane Pracice Nurse Clinical Education*. 20 September 2013; Brisbane, Australia.

Brodaty H. Carers and dementia. *Academic Department for Aged Care Psychiatry Inservice*. 12th December 2012, Royal Hospital for Women.

Brodaty H. Ageing – the good and the bad: findings from the Sydney Memory and Ageing Study. *Centre for Healthy Brain Ageing Information Day 2013*. 4 May 2013; UNSW, Sydney.

Brodaty H. Healthy brains. Positive ageing. *2013 Business Seminar Series for the Italian Chamber of Commerce*. 15 August 2013; Kirribilli Club Lavender Bay, Sydney.

Chenoweth L. The impact of playfulness on staff and how it changes care. *The National Play-Up Convention*. 5-6 September, 2013.

Chenoweth L. A person-centred approach to care. *International Alzheimer's disease Conference Hong Kong,* 13 Dec. 2013; Hong Kong.

Chenoweth L. Carer coaching for families of persons with dementia. *International Alzheimer's disease Conference*. 14 Dec 2013; Macau.

Gates N. Neuroplasticity: improving brain function via mental and physical exercise. *Behavioral Medicine Lecture Series*. Westmead Hospital, 25 November 2013

Gates N. Neuroplasticity: a healthy brain and mind for life. *Golden Door,* 15 November 2013.

Gates N. Keeping the mind alive: exercise can build mental muscle. *Wolper,* 6 May 2013.

Gates N. Secretes to a long and happy life. *Sydney City Council Seniors Week,* March 2013.

Kochan N. Diagnostic issues in Mild Cognitive Impairment. *Sydney Neuropsychology Case Rounds*, POWH, November 2013.

Kochan N. Reaction time measures predict dementia over 4 years, The Sydney Memory and Ageing Study. *Alzheimer's Association International Conference*. July 2013; Boston, USA.

Kochan N. The Australian Neuropsychological Normative Study of Older Persons, The Sydney Memory and Ageing Study. *College of Clinical Neuropsychologists Annual Conference*. November 2013; Brisbane.

Kochan N. Reaction time measures predict dementia over 4 years, The Sydney Memory and Ageing Study. *College of Clinical Neuropsychologists Annual Conference*. November 2013; Brisbane.

Low L-F. Young scholar's session; developing a viable career in dementia research: realities and rewards. *Dementia Research Forum*. 21-22 September 2013; Brisbane, Australia.

Low L-F. Special groups and quality dementia care. *Aged care reform: advancing quality in dementia care symposium*. 21 June 2013; University of Sydney.

Low L-F. Prevention of depression in later life. *Australian Rotary Health Symposium. Prevention of mental disorders across the lifespan: setting new directions for research and implementation*. 1-3 May 2013; Canberra (all expenses paid).

Low L-F. The Sydney Multisite Intervention of LaughterBosses and Elderclowns (SMILE) study an overview of results and reflection on the components of the intervention. *19th Australian Humour Studies Network Colloquium*, 7-9 February 2013; University of Newcastle.

Low L-F. Psychosocial approaches with people with dementia. *Redleaf Leisure and Lifestyle Seminar*. 30-31 October 2013.

Low L-F. Interpretation of research results. *Dementia Services Evaluation Grants Program Workshop 3*. 30 May 2013.

Low L-F. Introduction to statistics. *Dementia Services Evaluation Program Workshop*. 22 November 2012.

Low L-F. Home care evaluation – evidence and issues. *Home Care Quality Indicators Workshop*. 14 Nov 2013; St Luke's Hospital.

Low L-F. Non-pharmacological interventions for persons with dementia: what works and how to make it work for you (Plenary session). *Better Practice 2013*, 17-18 October 2013; Perth.

Low L-F. The results of SMILE and implications for better aged care practice. *The Play Up Convention*, 5-6 September 2013; Sydney.

Low L-F. Dementia prevention: what, when and why? *Leading Aged Services Australia (LASA) Congress*, 5-7 August 2013; Sydney.

Low L-F. Non-pharmacological interventions for persons with dementia: what works and how to make it work for you (Plenary session). *Better Practice 2013*, 25-26 July 2013; Sydney.

Low L-F. Design of LEAP for life: a community care training program to improve engagement and wellbeing of residents. *Centre for Healthy Brain Ageing (CHeBA) forum*. 24 May 2013; UNSW.

Low L-F. Can we make nursing homes more fun? The SMILE study. *Centre for Healthy Brain Ageing (CHEBA) public information day*. 4 May 2013; Sydney.

Low L-F. Humour in aged care. *Australian Nursing Home Foundation staff development day*, 23 March 2013; Sydney.

Low L-F. Friendships and persons with dementia: what new services can we provide? *Alzheimer's Australia NSW Inservice*, 13 Dec 2012; North Ryde.

Mather KA. Searching for genes related to early markers of dementia: the studies of the Centre for Healthy Brain Ageing. Invited presentation at the *St. George Hospital Psychiatry Academic Meetings*, 2013. Kogarah, Australia.

Menant J. Invited talk on research update on falls prevention. *NSW Rural Falls Network Meeting*, 24 October 2013; Bateman's Bay, NSW.

Menant J. Invited seminar talk on dual-task studies in aging and clinical groups. *Cognitive Neuroscience Research Group*, 23 September 2013; Aix-Marseille University, Marseille, France.

Müenchhoff J, Song F, Poljak A, Kochan NA, Brodaty H, Smythe GA, Attia J, Schofield PW, Sachdev PS. iTRAQ-based plasma protein profiling of Mild Cognitive Impairment across two independent cohorts. *Invited seminar at the Bioanalytical Mass Spectrometry Facility*. 2013; Sydney, Australia.

Sachdev P. Ageing and brain networks. *XII Annual Meeting of the International College of Geriatric Psychoneuropharmacology (ICGP),* 24-27 October 2012; Seville Spain. [Invited Speaker]

Sachdev P. The classification of neurocognitive disorders – the DSM-5 approach. *XII Annual Meeting of the International College of Geriatric Psychoneuropharmacology (ICGP)*, 24-27 October 2012; Seville Spain. [Plenary Speaker]

Sachdev P. The narrative in neurology and psychiatry. *Grand Rounds*, 21 March 2013; Liverpool Hospital, Liverpool.

Sachdev P. Is Alzheimer's a disease of white matter? *Brain Sciences Colloquium,* 25 March 2013; Black Dog Institute, Sydney.

Sachdev P. Recent developments in vascular cognitive impairment. *3rd Singapore International Neurocognitive Symposium, National Neuroscience Institute (NNI),* 5-6 April 2013; Singapore. [Plenary Speaker]

Sachdev P. Classification of neurocognitive disorders: the DSM-5 approach. *3rd Singapore International Neurocognitive Symposium, National Neuroscience Institute (NNI),* 5-6 April 2013; Singapore. [Plenary Speaker]

Sachdev P. Prevention of neuropsychiatric disorders in the elderly: status of the evidence. *Australian Rotary Health Symposium on the Prevention of Mental Disorders,* 1-3 May 2013; University House, Canberra. [Invited Speaker]

Sachdev P. Medical perspectives on Tourette syndrome. *The Tourette Syndrome Association of Australia Seminar*, 4 May 2013; Burwood RSL Club, Burwood.

Sachdev P. Does brain training really work: examining the scientific evidence. *The Wolper Jewish Hospital Keeping the Mind Alive Seminar*, 7 May, 2013; Easts Leagues Club, Bondi Junction.

Sachdev P. The centenarian as a model of successful ageing. *American Psychiatric Association (APA) Annual Meeting*, 18-22 May 2013; San Francisco, USA. [Invited Speaker]

Sachdev P. Classifying vascular cognitive disorders: current challenges and potential solutions. *VASCOG*, 25-28 June 2013; Toronto, Canada. [Invited Speaker]

Sachdev P. Healthy minds at 100. Canberra Centenarians: Statistics, Science and Stories. *Australian Association of Gerontology (ACT Division)*, 2 August, 2013. [Invited Speaker]

Sachdev P. What twins can tell us about ageing: insights from the Older Australian Twins Study. *Melbourne Neuroscience Seminar Series*, 4 September 2013; Melbourne Brain Centre, University of Melbourne, Victoria,. [Invited Speaker]

Sachdev P. The world-wide burden of neuropsychiatric disorders. *8th International Neuropsychiatric Congress*, 23-27 Sep 2013; Chicago, USA. [Invited Plenary Speaker]

Sachdev P. Changing lifestyle to prevent dementia. *Integrative Mental Health 2013 Forum*, 23 Nov 2013; UNSW, Sydney. [Invited Speaker]

Seeher K. The Scarlet RoAD study and other clinical trials. *Public forum hosted by the Sydney Centre for Clinical Cognitive Research at Prince of Wales Hospital,* 5 November 2012; Randwick. [Invited Speaker]

Seeher K. How clinical trials work. *Public forum Worried about memory loss? hosted by the Sydney Centre for Clinical Cognitive Research,* 5 June 2013; Prince of Wales Hospital, Randwick. **[Invited Speaker]**

Seeher K. Memory. *VibeWire's FastBreak powered by The Powerhouse Museum*, 27 September 2013; Sydney. [Invited Speaker]

Sidhu KS, Chung H, Sachdev PS. Patient-derived stem cells as model for Alzheimer's disease. *10th Annual Congress SBMT*, 2013; Baltimore, USA. [Invited Speaker]

Wen W. Invited speaker for the *Official Opening & MRI Symposium*, May 2013; BRIL Mark WainWright Analytical Centre, UNSW.

Wen W. Invited speaker at the *7th Alzheimer's and Parkinson's Disease Symposium*, Sept 2013; Queensland Brain Institute, University of Queensland.

Wen W. Invited speaker at the *Brain Donor Program Meeting*, Oct 2013; Brain and Mind Institute, University of Sydney.