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Chairperson’s Report: Dagmar Schmidmaier AM

2014 has been a year of remarkable findings and advancements at CHaBA.

One of the great strengths of CHaBA continues to be its multidisciplinary, comprehensive approach to brain ageing issues. This is exemplified by the 2014 achievements in broad-ranging areas such as the identification of a potential natural model for Alzheimer’s disease using the rodent Octodon degus, to the publication of the report, “Is the incidence of dementia declining?”, authored by Professor Sachdev, which provides evidence that preventative health strategies could lower the risk of dementia for future generations.

In 2014, the exemplary work of Professors Sachdev and Brodaty lead a high calibre, dedicated group of researchers who bring a diverse set of skills to address research issues in brain ageing and dementia. Since its launch, CHaBA has continued to build its own unique identity as a leading research centre, with internationally competitive programs in many aspects of this field. This has been achieved with limited infrastructure and the lack of one place they can call home.

A key focus for the Advisory Committee in 2014 has been to generate new funding avenues for CHaBA to harness the talent and dedication of the researchers.

Dementia research is heavily funded under its prevalence is taken into account: at the last estimate, dementia funding amounted to $1 for every $7 for their commitment. We remain committed to assisting CHaBA continue its strong presence in the community, largely thanks to the tireless work of Heidi Mitchell, our Marketing & Communications Officer & Karen Mother who was awarded the International Pioneer in Medicine award. Dr Nady Braidy who was selected to attend the prestigious Lindau Nobel Laureate Meeting and Kuldip Sidhu who was awarded the International Pioneer in Medicine award. Dr Nady Braidy who was selected to attend the prestigious Lindau Nobel Laureate Meeting and Kuldip Sidhu who was awarded the International Pioneer in Medicine award. Dr Nady Braidy who was selected to attend the prestigious Lindau Nobel Laureate Meeting and Kuldip Sidhu who was awarded the International Pioneer in Medicine award. Dr Nady Braidy who was selected to attend the prestigious Lindau Nobel Laureate Meeting and Kuldip Sidhu who was awarded the International Pioneer in Medicine award. Dr Nady Braidy who was selected to attend the prestigious Lindau Nobel Laureate Meeting and Kuldip Sidhu who was awarded the International Pioneer in Medicine award. Dr Nady Braidy who was selected to attend the prestigious Lindau Nobel Laureate Meeting and Kuldip Sidhu who was awarded the International Pioneer in Medicine award. Dr Nady Braidy who was selected to attend the prestigious Lindau Nobel Laureate Meeting and Kuldip Sidhu who was awarded the International Pioneer in Medicine award. Dr Nady Braidy who was selected to attend the prestigious Lindau Nobel Laureate Meeting and Kuldip Sidhu who was awarded the International Pioneer in Medicine award.

Similarly, global projection figures are estimated to reach 135 million by 2050, with costs to grow exponentially from the current amount of $600 billion annually. With rising figures representing an enormous social and economic burden and no available cure, dementia prevention is widely recognised as a critical area for research development. We are heartened by the World Dementia Council’s statement calling on governments to adopt a risk reduction approach in public health policies and campaigns, and to increase investment for population level research into dementia risk. This aligns with our belief that dementia is at least partially preventable through strategies that will push back its onset.

Accordingly, a major focus for CHaBA in 2014 was the leadership and expansion of a number of international consortia – COSMIC, ICC-Dementia, STROKID and PROMOTE - examining epidemiological, genetic and psychosocial factors related to dementia. Establishing international consortia is an innovative approach which allows the pooling of data from studies across the world to generate more robust statistical models of multiple risk and protective factors, and more precise estimates for potential factors with small effect. Running large-scale statistical analyses means we are better able to identify groups at risk and implement early intervention strategies to delay, ameliorate or stop the progression of dementia. A significant achievement for our consortia in 2014 was the expansion of STROKID, which now represents all continents, with a total sample size of more than 5000.

In 2014, CHaBA continued to consolidate its position as a leading centre of excellence in the field of brain ageing research. We outline some of our key research findings from 2014 in this report, including the development of a potential natural model for Alzheimer’s progression using the rodent Octodon degus, results from CHaBA Sydney Memory and Ageing Study showing the ability to metabolise glucose normally may help preserve brain structure and function, and results from the collaborative SMART trial demonstrating resilience training significantly improved global cognitive function.

We extend our congratulations to several of our researchers, whose innovative work was recognised in 2014: Honorary Associate Professor Kuldeep Sidhu who was awarded the International Pioneer in Medicine award. Dr Daryl Baker who was selected to attend the prestigious Lindau Nobel Laureate Meeting and Dr Karen Mother who was awarded the International Pioneer in Medicine award. Dr Nady Braidy who was selected to attend the prestigious Lindau Nobel Laureate Meeting and Kuldip Sidhu who was awarded the International Pioneer in Medicine award. Dr Nady Braidy who was selected to attend the prestigious Lindau Nobel Laureate Meeting and Kuldip Sidhu who was awarded the International Pioneer in Medicine award. Dr Nady Braidy who was selected to attend the prestigious Lindau Nobel Laureate Meeting and Kuldip Sidhu who was awarded the International Pioneer in Medicine award. Dr Nady Braidy who was selected to attend the prestigious Lindau Nobel Laureate Meeting and Kuldip Sidhu who was awarded the International Pioneer in Medicine award. Dr Nady Braidy who was selected to attend the prestigious Lindau Nobel Laureate Meeting and Kuldip Sidhu who was awarded the International Pioneer in Medicine award.

"Our belief is that dementia is at least partially preventable through strategies that will push back its onset"
Momentum, a movement to bring researchers and the corporate and philanthropic community together to change the future of dementia incidence. Former CHiBA Advisory Committee member and corporate leader Mr Richard Gediman AM has been instrumental in the creation of this initiative and will continue to play an essential role as Spokesman. The Dementia Momentum seeks to raise $10 million over 5 years to advance CHiBA research into risk and protective factors using large-scale "big data" amassed through international consortia. Since CHiBA has already established a number of consortia, we are in an excellent position to make a world-wide difference to prevention, earlier diagnosis, and earlier and more effective interventions.

In 2015, CHiBA plans to create a registry of people with dementia nationally. We also hope to finalise a unified space for CHiBA in 2015 through our participation with the MindGardens initiative spearheaded by a UNSW/ELSD Health Sciences alliance. Lastly, we wish to thank our supporters, their movement and participation which helped make 2014 a successful year for CHiBA. We look forward to continuing to deliver outcomes to fulfil our objective of healthy brains for healthy lives in the years to come.

Sincerely,

Chair, after leading the Committee since CHiBA's inception in 2012. Similarly, our Steering Committee has helped drive CHiBA's strategy for this and the coming year. Ultimately, research is a team effort and our achievements in 2014 could not have been possible without an exceptionally dedicated team of research assistants, PhD scholars, post-doctoral research associates and our collaborators, as well as our Centre Manager Angie Russell who manages finances and administration to ensure the CHiBA engine runs smoothly. Dr Sophia Dean and Kate Crook provided invaluable research and administrative support.

We continue with ambitious, but achievable, plans for 2015 including targeting prevention of cognitive decline. According to the latest available figures, National Health and Medical Research Council funding for Alzheimer's and other dementias is about 13 per cent of the amount of money for cancer research, while government funding overall is not proportionate to the number of people affected and the projections going ahead. To partly redress this imbalance, in 2015 we will launch The Dementia

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

Our Purpose

CHiBA is positioned as a leader in multidisciplinary research into age-related brain diseases, particularly dementia, and an international hub for collaborative engagement. Its work extends from molecular work in the Genetics and Proteomics laboratories, to neuronal systems and networks in the Neuromaging Laboratory, to clinical, epidemiological and sociological research, to research on ageing health policy using strong links with teaching hospitals, aged care providers, state and federal governments and its established ageing cohort studies. It works strongly emphasises implementation, capacity building and translational research.

Our Aims

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

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

Our Mission

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

Our Vision

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

Our Functions & Goals

The functions of the Centre are to:

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

This will be achieved through:

- Strengthened collaborative research programs among staff and partners locally, nationally and internationally, supported by increased peer-reviewed grants and commissioned research.
- Development of specialised research facilities and laboratories that place the
It’s important as a community we come to grips more than we have with the implications of a rapidly ageing population. This is not only about funding that might be necessary. It’s also about commitment and hope that something can be done.

ROGER CORBETT AO
Current thinking suggests it takes 25 years for symptoms of dementia to show. If we can halve the rate of that process, and build it up over 50 years, we can actually delay it showing up in our lifetime at all.  

Professor Henry Brodaty
“The award to Perminder Sachdev and I is testimony to a wonderful, dedicated and hard-working team striving to achieve the goal of healthy brains for all of us as we age,” Professor Henry Brodaty.

This is the highest award made by UNSW Medicine in recognition of outstanding contribution and significant achievements. “The award to Perminder Sachdev and I is testimony to a wonderful, dedicated and hard-working team striving to achieve the goal of healthy brains for all of us as we age,” said Professor Brodaty.

Professor Braidy and Professor Sachdev founded the Centre for Healthy Brain-Aging in 2012, which has since established itself firmly as a pre-eminent centre in brain ageing research. Recent research breakthroughs have included the development of new diagnostic criteria for vascular cognitive disorders, findings that indicate one in four elderly people with mild cognitive impairment naturally revert to normal cognition, and world-first findings about the potential of white matter brain imaging measures as a cheaper and less invasive technique for the early diagnosis of Alzheimer’s disease.

In addition to founding and leading CHeBA, both Professors have a long and distinguished history of academic and professional contribution in the fields of mental health, neuropsychiatry, geniatrics, health care policy and community involvement.

ChEBA’s Co-Directors Professor Henry Brodaty and Professor Perminder Sachdev, were jointly awarded the 2014 UNSW Medicine Dean’s Award for Outstanding Achievement on 11 November 2014.

Dean’s Award for Outstanding Achievement

Dr Nady Braidy
Attended 2014 Lindau Nobel Laureate Meeting

Dr Nady Braidy was one of 15 Australian scientists selected by the Australian Academy of Science to attend the 2014 Nobel Laureate meeting in Lindau, Germany to meet with Nobel Prize winners in the fields of physiology and medicine.

The 64th Lindau Nobel Laureate Meeting (20 June – 4 July 2014) brought together 600 young researchers from 80 different countries to interact with giants in these fields and build networks with other researchers. Overall, 20,000 researchers applied worldwide. The 15 Australians chosen went through a rigorous selection process to be put forward by the Australian Academy of Science.

“We’re already working with one of the leading neuroscientists in South America,” he told The Australian newspaper. “The approach is paying dividends, with several research publications already in the pipeline.”

Dr Braidy is a National Health and Medical Research Council early career postdoctoral fellow at CHeBA. His work investigates the pathobiology of Alzheimer’s disease and is the first to link one of the longevity genes, NAD+, with ageing. Next, he hopes to show that NAD+ levels can be increased in animal models, possibly leading to a reversal of age-related brain diseases.

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Dr Braidy said he was “honoured and flabbergasted” to be selected, and he made the most of the Nobel Laureate opportunity to forge new collaborations.

Dr Karen Mather
Awarded Yulgilbar Post-Doctoral Excellence Award

Leader of CHeBA’s Genetics and Genomics Group, researcher

Dr Karen Mather, received a $20,000 post-doctoral excellence award from the Yulgilbar Foundation in 2014, as part of a $10 million philanthropic initiative to find a cure for Alzheimer’s disease.

Dr Mather’s research project is investigating the biological determinants of an early symptom of Alzheimer’s disease, memory loss. Using identical twins from CHeBA’s Older Australian Twins Study, her research aims to identify RNA differences between co-twins who differ in their performance on memory tests. RNA is one of the three major macromolecules (along with DNA and proteins) that are essential for life. RNA carries information from DNA, the genetic blueprint, to form proteins and perform other functions in the cell and the body, and is therefore a very important but less well understood part of the puzzle in understanding memory impairment and dementia. This study has the potential to increase understanding of the early development of late-onset Alzheimer’s disease and ultimately may suggest novel diagnostic, prognostic and treatment strategies.

The Yulgilbar Foundation, established by Sarah and Baillieu Myer through the Myer Family Company, provides funding to find a cure for Alzheimer’s disease and, to date, has awarded five post-doctoral excellence awards to top-up the salaries of young researchers who are working to cure, prevent or slow down the advancement of Alzheimer’s.

The Yulgilbar Foundation has called for donations from other philanthropists, pledging to match any donations received. “We think that this is a great opportunity for private philanthropy to value-add to the government program by bringing the innovation and young minds into the mix,” said Baillieu Myer.

Professor Sachdev and Braidy expressed their gratitude to Yulgilbar Foundation for their generous support of Dr Mather.

“With funding for dementia research grossly underfunded when its prevalence and disease burden are taken into account, it is extremely promising to see such a push for philanthropic funding in this area by the Myer Family Company. We hope it encourages other philanthropists to recognise the importance of supporting CHeBA’s research into age-related cognitive disorders,” said Professor Sachdev.

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Honorary Associate Professor Kuldip Sidhu

Receives International Pioneer in Medicine Award

Co-Leader of CHiMaia Molecular Biology & Stem Cells Group, Honorary Associate Professor Kuldip Sidhu was awarded the “International Pioneer in Medicine Award” at the World Congress of the Society of Brain Mapping and Therapeutics (SBMT) in Sydney, held on 17-19 March 2014.

“...This award is also recognition of an important area of research that is destined to bring a paradigm change in human medicine.”

HON. ASSOCIATE PROFESSOR KULDIP SIDHU

The International Pioneer in Medicine Award is presented to individuals who have significantly contributed to scientific advancement in the fields of medicine and image guided therapy through a multidisciplinary approach. Their groundbreaking work has made developments in state-of-the-art technology and scientific discovery a reality.

Hon. Associate Professor Sidhu received the award for his landmark contributions to stem cell research, including spearheading the building of a unique global consortium to study patient-derived stem cells, known as induced pluripotent stem cells (iPSC). He co-authored the findings with 2012 Nobel Prize winner Dr Shinya Yamanaka. This collaboration has resulted in a ground-breaking discovery in the field of regenerative medicine.

“This award is also recognition of an important area of research that is destined to bring a paradigm change in human medicine,” said Hon. Associate Professor Sidhu. “The awards committee has been impressed by the pioneering work of Hon. Associate Professor Sidhu.”

As part of the 2014 NHMRC Grant Success – World First Study

Professor Sachdev was awarded $625,000 to better understand how amyloid plaques in the brain affect cognitive function.

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As part of the 2014 NHMRC Grant Success – World First Study

Professor Sachdev was awarded $625,000 to better understand how amyloid plaques in the brain affect cognitive function. This funding will be used to study the relationship between plaques and cognitive function, and to shed light on how genes and environments contribute to the development of the plaques.

Plaques on the brain are one of the hallmark indicators of Alzheimer’s disease, but it is still not fully understood how they grow or how they are linked to cognitive decline. Professor Sachdev and his team will conduct the world’s first study using PET scans with amyloid imaging of 100 sets of twins aged 60+ to study the relationship between plaques and cognitive function, and to shed light on how genes and environments contribute to the development of the plaques.

Modern imaging techniques, like PET scans, have revolutionised research into normal and pathological brain ageing. Many people develop plaques made of the protein amyloid as well as neurofibrillary tangles – both believed to be primary culprits for dementia. However, their presence does not mean cognitive decline is certain.

“People with Alzheimer’s disease all have amyloid, but if brain scans are taken of people in their 70s and 80s you see it’s possible to have amyloid but not dementia,” explained Professor Sachdev.
A report released on 9 April 2014 by Alzheimer’s Australia and CHeBA, “Is the Incidence of Dementia Declining?”, suggested that action on preventative health could lower the risk of dementia for future generations.

Author of the report, Professor Sachdev, said “There is evidence from recent studies in Europe that the age-specific rates of dementia may be modifiable. It is possible that environmental and lifestyle factors, such as diet and exercise, could make a significant contribution to reducing the risk of developing dementia.

A recent study in the UK in 2011 found that the expected prevalence of dementia in people aged 65 years and older was estimated to be 8.1 per cent but the actual prevalence was found to be 6.5 per cent – a decrease of about 20 per cent from what was expected.”

Alzheimer’s Australia’s National President, Ita Buttrose, said that the report highlights the importance of changing the way Australians think about dementia.

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People of all ages can make simple lifestyle changes that may reduce their risk of dementia, such as increasing physical activity and controlling blood pressure and cholesterol,” Ms Buttrose said.

The report also cautions that the total numbers of people with dementia will continue to rise, even with changes in age-specific prevalence, because of the increasing numbers of older people in Australia.

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Role of Glucose in Preserving Brain Structure and Function

Professor Lynn Chenoweth

Profile picture of Professor Lynn Chenoweth

Professor Lynn Chenoweth, who was appointed a half-time professor position at CHeBA in 2013, brings a wealth of experience in aged care nursing, care models and healthy ageing and has strengthened CHeBA's collaborative relationships with a number of universities and industry care providers. In 2014, Professor Chenoweth worked on a wide range of projects in her role with CHeBA.

The researchers found that those participants who developed new glucose disorders such as diabetes or pre-diabetes (glucose levels higher than normal but not high enough to be considered diabetes) during the two year period, had an accelerated decline in brain volume and cognition over that two year period. In people with impaired fasting glucose – meaning their blood glucose levels are edging towards diabetes - oxidative stress and inflammation.

“Both these processes can damage brain cells and increase the risk of cognitive decline,” said Professor Sachdev. However, those who had pre-diabetes at the beginning of the study but maintained stable glucose levels over the two years did not show these same effects. Studies of longevity indicate that choosing carbohydrates wisely, eating a vegetable-rich diet with fish, olive oil and small amounts of lean meat, exercising and maintaining a healthy weight are all beneficial, said Professor Sachdev.

The authors of the study believe that one way of reducing the risk of dementia is also by reducing diabetes, particularly in the elderly.

Prevention of diabetes is also a strategy for the prevention of dementia,” said Professor Sachdev.

1. The Home Project Undertaking research in nursing homes requires managers, nurses, residents and their families to participate and is logistically difficult. By contrast, doing experiments in virtual space could reduce costs and simplify research. Professor Chenoweth and colleagues have been developing an Home computer model (a virtual residential aged care facility) using existing data sets to populate the model. The team makes adjustments to the characteristics of residents, staff and care environment, to reflect the diversity in aged care facility design, in order to run virtual experiments. The aim is to identify best practice in the real world setting to produce quality outcomes for people with dementia.

2. Evaluating the Benefits of Smart Technology in In-Home Care Practice This project aims to develop and evaluate assistive technologies to support navigation, localization and shadowing for older people living in the community and in residential care. Navigation technology has the capacity to take a device or a person to a desired destination, for example the dining room, while safely negotiating doorways, corridors and inclines. Localization is a technique to determine the position of people or devices. This enables carers to know the whereabouts of a person or a device. Shadowing technology enables a device to safely follow a user, allowing the user to move efficiently from task to task. To date, first-level construction of the navigation prototype has been completed and localization and shadowing prototypes are under construction.

3. Clinical Leadership in Aged Care (CLiAC) Project Leadership is key in any organisation and residential care facilities are no exception. Professor Chenoweth is part of a team conducting a cluster randomised controlled trial to test the effectiveness of an aged care clinical leadership program for middle managers, aiming to improve their managerial competencies and effectiveness in aged care practice.

4. National Quality of Life in Residential Aged Care Professor Chenoweth is leading a national Australian study to: (a) investigate quality of life (QoL) for people with dementia in Australian residential aged care facilities (RACFs) from multiple perspectives; (b) explore the relationship between facility characteristics, staff care, family member and resident factors and QoL for people with dementia in Australian RACFs; and (c) assess the effectiveness of self-report instruments for measuring QoL of persons with dementia in RACFs.

5. DCM EPIC Trial A team from the UK invited Professor Lynn Chenoweth to join them in a replication of the CADRES study which she led. The UK study is a cluster randomised controlled trial across 20 sites evaluating the clinical and cost-effectiveness of Dementia Care Mapping (DCM) in addition to usual care versus usual care. Alone for people with dementia living in care homes in the UK.

Results from CHeBA’s Sydney Memory and Ageing Study have shown that the ability to metabolise glucose normally may help preserve brain structure and function.

The findings were published in the January 2014 edition of the journal, Age. As part of the study, researchers assessed the brain function of 880 people aged between 70-90 years of age (and without dementia) with a variety of memory tests and brain scans.

“Knowing that poor control of glucose can harm the brain means that doing all we can to keep glucose levels healthy with the right food and exercise gives us a better chance of avoiding dementia.” - PROFESSOR PERMANDER SACHDEV

The researchers found that those participants who developed new glucose disorders such as diabetes or pre-diabetes (glucose levels higher than normal but not high enough to be considered diabetes) during the course of the study, had an accelerated decline in brain volume and cognition over the two year period. In people with impaired fasting glucose - meaning their blood glucose levels are edging towards diabetes - some had signs of two problems caused by rising blood glucose: oxidative stress and inflammation.

1. The Home Project

2. Evaluating the Benefits of Smart Technology in In-Home Care Practice

3. Clinical Leadership in Aged Care (CLiAC) Project

4. National Quality of Life in Residential Aged Care

5. DCM EPIC Trial

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6. IDEAL Study Care for dementia at the end of life presents different challenges. This cluster randomised controlled trial is evaluating the effectiveness and cost of facilitated case conferencing versus usual care for improving end of life outcomes in aged care residents with advanced dementia in aged care facilities and their families. Facilitated case conferencing occurs over three months for all intervention sites and includes families, GPs and palliative care specialists.

7. HALT Study (Metting Antipsychotic Use in Long-Term Care) Professor Chenoweth has been a key member of the team led by Professor Brodaty on a Department of Health and Ageing funded project to reduce use of antipsychotics in nursing homes. Antipsychotics which are prescribed to over a quarter of nursing home residents are associated with side effects such as stroke and death. The HALT study collaborates with dementia care specialists, GPs, nurses and aged care workers to reduce inappropriately antipsychotic medication use in long-term resident users and correspondingly to reduce complications, rates of decline and mortality without consequently increasing behavioural and psychological symptoms, and to demonstrates that HALT is a nationally applicable and sustainable model. Professor Chenoweth provides training to nurse champions on how to manage behavioural and psychological symptoms of dementia; the champions in turn train the nurses.

8. Transitional Care for Patients with Dementia This study is examining the hospital discharge process and transitional care occurring for patients with dementia and their carers.

9. Living with Dementia: Retirement Villages: Investigating the Experiences of Retirement Village Residents with Dementia Little is known about the experiences of people with dementia living in retirement villages. Professor Chenoweth is ascertaining the extent to which people with dementia are well supported to age in place through the provision of community care services and informal support from other members of the village community.

10. PAIN-ED: Assessment and Management of the Painfully Impaired Older Person Presenting to Emergency Departments with Musculoskeletal Conditions or Injuries Previous research demonstrated that older people with cognitive impairment presenting to ED with musculoskeletal conditions of injuries take longer to receive analgesia compared to younger or non-impaired patients. This study is a cluster randomised controlled trial that compares pain scores and analgesic administration of cognitively impaired and cognitively intact older people diagnosed with a long bone fracture. Second Phase Project (Halting Antipsychotic Use in Nursing Homes) – Professor Chenoweth to evaluate the quality of organisational culture, care and health services and care environments of their retirement villages, aged care services facilities against person-centred standards, and evaluate achievements against recommended improvements. A report has been submitted to the ARR funding body.

11. The Montefiore Home Aged Care Facilities engaged Professor Chenoweth to evaluate the quality of their organisational culture, care services and care environments against person-centred standards, and evaluate achievements against recommended improvements.

12. PCECAT Project A report was submitted to the ARR funding body.
An international research team, including CHeBA scientists, has found that a Chilean rodent, *Octodon degus*, may provide a natural model for Alzheimer’s disease.

The world-first study, published in the journal *Brain Pathology*, shows that pathological changes observed in *Octodon degus* closely correlate with the progression of Alzheimer’s disease in humans. The *Octodon degus* live longer than more common rat species (typically seven years or more) and the amyloid-beta protein found in their brains more closely resembles that of humans (amyloid-beta protein is the main component of the brain plaques found in Alzheimer’s patients).

CHeBA’s Dr Braidy says research into neurodegenerative disorders such as Alzheimer’s disease, has been limited by the reliability of available disease models. “None of the current models mimic the full-range of changes occurring during Alzheimer’s disease. In fact, several models rely on introducing foreign genes into organisms, so we don’t know how reliable they are and the success rate of therapeutic treatments using these models has been poor.”

Professor Sachdev and co-author of the paper, says, “Naturalistic models of later onset Alzheimer’s disease are urgently needed and the degu looks promising in this regard. Since this animal does not live in Australia, and importation for research may prove to be difficult, our collaboration with the Chilean researchers is of great scientific value.”

Stroke is a leading cause of chronic disability and second leading cause of death globally. Vascular cognitive impairment (VCI) is one of the major sequelae of stroke and transient ischemic attack (TIA) with negative functional impact and elevated risk for institutionalization, dependency and death. Therefore, the overarching aim of this thesis is to characterize neuropsychological patterns of post-stroke VCI and improve outcome after stroke by establishing optimal VCI screening, prognosticating cognitive and functional outcome and investigating the efficacy of the external carotid–internal carotid (EC–IC) bypass revascularization neurosurgical intervention. The findings include, firstly, the widely used cognitive screening instruments, both the Montreal Cognitive Assessment (MoCA) and the Mini-Mental Status Examination (MMSE), were equivalent and moderately sensitive in detecting VCI 3–6 months after stroke. However, the addition of a visuomotor processing speed measure can improve the accuracy of VCI screening. Secondly, the neurocognitive status measured by the MoCA and the MMSE at the subacute stroke phase (i.e., within two weeks after vascular events) could predict both cognitive outcome and functional outcome at 3–6 months later. Thirdly, the cognitive performance of ischemic stroke/TIA patients was worse than stroke-free non-demented controls, globally as well as in individual domains except the episodic verbal memory, which was relatively spared. This study also supports the impact of lesion location and severity on the pattern of cognitive deficits. Finally, the EC–IC bypass surgery in carefully selected severe intracranial steno-occlusive disease patients could result in significant improvement in cerebral hemodynamics and performance in verbal memory and executive function. These findings provide evidence for routine VCI screening, customized rehabilitation and discharge planning at the subacute stroke phase for better prognosis in patients at a higher risk for significant VCI and/or functional decline. It also provides a well-characterized neuropsychological profile to aid differential diagnoses in post-stroke VCI and effective cognitive and point measures in therapeutic intervention, as well as the preliminary evidence of EC–IC revascularization as a promising intervention for patients with severe steno-occlusive disease.
CHeBA was awarded one of two $50,000 cheques given by the Dick Smith Foods Foundation in their 2014 “1 million to charity” competition.

"With grant funding becoming increasingly competitive, support from the community in philanthropic endeavours is crucial to advance our research projects and work toward healthier brain ageing." Professor Perminder Sachdev

The CHeBA community proved to be formidable competition, staying neck and neck throughout the final stages of the first wave with joint winner Top Blokes Foundation. An additional 36 charities received smaller donations.

The degree of support from the community for CHeBA’s research was overwhelming and encouraging.

"With grant funding becoming increasingly competitive, support from the community in philanthropic endeavours is crucial to advance our research projects and work toward healthier brain ageing and better clinical care of age-related diseases such as Alzheimer’s and other dementias,” said Professor Sachdev.

CHeBA currently has five longitudinal studies examining various aspects of cognitive ageing and dementia, including neuroepidemiology, neuropsychology, neuromaging, genomics, proteomics, stem cells, metabolomics and neuroinflammation. Recently CHeBA was successful in identifying genetic markers that predict levels of a blood protein marker of cognitive ageing and early dementia. Since the official launch of CHeBA in 2012, there has been a significant increase in collaboration and the development of a number of international partnerships with consortia. The intention at CHeBA is to build upon these resources and develop novel and innovative research themes. A major focus will be on biomarker research using genomics, proteomics and neuroimaging. In addition, promising post-doctoral fellows at CHeBA will give a new impetus to the bench-to-community approach allowing for translation of the research.
24

Climb for a Cause

On 16 March 2014 CheBA Champion Stephanie Campbell endured an horrific skydiving accident. Coming in to land on her 57th solo skydive, Stephanie’s parachute passed through turbulent air and collapsed high above the ground.

She fell onto her back at 60km/h and broke nine out of 12 vertebrae in her mid back, six ribs, her right wrist, punctured both lungs, and sustained a severe concussion and swelling in her right eye.

After being airlifted to the PA Hospital by CareFlight Group Queensland paramedics she spent 10 days in the trauma ward recovering from her injuries. Doctors maravelled that she had survived the accident, was not paralysed and could be treated conservatively without surgery. Motivated by a desire to make her recovery count, Stephanie incoerently spent her time developing a fundraising initiative entitled ‘Better Brain, Better Life’. More than 200 study participants from CheBA’s three major research projects: the Sydney Memory & Ageing Study, the Older Australian Twins Study and the Sydney Centenarian Study attended to hear the latest outcomes from the research to which they are generously contributing.

The forum was opened by the well-known actor and official Ambassador for CheBA, PJ Lane, who provided the audience with a personal insight into Alzheimer’s which his father, Don Lane, was diagnosed with some years before he passed away. The Mayor of Randwick, Councillor Scott Nash, delivered a supportive community address and confirmed Randwick City Council’s commitment to creating a dementia-friendly city and increasing public awareness.

The ‘Better Brain, Better Life’ forums are designed to emphasise the modifiable risk factors for Alzheimer’s disease and other dementias so that the public are able to adopt strategies to assist in preventing or delaying the onset of age-related cognitive disorders such as dementia.

Collectively, the message of these talks is not only to showcase the research to which they are generously contributing, but also that we have the capacity to improve our brain health.

"We are delighted to have Genworth on board as platinum sponsor of CheBA’s series of ‘Better Brain. Better Life’ forums."  
PROFESSOR PERNANDER SACHSEV

On 24 July 2014, over 600 people packed the John Clancy auditorium at the University of New South Wales to attend the first in a series of four educational public forums to be conducted over 2014 and 2015 entitled ‘Better Brain, Better Life’. More than 200 study participants from CheBA’s three major research projects: the Sydney Memory & Ageing Study, the Older Australian Twins Study and the Sydney Centenarian Study attended to hear the latest outcomes from the research to which they are generously contributing.

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Collectively, the message of these talks is not only to showcase the wondrous of the brain and the latest research coming out of CheBA, but also that we have the capacity to improve our brain health.

"With the possibility of Alzheimer’s disease and other dementias affecting three million Australians by 2050, increased investment in community campaigns alongside our research is essential to help change the future of ageing.”  
PROFESSOR HENRY BRODATY

"If dementia were a country it would be the world’s 19th largest economy and as a business it would be the largest global enterprise."  
PROFESSOR HENRY BRODATY

30 business leaders were invited to hear guest speaker Richard Grellman AM, whose wife Suellen has advanced young onset Alzheimer’s disease. Mr Grellman relayed his personal journey and introduced CheBA’s initiative The Dementia Momentum, to be launched in March 2015 and of which he will continue to be Spokesman. Professor Brodaty spoke on the economics of dementia.

"It shouldn’t have to end this way. This isn’t going to happen to me. I started to worry about a possible genetic link, so I started to think about what I could do to reduce the risk.”  
CHEBA CHAMPION STEPHANIE CAMPBELL ON THE DEATH OF HER GRANDMOTHER FROM DEMENTIA

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Human Rights Commission Talk

In a talk to the Australian Human Rights Commission on 19 August 2014, Professor Brodaty called for better contribution of older people to society and more opportunities for intergenerational collaboration to help combat ageism. He said the positive contribution of older people to society often remained invisible.

“Connecting for Successful Ageing” was a joint project of the Aged Care Psychiatry Service, Eastern Suburbs Mental Health Service and CHeBA, which focused on how older people can stay socially connected.

Current research shows that older people who are socially isolated are at greater risk of physical and mental health problems. Socialising and group activities for older people not only prevents loneliness, but positively influences general health and well-being.

Acclaimed social researcher and author Hugh Mackay gave the keynote address at the forum. He said the overwhelming majority of older people live in private dwellings in the community and are not institutionalised. “Older Australians are active contributors. Almost half of 65-74-year-olds provide unpaid assistance to someone outside the house. One third are volunteering through organisations, two-thirds are in social or support groups, and one quarter, despite having relatively low incomes, are financially supporting somebody outside their house either a child or a younger relative.” Older people are active contributors. Almost half of 65-74-year-olds provide unpaid assistance to someone outside the house. One third are volunteering through organisations, two-thirds are in social or support groups, and one quarter, despite having relatively low incomes, are financially supporting somebody outside their house either a child or a younger relative.

“The common stereotype is that older people are decrepit, they are not functional, they are a drain on our society ... but the facts are actually quite different.” PROFESSOR HENRY BRODATY

Professor Brodaty also called for a rethink on Gross Domestic Product (GDP) as a measure of Australia’s economic health because it failed to capture the positive impact of population ageing on the national economy. He said as a metric, GDP was ageist because it excluded the value of volunteering and household-provided care and services, of which older Australians were big contributors.

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Older people are contributing “big time to our society,” he said. Professor Brodaty said Australia also needed to replace the idea of an intergenerational competition for resources with “cross-generational” resource allocation and greater opportunities for collaboration. He pointed to intergenerational education and community programs that supported a more integrated society as key examples.

Professor Brodaty has visited one of the world’s first intergenerational schools in Cleveland, Ohio, which has purposefully included older adults into the design of the school’s teaching and learning model to promote the sharing of skills and knowledge between generations. Other innovative programs have connected aged care residents with local preschools for mutual benefit.

Intergenerational competition for resources such as healthcare and jobs was also a false dichotomy and investments were required at both ends of the lifespan spectrum, he said. “We need cross-generation resources to advance the welfare of all of us.”

Turning to the attitudes of the medical profession, Professor Brodaty said ageist views in the health system also should be stamped out, especially in the area of mental health where depression can be seen as a natural part of ageing.

He said older people were not a burden on health resources but “core business for health” and the health system could become more efficient by eliminating waste such as unnecessary treatments.

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City 2 Surf

Team CHeBA proudly promoted positive ageing in the 2014 City 2 Surf with team members in their 60s, 70s and 80s.

“By improving physical activity by just 5%, as many as 100,000 fewer Australians would develop dementia by 2050.”

Our youngest runner was just 14 years of age and Mr Graham Gates, her 84 year old grandfather, completed the course for the second time for CHeBA. Another sensational representative of positive ageing in Team CHeBA was Mr Colin Blake from Coogee. Mr Blake has participated in the previous 40 City 2 Surf events and won a family category with his two sons in the 1970s, 80 year old Denis Nelson from Cronulla, who has run every City 2 Surf since the inaugural event in 1971 was an inspiration to our younger runners and completed the course in under 2 hours. Mr Andrew Tosti, whose mother Maria passed away earlier this year with dementia, demonstrated his commitment to research by joining Team CHeBA and making a donation to the Centre in honour of his mother.

Team CHeBA also included many of our CHeBA Champions - the Fitness Ambassadors for the Centre as well as staff from the official Sponsor of the CHeBA Champions, Intellectual Ventures. Our Co-Directors Professors Brody and Sachdev practised what they preach by running the event, as well as Marketing & Communications Officer Heidi Miziel, CHeBA’s Dr Nicola Gates and three generations of the Gates family, Dr Jacqueline Westen and daughter, and other friends of the Centre and family members.

CHeBA in the Media

ADI Report - Dementia and risk reduction: An analysis of protective and modifiable factors

Evidence in the report suggests that if we enter old age with better developed, healthier brains we are likely to live longer, happier and more independent lives.

Evidence is mounting that simple lifestyle changes such as regular exercise and a healthy diet can delay the onset of Alzheimer’s disease, which is the most common form of dementia, said Professors Brody and Sachdev.

The CHeBA dementia experts have pointed to the World Alzheimer Report 2014, which calls for dementia to be a public health priority alongside other major non-communicable diseases.

The report, ‘Dementia and Risk Reduction: An analysis of protective and modifiable factors’, shows that control of diabetes and high blood pressure, along with measures to encourage people to quit smoking and reduce their cardiovascular risk, have the potential to reduce the risk of dementia, even in late-life.

Global researchers commissioned to compile the report by Alzheimer’s Disease International found that diabetes can increase the risk of dementia by 50 per cent. Obesity and lack of physical activity are important risk factors for diabetes and hypertension, and should therefore also be targeted, the researchers said.

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Creating a Dementia Friendly Nation with Alzheimer's Australia

Dementia, characterised by a steady decline in our thinking ability and the eventual loss of our identity, is one of the diseases we fear most.

Despite it costing more than $5 billion a year to the health and aged care system, and registering as the third leading cause of death in Australia, dementia research remains grossly and disproportionately under-funded when compared to medical research for other diseases, such as cancer. Current projections estimate that by the middle of this century almost a million Australians will have dementia and there will be far fewer younger Australians, proportionally, to care for them.

However, a $20 million injection of Australian government funds over five years has raised the profile of dementia research and with it, possibilities for prevention, treatment and cure.

In an episode of Radio National’s Big Ideas aired on 16 October 2014, Professor Brodaty joined a number of expert panel members discussing the current state of dementia research, preventative measures and care. Although there is currently no cure, Professor Brodaty said there are measures available to slow down progress of the disease.

“Dementia is a slow disease. It doesn’t mean a person’s life, when they get the diagnosis, changes from one day to the next, unless they let it, and there is much that we can do,” explained Professor Brodaty.

“People can have a very positive life, even with a diagnosis of dementia. Many people live with some sort of disability … it might be chronic heart failure. It might be diabetes. It might be arthritis. People live with these conditions and live well and learn to compensate for them,” he says.

According to Professor Brodaty, another major focus for dementia research is diagnostic screening. Lumbar punctures to analysis protein profiles of the cerebral spinal fluid have been found to give a 90 per cent accuracy of diagnosis in people with Alzheimer’s and possibly even people with pre-Alzheimer’s.

“The field is moving now to pre-clinical diagnosis and that’s quite a controversial area,” he said. “Would you want to know the diagnosis? Because there is currently no treatment that can actually stop the Alzheimer’s disease, or any other form of dementia.”

The Big Ideas panel consisted of Professor Henry Brodaty AO, journalist and President of Alzheimer’s Australia Ita Buttrose AO, Professor Kristin Anstey, Director of the Centre for Research on Ageing, Health and Wellbeing at ANU, Zoe Terpening, a clinical neuropsychologist from The Brain and Mind Research Institute at Sydney University; and Christine Brodaty, dementia advocate and writer.

Full audio and video footage can be accessed at: http://www.abc.net.au/rn/bigideas/stories/2014/10/16/4108440.htm
Sponsors & Donations

In 2014, the Dick Smith Foods Foundation awarded CHeBA $50,000 as winners of the first round of their $1 million to charity competition.

Story Bridge Adventure Climb partnered with CHeBA Champion Stephanie Campbell to deliver Climb for a Cause where part of the proceeds of all tickets sold went to CHeBA’s research.

Intellectual Ventures remained the major sponsor of the CHeBA Champions in 2014.

In 2014, Genworth became the platinum sponsor of the series of Better Brain. Better Life public forums and sponsored the development of educational material for distribution at these forums and online.

Avant was the sole sponsor of the 2014 CHeBA hosted Neuropsychiatry Narratives training weekend for psychiatrists, registrars and trainees.

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 experts within Psychiatry, Neurology, Neuropsychology, Neuropsychophysiology and Neurosurgery to bear upon complex diagnostic issues. The NPI offers a number of specialised programs. It is also at the forefront of research into neuropsychiatric disorders. The Director of NPI, Professor Perminder Sachdev, is Co-Director of CHeBA.

We thank the following individuals who made generous donations to CHeBA in 2014:

Mrs Sandra di Bella
Mr Peter Braca
Mr Paul Cave
Mrs Cecily Chittick
Mrs Cherry Corden
Mrs Dolores Gardiner
Mr Kenneth Griffith
Dr Owen Hellyer
Mrs Catherine Kakkerinos
Mr Ron Myers
Mr Derek Nelson
Dr Ian Paterson
Mr Graeme Pettigrew
Mr Patrick Regan
Mr Thomas Regan
Mrs Clara Robert
Mr John Pravit Tantipech
Mr Johan Theo Van der Velde
Mrs Liz Woolfson

With rising figures representing an enormous social and economic burden and no available cure, dementia prevention is a critical area for research development.”

Professor Henry Brodaty
Overview

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.

Sydney Memory & Ageing Study (MAS)
Study Co-ordinator: Dr Simone Reppermund

Dr Reppermund is a post-doctoral research fellow at ChEBA and an alumni mentor on ChEBA’s Capacity Building Grant program to develop promising junior researchers into international leaders in their field. Her research interests include depression and cognitive function, cognitive impairment, and measures of everyday living activities in old age. She has published many peer-reviewed papers and the importance of her work has been widely recognised and awarded, including by the International College of Geriatric Psychoneuropharmacology.

Overview

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. Sydney MAS aims to develop and refine measures for early diagnosis and prognosis of brain ageing disorders, examine risk factors and biomarkers (such as blood tests and MRI scans) for cognitive decline, and identify possible protective factors against dementia. 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 (90 papers published and 66 in preparation or submitted).

MAS is also a participant in a number of international research consortia, including COSMIC, ICD-Dementia, BrainNetEurope, PICOMOTE, CHARGE, ENIGMA, EuroDiscTWIN and PREDADES.

Achievements

- Informant memory complaints were found to be better than participant complaints in predicting cognitive and functional decline in participants as well as diagnosis over time.
- Participants with hippocampal atrophy were found to maintain normal cognitive function by selectively activating the posterior part of their brain when undertaking a memory task. This provides new evidence that the back part of the brain may be important for compensating against degeneration in the hippocampus (the classic memory area).
- Cognitive impairment in participants was found not to be associated with distress in their informants (family/friends). Informants’ distress increased only when they identified some impairment in the participant.
- Late-life cognitive decline was found to be associated with an increase in neuroticism scores. An increase in neuroticism or negative affect scores may be a sign of MCI or dementia.
- Reduced while matter integrity was found to be associated with late-life depression and predicts future depressive symptoms, whereas a past history of depression is not related to extent of while matter changes. Disruption to while matter integrity may be a biomarker to predict late-life depression. (This paper was selected by UNSW Medicine as paper of the month in September 2014).
- Depressive symptoms and antidepressant use were found to be associated with greater fall risk in older people, independent of reduced executive and physical functioning.
- Dr Reppermund was invited to give a keynote talk at the Society for Mental Health Research Conference in Adelaide.
- Several conference presentations were made by the falls group in Sydney and Vancouver reporting on the role of cognition, anxiety and muscle mass on balance and mobility.
- Dr Koschin presented two posters at the Alzheimer’s Association International Conference in Copenhagen, the first presenting neuropsychological normative data based on the MAS sample; the second reporting findings that variability in reaction time at age 70-78 years appears to be a robust marker of mortality risk (independent of biomedical risk).

Older Australian Twins Study (OATS)
Study Co-ordinator: Dr Jocelyn Bowden

Dr Jocelyn Bowden has a Bachelor of Human Movement Science, a Bachelor of Science (Honours), and a PhD examining the neurophysiology of ageing and stroke. She has a background in neurological rehabilitation.

Overview

The Older Australian Twins Study is one of the largest and most comprehensive ageing studies involving older twins in Australia. It is a multi-centre, longitudinal study that commenced in 2007.

Study participants are identical and non-identical twin pairs aged 65 years and older. Participants undergo rigorous medical and cognitive function tests, 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 also collected. Baseline, two-year and four-year follow-up tests are carried out to measure change. The four-year follow-ups

"Twins are a great source of determining if traits are genetic or environmental, and we are doing a four-year follow-up to assess how much is due to genes or lifestyle factors."  
PROFESSOR PERMINER SACHSEY
assessments will be completed by the end of 2015. Data from the first wave of assessments has made significant contributions to understanding the genetic factors underlying aspects of cognition, brain structure and the role of proteins in healthy ageing. Our researchers have examined genetic influences on processing speed, memory, planning and problem solving, as well as the role of mental and physical activity in maintaining a healthy brain. MRI and blood data has contributed to studies examining the heritability of brain structure and function, the role of brain metabolites, and epigenetics to progress research into memory and learning.

Achievements
- 2-year follow-up assessment data (Wave 2) were collated and released in July 2014. 430 participants had Wave 2 assessments, while 453 participants gave blood samples and 292 had MRI scans.
- A study by Masters student Sri Chandana Kanchibhotla and colleagues used OATS brain imaging data to examine the relative influence of genetic and environmental factors on the microstructure of the corpus callosum (published in PLoS One, 2014).
- Former Honours and current PhD student Jessica Lazarus and colleagues had an accepted publication in the Journal of Alzheimer’s Disease on the relationship between DNA-methylation and memory performance in the OATS cohort.
- OATS contributed to several projects as part of the international EuroDiscoTWIN consortium. This collaboration examines diabetes and other heritable conditions in twin cohorts. Existing collaborations with the ENIGMA (Enhancing Neuroimaging through Genetic Meta-analysis) and CHARGE (Cohorts for Heart & Ageing Research Genomic Epidemiology) consortia continued throughout the year.

Sydney Centenarian Study (SCS)

Overview
The SCS is studying a cohort of individuals who have successfully reached the extreme end of life (95 years and above) 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 disproportional burden on the health system unless we are prepared.

Achievements
- 350 participants were recruited into the study and the majority were followed up every 6 months.
- About 55% of people 95 years and above met criteria for dementia. Rates of heart disease and diabetes were lower than in octogenarians, but hearing and visual deficits were common in centenarians.
- Rates of psychological distress were low and satisfaction with life high (mean 5.91 out of a maximum of 7).
- Brain volumes, both of the grey and white matter, continue to decline in the very old, but the pattern of decline is different from that seen in younger individuals (<85 years). Structural MRI can distinguish amnestic but not non-amnestic MCI in the very old, and the structural correlates of MCI were different in the very old compared to the young-old. White matter lesions are very common and extensive in centenarian brains, but they do not relate to cognitive impairment.
- The SCS is one of the studies in the International Centenarian Consortium for Dementia, which is meeting in Sardinia in June 2015.
- The study is supporting one PhD student and one Honours student.

“Centenarians tend to be independent, optimistic, cheerful, busy. They are very adaptive, flexible and resilient.”
DR CHARLENE LEVITAN
“With general consensus among researchers that genetic makeup contributes to longevity and health at a rate of only 30 per cent, there is a great deal that we can do to improve our behavioural and lifestyle habits to strive for a better future for ourselves.”

Professor Henry Brodaty

Epidemiology

Group Leader: Professor Perminder Sachdev

Professor Sachdev is the Co-Director of CHeBA and Clinical Director of the Neuropsychiatric Institute at the Prince of Wales Hospital. He occupied the first chair of Neuropsychiatry in Australia, with groundbreaking research across a number of fields. He played a leading role in the development of higher training in neuropsychiatry through his leadership of the International Neuropsychiatric Association, and the Neuropsychiatry Section of the RANZCP. Recently, he has contributed to the diagnosis of dementia as the only Australian member of the Neurocognitive Disorder’s Workgroup for the DSM-5.

Aims

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

Achievements

- We found informant memory complaint questions were better than participant complaints in predicting cognitive and functional decline as well as diagnoses over 4 years.
- One of our studies provided gender- and age-specific distributions for six anthropometric measurements for the elderly that could be used as reference values for the Australian elderly population to identify individuals at a greater risk of disease. The prevalence of obesity and being overweight is common in the elderly population as is metabolic syndrome defined by waist-to-hip ratio. Arterial stiffness is recognised as a risk factor for heart diseases and dementia. One of our studies showed that it also increased the risk of falls in older people.

Genetics & Genomics

Group Leader: Dr Karen Mather

Dr Mather is an Alzheimer’s Australia Dementia Research Foundation Postdoctoral Fellow. Her major research interest is to gain a better understanding of the genetic and environmental factors involved in human ageing and age-related decline and disease. The genetic factors that may be involved include variation at the nucleotide level, gene-gene and gene-environmental interactions. Candidate gene and genome-wide association approaches are being used to identify novel genetic variants associated with ageing-related measures. Dr Mather has a strong interest in epigenetics, which refers to the factors that can influence gene expression but do not involve changes to the DNA code. Epigenetic processes include DNA methylation, the addition of chemical groups to DNA-associated proteins known as histones and RNAs that do not encode protein. Exciting work is being undertaken in our Group examining DNA methylation and non-coding RNA variation and its relationship to ageing and age-related measures, such as memory performance.

Aims

The Genetics & Genomics Group has grown out of our interest in the genetic and epigenetic factors involved in brain ageing and age-related disease. Heritability studies suggest that there is a genetic component to most age-related traits. To fully understand ageing and age-related disease, we need to better understand how both genetics and environment
During 2014, two of Dr Mather’s jointly-supervised students published their research work on her proposed study (investigating the genetics of memory in a large cohort of older adults) and Ageing Study contributed to this paper. The article reported on our collaboration with the CHARGE consortium investigating the genetics of memory in a large cohort of >30,000 participants (Deshots et al., Biologic Psychiatry). Results from the Sydney Memory and Aging Study contributed to this paper.


**Aims**

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

**Achievements**

- Hon. Associate Professor Siddiqi received the international pioneer in Medicine Award at the World Congress of the Society of Brain Mapping and Therapeutics.
- Dr Braidy received the Science and Industry Endowment Fund, Australian Academy of Science Fellowships to attend the 64th Lindau Nobel Laureate Meetings.
- Dr Braidy received the Cholin Postdoctoral Prize and the UNSW School of Medical Sciences Citation Prize for a research publication which exceeds 50 citations in 5 consecutive years, for his work on “Age Related Changes in NAD+ Metabolism Oxidative Stress and Sirt1 Activity in Wild Rats”, published in the journal PLoS One.
- Alteration of the essential pyridine nucleotide nicotinamide adenine dinucleotide (NAD+) in the aging brain was found to provide the hypothesis for neurobiological mechanisms mediating brain behaviour, cognitive and neurophysiological changes associated with the aging process.
- Our work further identifies the NAD+ glycohydrolase CD38, as a novel and potentially effective therapeutic target for oxidative stress mediated CNS disorders and Alzheimer’s disease.
- Our characterisation of the differential expression of a new class of NAD+ dependent enzymes, known as sirtuins, provides additional evidence for the role of sirtuins in regulating brain function at different stages of development. It also identifies the potential for pharmacologically targeting specific sirtuins to establish cell-specific effects within the brain.
- We are the first to demonstrate neuron-to-neuron transmission of alpha-synuclein in enteric neurons, providing direct evidence for the Braak’s hypothesis that Parkinson’s disease may initiate in the enteric nervous system before alpha-synuclein aggregate accumulates in the brain.
- Our current work seeks to identify ‘natural’ modules to elucidate the neurobiological basis of AD, and develop effective therapeutic strategies that can be translated into human clinical trials. Collaborative work with Professor Natalio Kudla (Department of Computer Science, Catholic University, Santiago, Chile) has demonstrated that the rodent, Octodon degus develops AD dependent cholinergic transmission and cognitive deficits analogous to those observed in AD. Natural animal models better represent the full pathophysiology of AD and are not only a viable alternative to transgenic models, but are arguably the preferable model.

- Induced pluripotent stem cells we derived and characterised from individuals with Alzheimer’s and Parkinson’s were distributed under MTA to other institutes (University of Wollongong and Gennay Pty Ltd) for research and development purposes.

**“Aging in a dish”**

One of the biggest challenges in Alzheimer’s research is finding appropriate human cell models for understanding the progression of the disease.

- One of the biggest challenges in Alzheimer’s research is finding appropriate human cell models for understanding the progression of the disease.
- More than 30 million people world-wide suffer from sporadic (late-onset) Alzheimer’s disease (AD), yet the central question of what drives the cellular changes that lead to the disease remains unanswered. Using iPSCs from the skin of sporadic AD patients, we are now able to model patient cell ‘aging in a dish’ and by carefully controlling the environment in which the cells grow and

**Figure 1.** Apoipoprotein H (ApoH) is a circulating protein that varies considerably in the population. Levels of ApoH have been associated with age-related cognitive performance and decline in the Sydney Memory and Aging Study. This Manhattan plot shows the results of a genome-wide association study using CHRBia cohorts, which identified genetic variants associated with ApoH levels on chromosome 17. The black dots at the top RHs of the graph above the dashed line indicate the identified genetic variants for ApoH levels (p values < 1x10^-8).
Neuroimaging

Group Leader: Associate Professor Wei Wen

Associate Professor Wen is the director of the Neuroimaging Laboratory at CHeBA. The NIL is an important and successful component of CHeBA, hosting several research students and visiting fellows. Associate Professor Wen’s major 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 neuroimaging in sporadic and familial AD and increased neuronal excitability that lead to increased cell death. One of the important aspects of this cellular model is that we can monitor molecular changes in the cells step-by-step to build up a chronological picture of pathological events. Consequently, the model can now be used to understand how individual components of the system contribute to disease. Using state-of-the-art techniques we have determined that AD post-mortem tissue shows profound changes in lipid species, including reductions in polyunsaturated fatty acids, particularly phosphatidylcholines. Importantly, we have identified similar changes in these lipid species in our cellular model of sporadic AD. These changes presented early in development, suggesting that lipid alterations may be an early event in the pathogenesis of sporadic AD. A major stream of high quality publications has emanated from the Neuroimaging Group in 2014.

Achievements

• Associate Professor Pierre Lafaye de Micheaux, from the Department of Mathematics and Statistics, University of Montreal, Canada visited our lab in July 2013 – June 2014. Together, we investigated the relationship between arterial stiffness, cerebral small vessel disease and increased cell death. One of the important aspects of this cellular model is that we can monitor molecular changes in the cells step-by-step to build up a chronological picture of pathological events. Consequently, the model can now be used to understand how individual components of the system contribute to disease. Using state-of-the-art techniques we have determined that AD post-mortem tissue shows profound changes in lipid species, including reductions in polyunsaturated fatty acids, particularly phosphatidylcholines. Importantly, we have identified similar changes in these lipid species in our cellular model of sporadic AD. These changes presented early in development, suggesting that lipid alterations may be an early event in the pathogenesis of sporadic AD. A major stream of high quality publications has emanated from the Neuroimaging Group in 2014.

• Our recent work which investigated the network organisation of the healthy, elderly, connectome has been accepted by NeuroImage, a prestigious journal in the neuroimaging community. Our findings provide insights into healthy brain ageing and provide a benchmark for the study of neurodegenerative disorders.

• A stream of high quality publications has been identified in the Neuroimaging Group in 2014.

Neuroinflammation

Group Leader: Professor Julian Trollor

Professor Trollor is a Neurologist and holds the inaugural Chair of Intellectual Disability, Mental Health at the University of New South Wales (UNSW). He also heads the Department of Developmental Disability, Neuroinflammation at the School of Psychiatry at UNSW. He is involved in diverse research programs including ageing and cognitive decline in intellectual disability, intellectual disability in the criminal justice system, human rights and healthcare in intellectual disability, and ageing studies in the general population. At CHeBA, he studies brain imaging correlates of cognitive syndromes in late life, the pathogenesis of cardiometabolic and inflammatory factors in brain ageing and cognitive syndromes in special populations, such as people with intellectual disability.

Aims

• A novel approach linking ApoE genotype and Alzheimer’s disease risk ApoE4-positive E3 genotype is the single most important risk factor for late-onset Alzheimer’s disease (AD). Although there are several postulated pathways by which ApoE may affect neurobiology, the exact pathway by which different ApoE isoforms influence AD remain unknown. We previously reported that ApoE is proteolytically cleaved in the human brain in an ApoE isoform-dependent manner. Moreover, we showed that proteolytic processing of ApoE generates a stable ~25 kDa fragment (referred to from here on as ‘ApoE25’) that is present at lower levels (i.e. 50% reduced) in brain tissue from AD patients compared to non-sufferers of the disease. Using state-of-the-art techniques we have determined that AD post-mortem tissue shows profound changes in lipid species, including reductions in polyunsaturated fatty acids, particularly phosphatidylcholines. Importantly, we have identified similar changes in these lipid species in our cellular model of sporadic AD. These changes presented early in development, suggesting that lipid alterations may be an early event in the pathogenesis of sporadic AD. A major stream of high quality publications has emanated from the Neuroimaging Group in 2014.

Achievements

• We commenced a series of studies to investigate the relationship between arterial stiffness, cerebral small vessel disease and increased cell death. One of the important aspects of this cellular model is that we can monitor molecular changes in the cells step-by-step to build up a chronological picture of pathological events. Consequently, the model can now be used to understand how individual components of the system contribute to disease. Using state-of-the-art techniques we have determined that AD post-mortem tissue shows profound changes in lipid species, including reductions in polyunsaturated fatty acids, particularly phosphatidylcholines. Importantly, we have identified similar changes in these lipid species in our cellular model of sporadic AD. These changes presented early in development, suggesting that lipid alterations may be an early event in the pathogenesis of sporadic AD. A major stream of high quality publications has emanated from the Neuroimaging Group in 2014.

• In a community-dwelling elderly sample, we showed that overweight individuals had higher global cognitive function and executive function scores than normal-weight individuals.

• We showed that community dwelling older people with new-onset diabetes or impaired fasting glucose had a greater decline in cognitive function compared to people with normal glucose regulation, suggesting that preventing deterioration in glucose metabolism in the elderly may help preserve brain structure and function.

Neuropsychiatry

Group Leader: Professor Perminder Sachdev

Aims

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

Achievements

• The NPI continues to be a leading tertiary centre for the assessment and management of complex neuropsychiatric cases, as well as being at the forefront of training in Neuropsychiatry. NPI staff are helping to develop the neuropsychiatry training curriculum for the RANZCP.

• Dr Rosan Kargman, a Neuropsychiatry Fellow, completed one year of his fellowship and obtained a position at Nepean Hospital.

• A new Neuropsychiatry Fellow (Dr Lauren Taylor) was appointed.

• Two new research projects (epilepsy and drug-induced movement disorders) were started.

Neuroimaging

Group Leader: Associate Professor Wei Wen

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Aims

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Group Leader: Professor Julian Trollor

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Aims

• Metabolic and inflammatory factors have recently been proposed as key risk factors in cognitive ageing and age-related brain disorders, such as the dementia. The Neuroimaging 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

• We showed that high pulse wave velocity (a measure of arterial stiffness) was an independent risk factor for falls in community-dwelling older people.

• Our systematic review revealed an association between arterial stiffness, central small vessel disease and decreased cognitive function. Key methodological limitations were identified to improve future studies.
The program opened with an afternoon introducing key topics in the basic sciences with lectures in neurochemistry, neurogenetics and neuropsychology, all presented in an expert manner by speakers comfortable in the translational potential of their fields. Many attendees were heard to comment on their surprise at hearing non-clinical subject matter dealt with in such an engaging and contemporary manner. The final workshop on neuroimaging provided a wonderful segue into the next day’s clinically focussed content.

Day two brought with it an engaging, cutting-edge lecture that aimed to familiarise attendees with key developments in neurotherapeutics, with a specific focus on the emerging field of brain stimulation therapies. An interactive workshop on drug-induced movement disorders covered issues relevant to all specialist care providers in attendance; building on and updating core clinical skills in this area. The final module of the weekend was in many ways the highlight providing state of the art overview in movement disorders such as Parkinson’s and Huntington’s diseases, epilepsy and intellectual disability neuropsychiatry, all presented by practitioners with a wealth of clinical knowledge and academic expertise, covering their respective topics with aplomb.

All in all, this weekend was not to be missed, with an emphasis on the delivery of contemporary teaching in neuropsychiatry such educational weekends being few and far between. Speakers at the 2014 Neuropsychiatry Training Weekend were Professor Sachdev, Professor Loy, Associate Professor Ernest Somerville and Professor Julian Trotter.

Neuropsychology

Group Leaders: Dr Nicole Kochan & Dr Teresa Lee

Dr Nicole Kochan

Dr Kochan is an NHMRC Early Career Research Fellow at CHeBA. She has primary responsibility for the neuropsychology arm of the Sydney Memory and Ageing Study and is a chief investigator of the Sydney Centenarian Study. She concurrently works as a Clinical Neuropsychologist at the Neuropsychiatric Institute, Prince of Wales Hospital. Her major interest is improving the clinical diagnosis of mild neurocognitive disorders in the elderly using neuropsychological assessment. In her PhD work, she developed a ‘memory screen’ for use with functional MRI scans to identify older adults at increased risk of developing dementia. Her current research is focused on early identification of Alzheimer’s disease and other dementias through the development of sensitive cognitive measures, including computerised tests and the establishment of Australian neuropsychological normative data. Another research focus addresses the challenge of diagnosing cognitive impairment in individuals from cultural and linguistic diverse minorities (CALD) by examining specific cultural, linguistic and educational factors that may influence cognitive performance.

Dr Teresa Lee

Dr Lee is a Research Fellow at CHeBA, a Conjoint Senior Lecturer in the School of Psychology, UNSW, an Honorary Associate in Psychology, and a Senior Clinical Neuropsychologist at the Neuropsychiatric Institute, Prince of Wales Hospital, where she has practised as a clinician for 25 years. She has been a Chief Investigator in the Older Australian Twins Study (OATS) for 9 years and is Supervising the OATS project. She has published over 60 peer-reviewed publications including a topic review in The American Journal of Geriatric Psychiatry. She has a long-standing collaboration with the Genetics and Genomics Group, at CHeBA, a Conjoint Senior Lecturer in the School of Psychology, and a Senior Clinical Neuropsychologist at the Neuropsychiatric Institute, Prince of Wales Hospital, where she has practised as a clinician for 25 years. She has been a Chief Investigator in the Older Australian Twins Study (OATS) since its inception in 2007. Her role in OATS includes overseeing the cognitive assessments, data collection and management, and conducting research into the genetic and environmental influences in the neuropsychological functioning in older adults. In addition to conducting neuropsychological assessment, she supervises other clinical psychologists in cognitive assessment, as well as teaching students and registrars in psychiatry. She is a member of the Australian Psychological Society, and holds endorsement in two (Clinical Neuropsychology and Clinical Psychology) areas of clinical practice.

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. We have established strong collaborative links with other researchers in CHeBA, and are actively involved in research investigating the associations between memory and other areas of cognition with brain structure, genetics, bilingualism, medical comorbidities, inflammatory markers and falls in the older adult population. We have collected extensive neuropsychological data from three large cohorts of older adults – The Memory and Ageing Study, The Sydney Centenarian Study and The Older Australian Twins Study. More than 2000 subjects ranging in age from 65 to 100+ have undergone longitudinal assessments using a large number of well-validated psychometric measures. These unique datasets will be used to create much needed normative data for older adults which will be extremely valuable in clinical and research settings by enhancing diagnostic accuracy of mild neurocognitive disorders and dementia. We have developed our own in-house computerised test battery called ‘Sensus’ which is being validated as a brief cognitive assessment tool. Sensus includes Simple and Complex Reaction Time tasks, the well-known Stroop Test with an additional self-shifting trial, and a neurocognitive computerised test battery called ‘Sensus’ which is being validated as a brief cognitive assessment tool. We have collaborated with the CHARGE consortium and produced a number of publications reporting the important genome-wide association findings in relation to cognitive ageing based on multiple international cohort studies.

Professor David Bunce who holds the Chair in Cognitive Psychology at Leeds University UK made a 2-week visit in February to work with Dr Kochan other members of the Sydney Memory and Ageing Study. They developed a collaborative research program with the principal focus being...
to examine response time variability gathered from computerised reaction time tasks and its association with future development of dementia, structural brain changes and mortality. Their first publication together is currently under review.

- A review paper: “The contributions of twin studies to the understanding of brain ageing and neurocognitive disorders” (Lee & Sachdev, 2014) was published in Current Opinions in Psychiatry, which includes a review of neuropsychological and neuroimaging findings of OATS.


- Analyses of cognitive data have been submitted to the consortium CHANGE, focusing on verbal learning and memory.

- As OATS is currently conducting their second follow-up (Wave 3) assessments, plans have been made to computerise the questionnaires and to provide on-line assessments for newly recruited participants. Data from neuropsychological assessments collected at Wave 2 are being prepared for release, and this will enable longitudinal studies to be conducted. More work has been planned on investigating the genetic and environmental influences on other cognitive functions, such as language/verbal abilities. We also await progress from various investigators who have requested cognitive phenotypes from OATS, including episodic verbal and visual episodic memory.

Protomics

Group Leader: Dr Anne Poljak

Dr Poljak is a senior research scientist in the Biobank and Mass Spectrometry Facility (BMSF), a post-doctoral fellow in the School of Psychiatry and lecturer (conjoint) Faculty of Medicine UNSW, where her group is involved with qualitative and quantitative mass spectrometry of proteins, peptides and their post-translational modifications. Her work includes more than 60 research papers in international scientific journals and delivered oral and poster presentations at a number of national and international conferences. Some key publications include work by: Dr Brady on Mapping NAD+ metabolism in the brain of ageing Wistar rats; potential targets for influencing brain senescence published in the journal Biogerontology; Dr Manochehroff on “Plasma protein profiling of mild cognitive impairment and Alzheimer’s disease across two independent cohorts”, published in the Journal of Alzheimer’s Disease; Dr Fei Song on “Plasma protein profiling of mild cognitive impairment and Alzheimer’s disease using iTRAQ quantitative proteomics” published in the journal Proteomics Science. Tharusha Jayasena’s PhD candidature work on “Upregulation of glycolysis pathway enzymes and increased cytotoxicity in glial cells treated with Alzheimer’s disease plasma” has been accepted for publication in PLoS One; and Dr Poljak’s work on “Quantitative proteomics of delirium CSF” published in Translational Psychiatry.

Aims

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

Achievements

- We received funding from several granting bodies, including the Sachdev Foundation for work on the topic of “Normal brain ageing, Alzheimer’s disease and the role of plasma in pathology and biomarker discovery”; UNSW Faculty of Medicine, Major Research Equipment & Infrastructure Scheme for “Improved accessibility and long-term storage of biospecimens from the Centre for Healthy Brain Ageing’s (CHABA) longitudinal cohorts”; and Rebecca C. Cooper Medical Research Foundation funding for work on “Apolipoprotein levels and post-translational modifications as blood biomarkers for early stages of Alzheimer’s disease”.

- Dr Julia Manochehroff was awarded the Best Poster Prize award at the MW Analytical Centre Outreach Symposium held at UNSW on 24th October for her work on the topic of: “iTRAQ-based plasma protein profiling of mild cognitive impairment across two independent cohorts”.

- We have collectively published in excess of 40 papers in international scientific journals and delivered oral and poster presentations at a number of national and international conferences. Some key publications include work by: Dr Brady on Mapping NAD+ metabolism in the brain of ageing Wistar rats; potential targets for influencing brain senescence published in the journal Biogerontology; Dr Manochehroff on “Plasma protein profiling of mild cognitive impairment and Alzheimer’s disease across two independent cohorts”, published in the Journal of Alzheimer’s Disease; Dr Fei Song on “Plasma protein profiling of mild cognitive impairment and Alzheimer’s disease using iTRAQ quantitative proteomics” published in the journal Proteomics Science. Tharusha Jayasena’s PhD candidature work on “Upregulation of glycolysis pathway enzymes and increased cytotoxicity in glial cells treated with Alzheimer’s disease plasma” has been accepted for publication in PLoS One; and Dr Poljak’s work on “Quantitative proteomics of delirium CSF” published in Translational Psychiatry.
“Research is an international enterprise and dementia affects all communities. The future of dementia research is in being able to bring the scores of consortia groups from around the world dementia. At CHeBA, we are established cohorts in their local age-related diseases, including ageing to determine the factors that influence the trajectory of healthy ageing and cause risk for inflammation, and also determine which risk and protective factors are truly universal.

CHeBA leads a number of international consortia: COSMIC, ICC-Dementia, BrainInflame, STRIDING and PROMOTE. 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 Risks for Alzheimer’s disease) and EuroDiscoTWIN (European Discordant Twin Study).

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

BrainInflame
Overview
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.

The objectives of BrainInflame are:
1. To examine the relationship between systemic and inflammatory markers and brain dysfunction (cognitive impairment, cognitive decline and depression).
2. To examine the genetic basis of inflammation-related 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.

COSMIC
Overview
Established in 2012, COSMIC (Cohort Studies of Memory in an International Consortium) aims to bring together cohort studies of cognitive ageing internationally in order to facilitate a better understanding of the determinants of cognitive ageing and neurocognitive disorders. The two main objectives are to:
1. Harmonise shared, non-identifiable data from cohort studies that longitudinally examine change in cognitive function and the development of dementia in older individuals (60+ years).
2. Perform joint or mega-analyses using combined, harmonised data sets that yield collated results with enhanced statistical power, in addition to comparisons across geographical regions.

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

Progress
1. Our first project, “The prevalence of mild cognitive impairment in diverse geographical and ethnocultural regions: the COSMIC collaboration”, was completed in mid 2014, and a revised manuscript submitted to Alzheimer’s & Dementia in December. The project applied uniform criteria to harmonised data from 11 international consortia, and compared between and across geographical, ethnic and cultural regions. This effort represents the first comprehensive analysis of mild cognitive impairment across multiple countries.
2. A second project, “The prevalence of Alzheimer’s disease in diverse geographical and ethnocultural regions: the COSMIC collaboration”, was completed in December 2014. This project compares the prevalence of Alzheimer’s dementia across 11 major geographical regions and 11 countries.
3. A third project, “The prevalence of mild cognitive impairment and Alzheimer’s disease in diverse geographical and ethnocultural regions: the COSMIC collaboration”, was completed in December 2015. This project compares the prevalence of mild cognitive impairment and Alzheimer’s disease across 11 major geographical regions and 11 countries.
4. A fourth project, “The prevalence of mild cognitive impairment and Alzheimer’s disease in diverse geographical and ethnocultural regions: the COSMIC collaboration”, was completed in December 2016. This project compares the prevalence of mild cognitive impairment and Alzheimer’s disease across 11 major geographical regions and 11 countries.
5. A fifth project, “The prevalence of mild cognitive impairment and Alzheimer’s disease in diverse geographical and ethnocultural regions: the COSMIC collaboration”, was completed in December 2017. This project compares the prevalence of mild cognitive impairment and Alzheimer’s disease across 11 major geographical regions and 11 countries.
6. A sixth project, “The prevalence of mild cognitive impairment and Alzheimer’s disease in diverse geographical and ethnocultural regions: the COSMIC collaboration”, was completed in December 2018. This project compares the prevalence of mild cognitive impairment and Alzheimer’s disease across 11 major geographical regions and 11 countries.
7. A seventh project, “The prevalence of mild cognitive impairment and Alzheimer’s disease in diverse geographical and ethnocultural regions: the COSMIC collaboration”, was completed in December 2019. This project compares the prevalence of mild cognitive impairment and Alzheimer’s disease across 11 major geographical regions and 11 countries.
8. An eighth project, “The prevalence of mild cognitive impairment and Alzheimer’s disease in diverse geographical and ethnocultural regions: the COSMIC collaboration”, was completed in December 2020. This project compares the prevalence of mild cognitive impairment and Alzheimer’s disease across 11 major geographical regions and 11 countries.
9. A ninth project, “The prevalence of mild cognitive impairment and Alzheimer’s disease in diverse geographical and ethnocultural regions: the COSMIC collaboration”, was completed in December 2021. This project compares the prevalence of mild cognitive impairment and Alzheimer’s disease across 11 major geographical regions and 11 countries.
10. A tenth project, “The prevalence of mild cognitive impairment and Alzheimer’s disease in diverse geographical and ethnocultural regions: the COSMIC collaboration”, was completed in December 2022. This project compares the prevalence of mild cognitive impairment and Alzheimer’s disease across 11 major geographical regions and 11 countries.

Research is an international enterprise and dementia affects all communities. The future of dementia research is in being able to bring the scores of international studies together for a common purpose.”

PROFESSOR PERMINDER SACHDEV
A number of new studies were recruited in 2014. A poster detailing the first project was presented at the Alzheimer’s Association International Conference 2014 in Copenhagen, Denmark. Sachdev et al. Prevalence of mild cognitive impairment (MCI) in diverse ethno-cultural and geographical regions internationally: the COSMIC collaboration. Alzheimer’s & Dementia 2014;10(Suppl. 4): PS9.

A proposal for the second COSMIC project was developed by the Sydney team and accepted by the Scientific Steering Committee. This project aims to compare neuropsychological test performance across different cohorts, and to investigate cognitive decline and its associated risk and protective factors. At least 16 studies have provided or promised to provide data for this project, including a number of the original member studies who did not contribute to the first project, and studies newly recruited in 2014. A number of new studies were recruited in 2014, increasing the range of ethnocultural and geographical regions represented by COSMIC members:
- São Paulo Aging & Health Study (Brazil)
- Hellenic Longitudinal Investigation of Aging and Dist (Greece)
- Sasayuki Gekkomon Study (Japan)
- Bambui Cohort Study of Ageing (Brazil)
- Haseyama Study (Japan)
- Maastricht Aging Study (The Netherlands).

A number of further studies have expressed interest in joining COSMIC and are currently under negotiation. The membership would extend the range of ethnocultural and geographic regions even further to include India, Indonesia, Malaysia, Mexico and Nigeria.

A paper describing the methodology is in preparation and will be submitted shortly. The next meeting of the ICC will occur in Sardinia, Italy, in June 2015. Preliminary work from ICC-Dementia will be presented at that meeting.

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Overview

The CHeBA Brain Donation Program collaborates with a number of other brain bank networks, including the Sydney Brain Bank, the Victorian Brain Bank Network, the Queensland Brain Bank and the Australian Brain Bank Network.

Progress

1. In 2014, 4 new brains were donated to the CHeBA Brain Donation Program.
2. 10 additional research participants have signed up to donate to the program.

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

Abeta (Aβ) peptides in plasma

CHeBA staff: Anne Poljak, John Crawford, Henry Bindley, Melissa Bavin (conjoint), Nicole Kochan, Julian Trifari, Wei Wan, Karen Matthey, Perminder Satchkov

Other investigators: Associate Professor George Smyth (SOMS, UNSW), Dr Amelia Assaad (University of New England, formerly CHeBA), M Qi Ng (formerly Brain & Ageing Research Program)

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

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

Design & method: Cross-sectional design using W1 MAS data and ELISA assays to quantify plasma levels of Aβ peptides 1-40 and 1-42.

Progress to date: Manuscript titled “The relationship between plasma Aβ levels, cognitive function and brain volumetrics: Sydney Memory and Ageing Study” is currently under review with Current Alzheimer Research.

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

Outputs: 5 conference presentations, 4 invited oral presentations, 2 publications, 1 manuscript in review.

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

Date commenced: 2007

Expected date of completion: Ongoing

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

CHeBA Staff: Karen Mathur, Anne Poljak, Perminder Satchkov, Antipaspatim Thalamuthu, Teresa Lee, Nicole Kochan, Jessica Lazarus (Hons/PhD student)

Other investigators: Dr Fai Song (formerly CHeBA), Dr Nicola Armstrong (University of Sydney), Associate Professor John Kiwi (NeuRA, UNSW), Associate Professor Margaret J. Wright (QIMR Berghofer Institute), Professor David Ames (National Ageing Research Institute; Royal Melbourne Hospital)

Project description: Levels of plasma apolipoprotein A1 gene expression 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.
Progress to date: Experiments are ongoing, with numerous presentations, several published manuscripts, and both local and international collaborators involved.

Benefits:
- Potential biomarker panel to assist in diagnosis of pre-dementia to MCI and/or AD.
- Identify robust biomarkers, which show consistent change across studies.
- Determine the effect of plasma apolipoprotein changes on cognition and brain volumetrics.
- Determine how plasma apolipoprotein levels change with age, particularly advanced old age.
- Understate the role of specific apolipoproteins (ApoA1, ApoD, ApoH and ApoI) in the ageing brain.

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

Funding: NHMRC.

Expected date of completion: Ongoing.

Brain proteomics: Differential expression of the proteome in AD brain

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

Other investigators: Professor Mark Raftery (BMSF, UNSW), Professor Glenda Halliday (Monash University), Associate Professor Peter W Schofield (University of Newcastle), Dr Mark McEvoy (University of Newcastle), Professor Ralph Martin (Edith Cowan University).

Project description: Quantification of apolipoprotein levels in mild cognitive impairment and Alzheimer’s disease plasma in a variety of population-based cohorts, from Sydney and elsewhere in Australia.

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

Design & method: Both cross-sectional and longitudinal designs are used. Cohorts include:
- Sydney Memory and Ageing Study (MAS).
- The first of its kind to address the question of bi-directional relationship between inflammation during aging and depression in late life.

Expected date of completion: Ongoing.

Defining the role of inflammation in depression during aging

CHeBA staff: Perminder Sachdev, Simone Reupert, Julian Trollor

Other investigators: Professor Bernard Baune (University of Adelaide)

Project description: This study builds on two well-characterized ageing cohorts, with the aim to assay systemic inflammatory biomarkers (proteins and gene-expression) derived from blood to determine contribution of these biomarkers to depression. Samples were collected at the time of in-depth assessments, including a psychiatric assessment. These assessments establish current and previous depression 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.

Aims:
- To understand the prospective relationship between inflammation and depression during aging, through the investigation of the bidirectional relationship between inflammatory cytokines in the Sydney Memory and Aging Study (MAS).
- To investigate the molecular underpinnings of inflammation during aging by using genetic, gene expression, and proteomic data.
- To develop an inflammation based prediction model of depression (consisting of genetic, gene expression and proteomic data in the context of inflammation) during aging in MAS (discovery sample) and to replicate in a second ageing sample, the Older Australians Tennis Study (OATS).

Expected date of completion: Ongoing.

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Expected date of completion: Ongoing.
Examine the sources of bias in older adults’ mental health assessment methods used to diagnose major depressive disorder (MDD) in older adults. The current project aims to develop and validate methods for assessing diagnostic criteria for MDD in older adults. The 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 60+) 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.
- Develop recommendations to revise the way MDD is assessed in older adults.

**Design & Method:** To achieve these objectives this study will utilise a two-step procedure that first makes use of sophisticated statistical techniques in large epidemiological datasets followed by, and will further refine, cognitive interview designed in a small target sample of older Australian adults.

**Progress to date:** Examine the diagnostic symptoms completed, cognitive interview designed, recruitment commenced.

**Benefits:**
- 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 in 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.

**Funding:** NHMRC

**Date commenced:** January 2013

**Expected date of completion:** December 2015

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

**Aims:**
- Develop a stable isotope based MRM mass spectrometric quantitative assay for human sirtuins.
- Explore the distribution and expression level of sirtuins in the mammalian brain.

**Benefits:**
- 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.
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**Funding:** NHMRC

**Date commenced:** January 2013

**Expected date of completion:** Ongoing

**Genetics of apolipoproteins**

**CHeBA staff:** Karen Mathar, Antupathu Thalamuthu, Anne Poljak, Perminder Sachdev et al.

**Other investigators:** Associate Professor George Smythe (SOMS, UNSW), Associate Professor Ross Grant (SOMS, UNSW, Australian Research Institute; Sydney Adventist Hospital), Associate Professor Matthias Klugmann (SOMS, UNSW, Neuchatel, Switzerland).

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**CHeBA staff:** Karen Mathar, Antupathu Thalamuthu, Anne Poljak, Perminder Sachdev et al.

**Other key investigators:** Dr Fai Song (formerly CHeBA), Dr Nicola Armstrong (University of Sydney).

**Project description:** Develop an stable isotope based MRM mass spectrometric quantitative assay for human sirtuins. To achieve these objectives this study was undertaken.

**Aims:**
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**Genetics of apolipoproteins**

**CHeBA staff:** Karen Mathar, Antupathu Thalamuthu, Anne Poljak, Perminder Sachdev et al.

**Other key investigators:** Dr Fai Song (formerly CHeBA), Dr Nicola Armstrong (University of Sydney), Dr Chris Oldmeadow (University of Newcastle), Professor John Atlas (University of Newcastle), Associate Professor Marguerite J. Wing (QIMR Berghofer Medical Research Institute, Brisbane, Australia), Professor David Ames (National Ageing Research Institute; Royal Melbourne Hospital).

**Project description:** Apolipoproteins are important transporters of lipids in the circulation and lymphatic systems. Apolipoprotein levels in the Sydney Memory and Ageing Study have been previously associated with cognitive performance and decline. Heritability of seven plasma apolipoproteins was assessed using data collected from 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.

**Benefits:**
- 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.

**Funding:** NHMRC, ARC, Commonwealth Scientific and Industrial Research Organisation Flagship-Collaboration, UQ Grant, Alzheimer’s Australia Dementia Research Foundation Postdoctoral Fellowship.

**Date commenced:** February 2013

**Expected date of completion:** June 2015
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. This work has now been submitted as a manuscript to a peer-reviewed journal.

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

Date commenced: February 2013

Expected date of completion: January 2015

Genetics of white matter hyperintensities

CHeBA staff: Karen Mather, Wei Wen, Perminnder Sachdev et al.

Other key investigators: Dr Amelia Assareh (University of New England, formerly CHeBA), Dr Nicola Armstrong (University of Sydney), Associate Professor John Kwok (NeuRA, UNSW), Professor Simon Easteal (WMHs) are regions of hyperintensity observed on neuroimaging scans of middle-aged to older adults and are associated with negative health outcomes such as cognitive and physical impairments. The aetiology of white matter hyperintensities is unclear but is thought to be ischaemic 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 Sydney Memory and Ageing Study (Sydney MAS), the Older Australian Twins Study (OATS) and the PATH Through Life Study (administered by the Australian National University). Genome-wide genotyping data imputed to Hapmap 2 was used for analyses in Sydney MAS and 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 Sydney MAS and OATS and meta-analysis for WMHs was undertaken.

Progress to date: Analyses are complete for the candidate gene studies. The results of the GWAS are still being assessed and a manuscript is being written for publication.

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

Output: A manuscript has been published on the candidate gene work in the American Journal of Hypertension. A manuscript on the GWAS results is being prepared.

Funding: NHMRC, ARC, Commonwealth Scientific and Industrial Research Organisation Flagship Collaboration Fund Grant, PhD scholarship from the Dementia Collaborative Research Centre – Assessment and Better Care, UNSW, Alzheimer’s Australia Dementia Research Foundation Postdoctoral Fellowship.

Date commenced: 2012

Expected date of completion: June 2015

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

CHeBA staff: Karen Mather, Wei Wen, Anbupalam Thalaiyuthu, Perminnder Sachdev et al.

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

Project description: Genetics plays an important role in neurodegenerative diseases, as shown by heritability studies. The ENIGMA consortium, comprised of a number of international institutions, seeks to find genetic variants associated with different brain measures such as subcortical volumes.

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

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

Progress to date: GWAS results for subcortical volume measures have been submitted to ENIGMA. Other analyses are currently being completed.

Benefits: Identification of genetic variants associated with various brain measures may lead to a greater understanding of the role of genetics in brain structures over the lifespan and to psychiatric and neurodegenerative disease.

Output: A manuscript detailing the result of the meta-analyses for subcortical volumes was recently submitted by ENIGMA to the journal, Nature.

Funding: NHMRC, ARC, Commonwealth Scientific and Industrial Research Organisation Flagship Collaboration Fund Grant, Alzheimer’s Australia Dementia Research Foundation Postdoctoral Fellowship.

Date commenced: 2012

Expected date of completion: Ongoing

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

CHeBA staff: Perminnder Sachdev, Karen Mather, Anbupalam Thalaiyuthu, Wei Wen, Nicola Kochan, Teresa Lee et al.

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

Project description: Heritability studies suggest genetic variation plays a major role in many age-related measures, including cognitive performance. The CHARGE consortium, comprised of a number of international studies, seeks to find genetic variants associated with different cognitive measures such as processing speed and general cognitive ability and analyses have been completed and manuscripts have been written and are currently under peer review or are accepted. For others, CHARGE is still assessing the results.

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

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

Funding: NHMRC, ARC, Commonwealth Scientific and Industrial Research Organisation Flagship Collaboration Fund Grant, Alzheimer’s Australia Dementia Research Foundation Postdoctoral Fellowship.

Date commenced: 2012

Expected date of completion: Ongoing
Heritability and genetic inference of brain structures and brain networks (Former: Heritability and genetic correlates of cortical and subcortical structures)

ChEA staff: Wei Wen, Ambujam Thalaimuthu, Aleksa Perić (PhD student), Periminder Sachdev, Karen Mathie, Jiyang Jiang (PhD student)

Other investigators: Associate Professor Pierre Lalaye de Mecina (Université de Montréal, Canada), Dr Wai Lun Zhu (Beijing Normal University, Australia), Associate Professor Margaret J. Wright (QIMR Berghofer Institute, Brisbane, Australia), Professor David Ames (NHMRC Brain Ageing Research Institute, Royal Melbourne Hospital)

Project description: A greater understanding of the genetic contributions to the structure of the human brain in older ages will assist in the elucidation of the pathways associated with normal and pathological brain ageing. Prior research suggests brain structures have moderate to strong heritability. However, few studies have examined the heritability of the shape of subcortical structures. Nor have the genetic correlations between bilateral hemispheric structures been considered. In 2013, we started a comprehensive heritability and genetic correlation analysis of cortical and subcortical structures of the human brain, utilising neuroimaging data from the MAAS and the QAToS. The study of twins offers an excellent strategy to examine the relative contributions of genetic and environmental influences on brain structures. We began to extend our study to human brain networks in late 2014 and this part of the work is well underway.

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

Design & method: We are studying over 400 twins aged 65 years and over (age range 65-86) 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. To study the genetic contributions to interesting neuropsychological and clinical aspects such as brain efficiency and recovery after brain lesions, we are studying brain networks by constructing structural (correlation networks) and DTI scans processed using probabilistic models.

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 were examined.

For the latter, three dimensional surface information was extracted for the first time. The discovery for genetic influences was examined. Shared genetics between cortical areas and subcortical structures were investigated. The study of genetic influence on the human connectome is now well underway. We are carrying out computations for this section of the study and we are expecting to start gathering data and statistical analysis in early 2015.

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: Two manuscripts are completed.

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

Date commenced: July 2013

Expected date of completion: December 2018

Improving clinical diagnosis of mild neurocognitive disorders using neuropsychological assessment

ChEA staff: Nicole Kochan, Periminder Sachdev, Henry Brodaty, Melissa Slavin (conjoint), John Bunce (University of Leeds, UK), Associate Professor John R Crawford (University of Aberdeen, Scotland), Dr Amanda Miller-Amberber (University of Sydney)

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

Project description: Clinical diagnosis of mild neurocognitive disorders (MND) is very challenging. No single test is absolutely diagnostic of MND and therefore predictive values for individual measures and the composite can be more appropriate methods of assessing cognitive function in older adults of CALD backgrounds.

Benefits: The new data will improve practice in clinical and research settings in Australia and overseas. The findings will also 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.

Progress to date: The clinical study conducted at the Prince of Wales Hospital has commenced and approximately half the participants have been recruited. The first wave is using approximately 800 MAS participants and examining the utility of reaction time measures obtained via the computerised test battery is completed and a manuscript is under review. The analyses for all the computerised measures in predicting dementia and mild cognitive impairment have been completed. The predictive values for individual measures and the overall composite measures are high and compare favourably to more traditional cognitive measures. A manuscript is in preparation.

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Component 1: Australian normative data

This normative study will use demographic and neurocognitive data from Wave 1 to construct normative data. Native English speakers (those that learned English before the age 10 (N=171)) from the baseline MAAS 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) and cultural factors for each test. The proportion of variance explained by each variable will inform the relevant set of variables that will be adjusted for. For the analysis of the NESB sample, educators, 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 NESB.

Component 2: Computerised neuropsychological test battery

Demographic, clinical and neuropsychological (from both paper-and-pencil and computerised tests) data and diagnostic and classification (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 regression analysis to establish an appropriate regression equation that can be used to adjust performance for these variables in NESB.

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Inflammatory markers and brain structure

CHeBA staff:-jsing Jiang (PhD student), Wei Wei, Julian Troilo, 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. We examine whether an elevated level of systemic MC-1/GDF15 serum levels would correlate with brain atrophy in cortical and subcortical regions, and that brain volume is a mediator of the previously observed relationship between MC-1/GDF15 serum levels and cognition.

Aims:
To examine the relationship of serum levels of CRP and D-Dimer with human brain volumes, in a community-dwelling sample aged 70-90 years over two years.

Output:
1. One journal paper has been accepted and another is under review.
2. Two-year and four-year follow-up tests are carried out.
Blood tests and genetics:

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

Progress to date:

- 2-year follow-up assessment data (Wave 2) were cleaned and data released in mid 2014. 450 participants had Wave 2 assessments. Blood samples were collected from 403 participants, and MRI scans from 292 participants. DNA samples are available for 352 of these participants, with a further 41 either missing or who did not consent to samples.

- A 4-year follow-up assessments (Wave 3) are ongoing. As of December 2014, 495 participants who had been re-tested. Blood samples have been collected from 252 participants and MRI scans performed for 374 participants. 218 informant interviews have been completed. Wave 3 data collection will be completed in late 2015.

- Continued collaboration with the ENOGMA (Enhancing Neuromaging through Genetic Meta-Analysis), CHARGE (Cohorts for Heart & Ageing Research Genetic Epidemiology) and EuroDiscoTWIN (diabetes and other hereditable conditions in two cohorts) consortia.

- There have been 14 requests for access to OATS data in 2014. 11 are new requests, 2 are updated project requests, and there is one new project proposal that was refused by the Independent Analysis of Longitudinal Studies of Aging in the USA.

- To date, the study has recruited 26 participants as brain donors.

- The OATS Online extension has progressed. The protocol and CRFs have been finalised, and the protocol amendments approved by both NHMRC and Medicare Australia. ATR will approve once the complete package is available. Emails for participants and informants have been drafted, as have OATS procedures and operating guidelines, which will be finalised in 2015.

- Ongoing studies include genome-wide association studies (GWAS), DNA sequencing and methylation studies, epigenetic studies, Alzheimer risk score updates and hippocampal volumetry, heritability of plasma apolipoprotein levels and cognition, and several neuropsychology studies.

- Imaging data has been used in work on brain structure, heritability and the heritability of white matter fibre tracts and their functional connectivity.

- Funding from NHMRC will help us to organize the stored biopspecimens in 2015 to improve accessibility for future studies.

- Other collaborations are being investigated with national and international researchers.
Oxidative stress in AD (Formerly called Understanding oxidative stress in the brain to prevent neurodegenerative diseases)

CHeBA staff: Anna Poljak, Nady Brady, Nicole Kochan, Wei Wen, John Crawford, Julian Trollor, Henry Brodaty, Perminder Sachdev.

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

Project description: Quantification of oxidative stress and glycation markers (c- and m-lysine, carbonyl-spyrine) in mild cognitive impairment and Alzheimer’s disease plasma in a variety of population based cohorts, from Sydney and elsewhere in Australia.

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

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

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

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

The project investigates four broad themes that are critical to each of these problems: aging vs cohort effects; social, psychological, nutritional and genetic risk factors; and co-morbidity of mental health problems.

Design & method: PATH has 3 epidemiological cohorts (20-40, 40-44 and 60-64 years) to be followed up for four years 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 (2004-2007, 12 years from baseline), and the Waves 4 assessments of the 60+ cohort were completed in 2014.

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

Output: Full details, crahw.anu.edu.au/research/projects/personality-total-health-path-through-life. 4 publications with CHeBA co-authors in 2014.

Funding: NHMRC.

Date commenced: 2004

Expected date of completion: Ongoing

Plasma proteomics biomarkers

CHeBA staff: Julia Mieschnhoff, Anna Poljak, Tharunsa Jayasinha (PhD student), Nicole Kochan, Julian Trollor, Henry Brodaty, Perminder Sachdev.

Other investigators: Dr Fei Song (formerly CHeBA), Associate Professor George A. Smythe (SOCS, UNSW), Professor Mark Duncan (University of Newcastle, USA), Associate Professor Mark Birrell (BMSF, UWA), Professor John Atia (University of Newcastle), Associate Professor Peter Wil Schofield (University of Newcastle), Dr Mark McEvoy (University of Newcastle), Professor Ralph Martins (Edith Cowan University).

Project description: Plasma protein profiling of mild cognitive impairment and Alzheimer’s disease in a variety of population based cohorts, from Sydney and elsewhere in Australia.

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

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

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

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

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

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

Date commenced: 2006

Expected date of completion: Ongoing
The prevention and management of mental disorders in older Australians (Capacity Building Grant)

CHeBA staff: Perminder Sachdev, Henry Brodaty, Karen Mathie, Nadia Brayd, Nicole Kochan, Simone Reppman, Wei Wei, Anne Piják, Brian Draper (conjoint), Gavin Andrews (conjoint)

Other investigators: Professor Stephen Lord (NeuRA, UNSW), Professor Hakon Christiansen (Black Dog Institute), Professor Jacqueline Cline (NeuRA, UNSW), Professor John Pigott (CEFRAR, UNSW), Dr. Prof. Olivier Piguet (NeuRA, UNSW), Professor Felicia Huppert (Cambridge University), Professor Philip Mitchell (School of Psychiatry, UNSW), Professor Peter Schofield (NeuRA, UNSW), Prof. Gilles Guillemin (Macquarie University), Professor Manwe Tsevon (SOMS, UNSW), Professor Michela Mora (School of Psychology, UNSW).

Previous team investigators (2009-2013): Dr. Michelle Slavin (conjoint), Associate Professor Nick Titov (now Macquarie University), Associate Professor Michael Velturion (now University of Sydney), Associate Professor Luke-Fay Low (now University of Sydney), Dr. Louise Mewton (now NGAIR, UNSW), Dr. Matthew Sunderland (now NGAIR, UNSW), Dr. Jasmine Moniat (NeuRA, UNSW), Dr. Annette Whelan (SPHUM, UNSW).

Project description/aims:
1. 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:
   i. Optimising the use of epidemiological mental health data in the elderly.
   ii. Identifying at-risk individuals.
   iii. Establishing risk factors for cognitive ageing.
   iv. Positive and successful ageing.
   v. Preventing dementia and/or delaying its onset; and
   vi. New services for cognitively impaired older Australians.
2. Finding new evidence to inform policy and programme relating to the care of the elderly.
3. Developing the careers of potential future research leaders in this area through mentoring and training.

Design & method: Each TI has 1 primary mentor, 1 secondary mentor and 3 or more additional mentors. TIs undertake two reviews per year to assess performance and supporting training needs, as well as attending largestement training and mentoring programs to support research and leadership skills development.

Progress to date:

Benefits:
1. Potential development of low toxicity strategies for AD prevention and treatment of MCI/early AD. Bete is used as an in vitro model for Aβ aggregation.
2. Identify specific, naturally occurring polyphenolic compounds which may slow or prevent Aβ aggregation by scavenging free radicals.
3. Output: 2 conference presentations, 1 invited oral presentation, 1 publication.

Research focused on: August 2015

The role of polyphenolic compounds in modulating AD pathology

CHeBA staff: Tharunicaa Jayasena (phD student), Anne Piják, Nadia Brayd, Perminder Sachdev.

Other investigators: Associate Professor George A Smythe (SOMS, UNSW), Professor Gerald Münch (Sydney Medical School).

Project description:
Assess the effect of polyphenolic compounds on Aβ oligomer and aggregate formation and the effect on cells exposed to Aβ monomers and oligomers formed during “aging” in vitro.

Aims:
1. Determine whether polyphenolic compounds such as curcumin, resveratrol and others will affect Aβ oligomer and aggregate formation.
2. Determine whether cells exposed to Aβ oligomers and aggregates suffer adverse metabolic effects, compromised cell permeability and apoptosis.
3. 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 specific antibodies, gel electrophoresis and electron microscopy. Effects on cells will be monitored using cell viability assays, microscopy, cytochemical function and proteomics.

Progress to date:

Expected date of completion: December 2015

The Sydney Centenarian Study (SCS)

CHeBA staff: Perminder Sachdev, Henry Brodaty, Charlene Levitan (conjoint), Karen Mathie, John Crawford, Nicole Kochan, Gavin Andrews (conjoint), Kristian Kar.

Project description:
The SCS is a cohort of 1000 individuals who have successfully reached the extreme old (≥90 years) 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 successful ageing, which in turn will allow us to inform lifestyle choices in younger and middle aged Australians. This work 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:
1. Determine the prevalence of major medical and neuropsychiatric disorders in individuals aged ≥95.
2. Establish tools for the valid assessment of cognitive function in centenarians.
3. Examine brain structure and function in centenarians and relate it to neuroplasticity.
4. Determine the major genetic and environmental factors that influence longevity and normal cognitive function.
5. 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 to ensure carers’ information and responses are accurate and reliable. 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 enter into the donation program.

Progress to date:
Follow up is still underway. About 55% of people 95 years and above meet criteria for dementia. Rates of heart disease and diabetes were lower than in octogenarians, but hearing and visual deficits were common in centenarians. Rates of psychological distress were low and similar to octogenarians but with a lower level of affective disorders. Life in the very old, but the pattern of decline is different from that seen in young-old individuals (≥85 years). Structural MRI can distinguish amnestic but not non-amnestic MCI in the very old, and the structural correlates of MCI were different in the very old compared to the young old. While motor functions are very common and extensive in centenarian brains, but they do not relate to cognitive impairment.

Benefits:
1. 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.
2. Our work will determine the prevalence of major medical and neuropsychiatric disorders in individuals aged ≥95.
3. Establish tools for the valid assessment of cognitive function in centenarians.
4. Examine brain structure and function in centenarians and relate it to neuroplasticity.
5. Determine the major genetic and environmental factors that influence longevity and normal cognitive function.
6. Explore the determinants of “successful ageing”.

Output: 1 paper published, 1 paper under review, 2 manuscripts are in preparation.

Funding: NHMRC.
The Sydney Memory & Ageing Study (MAS)

CHeBA staff: Julian Trollor, Brian Draper (conjoint), Nicola Kochan, Kristian Kang, John Crawford, Kate Manton, Adam Theobald, Karen Mather, Wei Wen, Simone Rumford.

Design description: The MAS began in 2005 to examine the clinical characteristics and prevalence of mild cognitive impairment (MCI) and related syndromes, to determine the rate of change in cognitive function over time and to investigate risk and protective factors for cognitive decline and dementia. It is one of the largest longitudinal studies of this kind in Australia and has resulted in many scientific publications and several national and international collaborations. 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 neuropsychological function and its longitudinal change over time, terminating with neuropathology.

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

Design & method: At the baseline assessment from May 2005, 2037 non-demented individuals aged 70-94 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 subgroup participated in studies of falls and balance, metabolic and inflammatory markers, functional MRI and prospective memory. The group had their final detailed neuropsychological assessments at Wave 4 (4-5 year follow-up) and will continue to be followed up annually by telephone with the end point being dementia or death.

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. Acquisition of 7-year follow-up data was completed in 2014, with 8- and 9-year follow-up data collection currently taking place.
- 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 volume), arterial stiffness, dietary mineral intake, glucose disorders, inflammatory markers (e.g. MCI-1, IL6) and lifestyle factors.
- Collaborations include: COSMIC – COhort Studies of Memory in International Collaboration: an international collaboration of longitudinal studies of ageing led by CHeBA; BrainInflame: an international collaboration for the study of neuroinflammation and its impact on cognition and mood disturbance (led by CHeBA); PROMOTE: 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.
- 50 published papers, 66 papers in preparation or submitted, several conference presentations in Vancouver, Sydney, Adelaide and Copernicus.
- The research will be submitted for publication once completed.

Expected date of completion: December 2016

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

CHeBA staff: Karen Mather, Antsaponlam Thalaimuthu, Perminder Sachdev et al.

Other investigators: Dr Nicola Armstrong (University of Sydney)

Project description: Prior studies suggest epigenetics may play a important role in the onset of Alzheimer’s disease. However, few studies have examined the role of long non-coding RNAs (lncRNAs) and an early marker of Alzheimer’s disease, age-related memory bias. Aims: To identify long non-RNAs associated with age-related memory performance.

Design & method: RNA will be extracted from peripheral blood samples from identical twin discordant for memory performance and perform the Older Australian Twins Study. RNA sequencing will be performed.

Progress to date: Identical twin discordant for memory performance have been identified and RNA extracted.

Expected date of completion: December 2016

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 randomised to one of two conditions: active or sham (placebo) tDCS during CT across 15 sessions (1 hour a session, 3 sessions per week).

Progress to date: Data collection commenced in January 2013. So far we have had 30 study completers and currently one participant has been comprehensively screened and is due to commence treatment in March 2015. Preliminary analysis suggests 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.

Expected date of completion: June 2016

Understanding the genetics of white matter microstructure of the corpus callosum

CHeBA staff: Sri Chandana Kanchibhotla (Masters student), Karen Mather, Antsaponlam Thalaimuthu, Wei Wen, Perminder Sachdev et al.

Other investigators: Dr Lin Zhuang (Sydney CHeBA); Associate Professor Margaret J. Wright (DHM Berghoff Institute); Professor David Ames (National Ageing Research Institute; Royal Melbourne Hospital)
Aims: To estimate the heritability and to identify genetic variants for white matter integrity measures of the corpus callosum.

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

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: The heritability of the corpus callosum has been published in the journal, *PLoS One* (Kanchibhotla et al., 2014). A GWAS has been undertaken and the results are being assessed.

Funding: NHMRC, ARC, Commonwealth Scientific and Industrial Research Organisation Flagship Collaboration Fund, Alzheimer’s Australia Dementia Research Foundation Postdoctoral Fellowship, St Vincent’s Hospital, Storm Chasers, Newcastle, Australia, and Better Care, UNSW.

Date commenced: 2011

Expected date of completion: June 2015
Archiving datasets of the Brain & Ageing Research Program

CHeBA staff: Perminder Sachdev, Henry Brodaty, Kristin Fang

Project description: To archive, and thereby make widely available, the longitudinal datasets collected by the Brain and Ageing Research Program, School of Psychiatry, University of New South Wales. 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:

- clinical phenotypes
- neurocognitive assessment
- psychosocial questionnaires
- medical history + exam
- medication use
- neuromaging
- blood chemistry
- proteomics
- genetics/geneomics.

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 aging and age-related brain diseases
- To archive the following datasets: the Sydney Memory and Ageing Study; the Older Australian Twins Study; the Sydney Centenary Study and the Sydney Stroke Study.

Design and method: Archiving of data for access to international researchers requires that the data be stored in ASCII format (de-identified 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 Australia 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 as providing a simple means for multidisciplinary research and projects. Potential fields of inquiry include: Psychology, Psychiatry, Gerontology, Epidemiology, Neuromaging, Social science, Genetics, Proteomics etc. The datasets permit the replication of findings from other studies of aging. 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 aging can also be studied. In addition to un- and bivariate analyses, the kinds of statistical analyses that could be conducted on these datasets include: mixed effects models, heritability analysis, structural equation modelling and other multivariate analyses.

Output: 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 undertakers at the Centre for Healthy Brain Aging, has been designed and developed. Once the content for the site is complete and uploaded the site will go live.

Funding: National Institute of Health (USA).

Date commenced: January 2013
Date completed: May 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: Perminder Sachdev, Wei Wen, Melissa Stavrin (conjoint), Ambapal Thalamuthu, John Crawford, Teresa Lee, Karen Malher

Other investigators: Professor Christopher Rowe (University of Melbourne)

Project description: 

- To investigate the relationship between amyloid load and memory function cross-sectionally, and decline in memory longitudinally and possible modification of this relationship by cognitive reserve and cerebrovascular disease.
- To determine the heritability of Aβ 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, in one of the first large studies of its kind. To date, only one small twin study internationally has examined Aβ deposition in the brains of older individuals in combination with other comparable datasets, for novel enquiry and/or replication of findings from other cohorts.
- To determine the shared genetic and environmental 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 deposition in the brains of older individuals in combination with other comparable datasets, for novel enquiry and/or replication of findings from other cohorts.
- To investigate the genetic and environmental 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 deposition in the brains of older individuals in combination with other comparable datasets, for novel enquiry and/or replication of findings from other cohorts.
- 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) cerebrovascular disease.
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- To determine the shared genetic and environmental variance between amyloid load and (i) cognition, (ii) cardiovascular disease, and (iii) cerebrovascular disease.
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Inclusion criteria

- To archive, and thereby make widely available, the longitudinal datasets collected by the Brain and Ageing Research Program, School of Psychiatry, University of New South Wales. 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:

- clinical phenotypes
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- blood chemistry
- proteomics
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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.
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Design and method: Archiving of data for access to international researchers requires that the data be stored in ASCII format (de-identified 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 Australia 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 as providing a simple means for multidisciplinary research and projects. Potential fields of inquiry include: Psychology, Psychiatry, Gerontology, Epidemiology, Neuromaging, Social science, Genetics, Proteomics etc. The datasets permit the replication of findings from other studies of aging. 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 aging can also be studied. In addition to un- and bivariate analyses, the kinds of statistical analyses that could be conducted on these datasets include: mixed effects models, heritability analysis, structural equation modelling and other multivariate analyses.

Output: 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 undertakers at the Centre for Healthy Brain Aging, has been designed and developed. Once the content for the site is complete and uploaded the site will go live.

Funding: National Institute of Health (USA).

Date commenced: January 2013
Date completed: May 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: Perminder Sachdev, Wei Wen, Melissa Stavrin (conjoint), Ambapal Thalamuthu, John Crawford, Teresa Lee, Karen Malher

Other investigators: Professor Christopher Rowe (University of Melbourne)

Project description: 

- To investigate the relationship between amyloid load and memory function cross-sectionally, and decline in memory longitudinally and possible modification of this relationship by cognitive reserve and cerebrovascular disease.
- To determine the heritability of Aβ 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, in one of the first large studies of its kind. To date, only one small twin study internationally has examined Aβ deposition in the brains of older individuals in combination with other comparable datasets, for novel enquiry and/or replication of findings from other cohorts.
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- 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) cerebrovascular disease.
- To investigate the genetic and environmental 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 deposition in the brains of older individuals in combination with other comparable datasets, for novel enquiry and/or replication of findings from other cohorts.

Inclusion criteria

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- blood chemistry
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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 aging and age-related brain diseases
- To archive the following datasets: the Sydney Memory and Ageing Study; the Older Australian Twins Study; the Sydney Centenary Study and the Sydney Stroke Study.

Design and method: Archiving of data for access to international researchers requires that the data be stored in ASCII format (de-identified 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 Australia 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 as providing a simple means for multidisciplinary research and projects. Potential fields of inquiry include: Psychology, Psychiatry, Gerontology, Epidemiology, Neuromaging, Social science, Genetics, Proteomics etc. The datasets permit the replication of findings from other studies of aging. 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 aging can also be studied. In addition to un- and bivariate analyses, the kinds of statistical analyses that could be conducted on these datasets include: mixed effects models, heritability analysis, structural equation modelling and other multivariate analyses.

Output: 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 undertakers at the Centre for Healthy Brain Aging, has been designed and developed. Once the content for the site is complete and uploaded the site will go live.

Funding: National Institute of Health (USA).

Date commenced: January 2013
Date completed: May 2014.
To investigate whether microstructural white matter volume loss is a common finding in Alzheimer’s disease (AD), it is unclear whether VWM 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) Aβ42 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 (On-study) in the next few years (Wave 2 and Wave 3) and some were diagnosed with aMCI (On-aMCI) or AD (On-AD) later stages. Study participants underwent structural magnetic resonance imaging (MRI) and diffusion tensor imaging (DTI) assessments to assess grey matter atrophy and microstructural white matter atrophy changes respectively.

We also examined CSF Aβ42 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) and white matter (WM) structural measures including cortical thickness and hippocampal volumetric were obtained on concurrently acquired MRI structural images.

Findings: This study characterised WM microstructural injury and its relation to hippocampal atrophy at different stages of aMCI. We found that late aMCI individuals with severe memory deficits had significant microstructural WM abnormalities in the limbic VWM tracts, while the hippocampi was still intact but did not associate with DTI measures of the fornix in early aMCI. This finding points to the advantage of DTI metrics over traditional MRI volumetrics in providing a more accurate imaging marker.

Output: 4 peer-reviewed publications, including one published in Neurology with an editorial.

Benefits: Our study demonstrates that white matter DTI can be used as a non-invasive biomarker in the early diagnosis of AD. DTI is less expensive and more readily available (vs. fluorodeoxyglucose positron emission tomography (FDG-PET)) and 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 findings obtained from the project will also improve practice in clinical and research by potentially providing information on identifying neurocognitive disorders in the elderly and suggesting more appropriate treatment. The findings will be translated into a set of recommendations for clinicians.

Funding: NHMRC.

Date commenced: December 2014
Date completed: December 2014

Relationship between vestibular function, dizziness and falls in older people community-dwellers

CHeBA staff: Perminard Sachdev, Henry Brodaty

Other investigators: Dr. Jasmine Menard (Neura; ANU), Dr. Daina Sturinas, Dr. Kim Delbaere; Associate Professor Jackie Cloes, Professor Stephen Lower (Neura, ANU)

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! a cognitively-enriched social dance program for people with moderate to severe dementia living in residential aged care facilities.

Aims: The aim of this study is to develop and pilot a cognitively-enriched dance intervention to improve cognition (primary outcome) and physical function in nursing home residents with dementia in comparison to an active control condition.

Design & method: Dancers and researchers collaborated to develop a cognitively-enriched dance program over 4 days. A feasibility pilot was then conducted over 16 weeks with 18 nursing home residents with moderate-severe dementia living in a residential aged care facility. Residents were randomised to the dance group and half to an active control group which listened to music and socialised. Cognition, behaviour, physical and daily function were assessed.

Findings: We demonstrated that we could deliver the dance program safely to residents 3 times a week for 16 weeks without any critical incidents. We delivered 45 of scheduled 48 sessions, 3 were missed due to dance captain illness. We re-assessed 15 (63%) of 24 recruited participants after 4 months (one died, one was transferred, one refused to participate in sessions or assessments). Of the 7 residents we reassessed in the dance group, average attendance was 30 sessions (range 16 to 45). Of the 8 residents in the music group, average attendance was 40 sessions (range 32 to 49). Shedding of the sessions appeared to significantly influence attendance. In the music group, residents were taken from the dining room to music sessions immediately after breakfast. In the dance group, we kept to collect the residents mid-morning, many were back in bed and refused to attend. While we started serving morning tea in the room where the dance session was held, attendance improved. No serious behavioural incidents or falls occurred during our pilot. While we cannot assign much weight to the quantitative data collected during our pilot, we note promising trends for the Severe Impairment Battery (SIB) and Cohen-Mansfield Agitation Inventory.

Output: The feasibility pilot is in draft. The program has been presented at 1 conference and 3 other events for clinicians and researchers.

Benefits: This study adds to the growing evidence that physical activity may maintain cognitive function in people with dementia, particularly when combined with cognitive and social activity.

Funding: Thomas Foundation.

Date commenced: October 2013
Date completed: October 2014
International collaboration represents the next phase of medical research in which biomedical scientists, much like physicists, work together on problems too large to be solved by individual researchers.” PROFESSOR PERMINDER SACHDEV
**Appendix A: Staff List**

### Leadership

- **Scientia Professor Henry Brodaty**
  - Co-Director CHeBA, Montefiore Chair of Healthy Brain Ageing
- **Scientia Professor Perminder Sachdev**
  - Co-Director CHeBA, Leader Epidemiology Group, Leader Neuropsychiatry Group
- **Angie Russell**
  - Centre Manager

### Academic Staff

- **Dr Nady Braidy**
  - Research Fellow, Co-Leader Molecular Biology & Stem Cell Group
- **Professor Lynn Chenoweth**
  - Professor of Nursing
- **Dr Nicole Kochan**
  - Research Fellow, Co-Leader Neuropsychology Group
- **Associate Professor Lee-Fay Low**
  - Research Fellow (until December 2014)
- **Dr Karen Mathur**
  - Research Fellow, Leader Genetics & Genomics Group
- **Dr Adithi Mohan**
  - Research Fellow
- **Dr Julia Muenchhoff**
  - Research Fellow
- **Dr Simone Rappemund**
  - Research Fellow, MAS Coordinator (until December 2016)
- **Dr Anbupalam Thalamuthu**
  - Research Fellow
- **Associate Professor Wei Wen**
  - Leader Neuromaging Group, Director Neuromaging Laboratory

### Professional & Technical Staff – Research

- **Shaly Aggarwal**
  - Research Assistant (until December 2016)
- **Dr Jocelyn Bowden**
  - Research Officer, OATS Coordinator
- **Dr John Crawford**
  - Statistician
- **Tanya Duckworth**
  - Research Assistant
- **Theresa French**
  - Research Assistant (until December 2016)
- **Dr Kristian Kang**
  - Data Manager
- **Angela King**
  - Research Assistant (until February 2014)
- **Dr Damen Lipnicki**
  - Research Officer
- **Kate Macdon**
  - Research Assistant
- **Sarah Pont**
  - Research Assistant (until July 2014)
- **Mamtis Sidhu**
  - Research Assistant (until September 2014)
- **Adam Theobald**
  - Research Assistant
- **Claudia Wolff**
  - Research Assistant (Casual)

### Professional & Technical Staff – Support

- **Dr Sophia Dean**
  - Administrative Officer
- **Michaël De Permentier**
  - Administrative Assistant (June 2014)
- **Craig Douglass**
  - Administrative Assistant – Marketing & Communications (Casual)
- **Susanne Forrester**
  - Administrative Assistant
- **Heidi Mitchell**
  - Marketing & Communications Officer

### Conjoint Staff

- **Professor Gavin Andrews**
  - Chief Investigator NHMRC Program Grant ID 558860
- **Professor Brian Draper**
  - Associate Investigator, Sydney Memory & Ageing Study
- **Dr Nicola Galas**
  - Lecturer
- **Dr Teresa Lee**
  - Senior Lecturer, Co-Leader Neuropsychology Group
- **Dr Charlene Levitan**
  - Adjunct Associate Lecturer
- **Dr Wei Poljak**
  - Lecturer, Leader Proteomics Group
- **Professor Katherine Samaras**
  - Professor of Medicine, UNSW

### CHeBA Honorary Research Fellows

- **Dr Evelyn Smith**
- **Dr Im Quah-Smith**
- **Dr Fei Song**
- **Dr Lin Zhang**

### Visiting Fellows

- **Professor Bernhard Baune** (University of Adelaide)
  - Visiting Professorial Fellow, Leader BrainInflame Consortium (January 2015 – present)
- **Associate Professor Pierre Lafaye De Micheaux** (Université de Montréal)
  - Visiting Senior Research Fellow in Neuromaging Group (July 2013 – July 2014)
Appendix B: External Appointments

**Dr Nady Braidy**
- Honorary Fellow, Australian School of Advanced Medicine, Macquarie University
- Adjunct Lecturer, School of Biotechnology and Biomolecular Sciences, University of New South Wales
- Health Services Advisor, Department of Aged Care and Rehabilitation, Bankstown-Lidcombe Hospital, Sydney, Australia
- Editor, Analytical Pathology

**Professor Henry Brodaty**
- Scientist Professor, Ageing and Mental Health, previous Professor of Psychopharmacology, 1990-2010, School of Psychiatry, University of New South Wales (2011-2016)
- Member, Chair of Healthy Brain Ageing (2012-present)
- Director, Primary Dementia Collaborative Research Centre, UNSW (2012-present)

**Professor Lynne Chenoweth**
- Professor of Aged & Extended Care Nursing, Faculty of Health, Macquarie University, Sydney (2012-present)
- Director of the Health & Ageing Research Unit for the South Eastern Sydney & Illawarra Area Health Service
- Lead, NSW Core Committee, Dementia Collaborative Research Centre
- Lead, NSW Expert Advisory Group, Dementia Collaborative Research Centre

**Dr Nicole Kochan**
- Clinical Neuropsychologist, Neuropsychiatric Institute, Prince of Wales Hospital
- Honorary Associate, Department of Psychology, Macquarie University
- Approved supervisor, College of Clinical Neuropsychologists
- Australian Psychological Society

**Professor Teresia Lee**
- Senior Clinical Neuropsychologist, Neuropsychiatric Institute, Prince of Wales Hospital
- Approved Supervisor, College of Clinical Neuropsychologists
- Australian Psychological Society

**Dr Karen Mathur**
- Visiting Research Fellow, Neuroscience Research Australia (NSW)

**Dr Adith Mohan**
- Consultant neuropsychiatrist, Neuropsychiatric Institute, Prince of Wales Hospital
- Member, Local Training Network Governance Committee (MOC) and site coordinator for Training for Psychiatry, Prince of Wales Hospital, South Eastern Sydney & Illawarra Psychiatry Training Network

**Dr Anne Poljak**
- Research Scientist, Brain Function, Australia (1989-present)

**Professor Lynn Chenoweth**
- Professor of Aged & Extended Care Nursing, Faculty of Nursing, Macquarie University, Sydney (2012-present)
- Director of the Health & Ageing Research Unit for the South Eastern Sydney & Illawarra Area Health Service
- Lead, NSW Core Committee, Dementia Collaborative Research Centre
- Lead, NSW Expert Advisory Group, Dementia Collaborative Research Centre

**Dr Simone Reppermund**
- Editorial board, Advances in Medicine

**Professor Perimidei Bachdev**
- Clinical Director, Neuropsychiatric Institute, Prince of Wales Hospital, Sydney (1987-present)
- Chief Medical Advisor to Alzheimer’s Australia (2014-present)
- Visiting Fellow, The Centre for Research on Ageing, Health and Wellbeing, Australian National University (2012-2014)
- Member of the F1000 Research Board Advisory Board – Neuropsychiatry panel (2015-current)
- President of the International College of Geriatric Psychiatry, Australia (2012-2014)
- Executive Member of the International Society of Vascular Behavioural and Cognitive Disorders (VASCODIC) (2012-present)
- Member, Neurocognitive Disorders Work Group, DSM-5 (2007-present)
- Founding Executive Committee Member of the Tourette Syndrome Association of Australia (1989-present)
- Scientific Advisory Committee Member of the Alzheimer’s Association of Australia (1995-present)
Appendix C: Postgraduate Research Students

CURRENT

Anne-Nicole Casey
Two degrees to social isolation: friendship schema & resident peer networks within a high-care residential aged care facility

PhD student
School of Psychology, Faculty of Medicine, UNSW

Supervisors: Dr Lee-Fay Low, Associate Professor Yun-Nee Jee, Professor Henry Brodaty

Sophie Chen
The relationship of diet to neurocognitive health

Masters by Research student
School of Psychology, Faculty of Medicine, UNSW

Supervisor: Professor Henry Brodaty, Dr Fiona O’Leary

Premilla Chinnappa-Quinn
The effect of physical illness and hospitalisation on cognition in older adults

PhD student
School of Psychology, Faculty of Medicine, UNSW

Supervisor: Professor Henry Brodaty, Dr Fiona O’Leary

Jessica Lazarus
Epigenetics and longevity

PhD student
School of Psychology, Faculty of Medicine, UNSW

Supervisors: Dr Karen Mathar, Associate Professor John Neve

Alien Lowe
Advanced characterisation of skin derived neuroprecursors

PhD student
School of Psychology, Faculty of Medicine, UNSW

Supervisors: Associate Professor Michael Valenzuela, Hon. Associate Professor Kuldeep Sidhu

Janet Mitchell
Service networks and their influence on the care of those with dementia in residential care

Masters by Research student
School of Psychology, Faculty of Medicine, UNSW

Supervisors: Professor Perminder Sachdev, Dr Karen Mathar, Professor Peter Schofield

Andrea Lammel
Heritability of episodic memory and its neuroanatomical correlates: An extended twin-design study

PhD student
Macquarie University

Tharusha Jayasena
The role of polyphenolic compounds in modulating symptoms and other pathways involved in Alzheimer’s disease

PhD student
School of Psychology, Faculty of Medicine, UNSW

Supervisors: Professor Arthur Shrier, Dr Jennifer Batchelor, Professor Perminder Sachdev

Professor Julian Trollor
Chair, Intellectual Disability Mental Health, School of Psychiatry, UNSW

Senior Medical Practitioner (Academic), Professor in Neuropsychiatry and Intellectual Disability, South Eastern Sydney Local Health District, Sydney

Visting Senior Research Fellow, Neuroscience Research Australia (NeurofA)

Member, NSW Institute of Psychiatry Board

Executive member, Intellectual and Developmental Disability Special Interest Group, RANZCP

Executive committee member, NSW Health Agency for Clinical Innovation, Intellectual Disability Health Network

Executive member, NSW Ministry of Health, Department of Family and Community Services, Joint Committee Intellectual Disability Mental Health

Member, Panel of Expert Advisors, Disability Deaths, NSW Ombudsman

Executive Member & immediate past Secretary & Treasurer, International Neuropsychiatric Association

International member, Neuropsychiatric Migrant Syndrome Information Service

Member, Australian Alliance for the Study of Intellectual Disability

Member, National Association for the Dually Diagnosed

Member, Joint Committee, NSW Health and Ageing Disability and Home Care, NSW Government Family and Community Services

Member, NSW Council for Intellectual Disability

Member, Research Advisory Committee, NSW Mental Health Commission

Member, Society for the Study of Behavioural Neurogenetics

Vice President & Member, Australian Association of Developmental Disability Medicine

Member, Neurocognitive Disorder Working Group, Diagnostic Manual for Intellectual Disability

Postgraduate Research Students

Appendix D: Awards

Appendix E: Research Grants & Funding

Appendix F: Statement of In-kind Contributions

Appendix G: Statement of Financial Performance

Appendix H: Publications

Appendix I: Conference Presentations

Appendix J: Workshops & Invited Lectures

Appendix K: Workshops & Invited Lectures

Appendix L: Staff List

Appendix M: Appointments

Appendix N: Annual Report

Appendix O: Annual Report
Supervisors: Professor Lindy Clemson, Professor Henry Brodaty.

Amanda Oley
- Obsessive compulsive disorder: a decision making model
- PhD student
- School of Psychiatry, Faculty of Medicine, UNSW
- Supervisors: Professor Perminder Sachdev, Professor Giri Mahi
- PhD submitted June 2014

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

Mary Revelas
- The genetics of exceptional longevity and successful ageing
- PhD student
- School of Psychiatry, Faculty of Medicine, UNSW
- Supervisors: Associate Professor Wei Wen, Professor Perminder Sachdev, Professor Michael Breakspear

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: Dr Karen Mather, Dr Anbupalam Thalamuthu, Professor Perminder Sachdev

COMPLETED

Yanhong (Catherine) Dong
- Cognitive outcome after stroke: Detection of vascular cognitive impairment, prognosis, neuropsychological patterns, and the efficacy of revascularization
- PhD student
- School of Psychiatry, Faculty of Medicine, UNSW

Willard 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 Mikos, Professor Henry Brodaty
- PhD submitted June 2014

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

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

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

Dr Nady Braidy
- The Science and Industry Endowment Fund – Australian Academy of Science Fellowship to the 84th Lindau Nobel Laureate Meetings
- Chilean National Postdoctoral Prize

Professor Henry Brodaty & Professor Perminder Sachdev
- Joint Recipients: Dean’s Award for Outstanding Achievement (Academics), UNSW
- Outstanding contribution to research and teaching in the Faculty of Medicine

Hon. Associate Professor Kuldip Sidhu
- International Pioneer in Medicine, Society of Brain Mapping & Therapeutics, USA

Professor Julian Trollor
- Promoted from Associate Professor to Professor

Dr Karen Mather
- National Post-Doctoral Excellence Award
Appendix E: Research Grants & Funding

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

**Funding Source**: NHMRC Project Grant

**Project ID**: RG122225

**Investigator/s**: Prof Perminder Sachdev, Dr Margie Wright, Prof David Ames, A/Prof Julian Trollor, A/Prof Wei Wen, Prof Bernhard Baunes, Dr Teresa Lee, Dr John Crawford

**Duration**: 3 years: 2013-2015

**Total Funds**: $912,022

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

**Funding Source**: Australian Research Council (ARC) Discovery Project

**Project ID**: RM10093

**Investigator/s**: Prof Perminder Sachdev, Dr Anna Poljak, Prof Mark Dunon, Prof John Atta, Prof Peter W Schofield, Dr John Crawford

**Duration**: 3 years: 2012-2014*

**Total Funds**: $330,000

*Extension granted to 31 March 2015

**Secondary analyses and archiving of social and behavioral databases in aging**

**Funding Source**: National Institutes of Health (USA)

**Project ID**: R01AG04653

**Investigator/s**: Dr Allan Snyder

**Duration**: 1 year: 2012-2013*

**Total Funds**: $26,402

*Project acquitted and closed January 2014

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

**Funding Source**: NHMRC Seed Funding Project Grant

**Project ID**: RM10658

**Investigator/s**: Prof A/Prof Wei Wen

**Duration**: 1 year: 2012-2013*

**Total Funds**: $144,708

*Project acquitted and closed September 2014

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

**Funding Source**: NHMRC Seed Funding Project Grant

**Project ID**: RM10657

**Investigator/s**: Dr Melissa J Sturin

**Duration**: 1 year: 2012-2013*

**Total Funds**: $181,265

*Project acquitted and closed May 2014

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**Appendix: Grants & Funding**

**Grants**

**Agilent 1200UHPLC equipment grant (Part 1)**

**Funding Source**: National Health & Medical Research Council (NHMRC)

**Project ID**: RG134156-B

**Investigator/s**: Prof Perminder Sachdev, Dr Anna Poljak, Dr Nady Braidy, Dr Julia Munchhoff, et al.

**Duration**: 1 year: 2014

**Total Funds**: $109,711

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

**Funding Source**: Yaylakir Foundation

**Project ID**: RG141699

**Investigator/s**: Dr Karen Malter

**Duration**: 1 year: 2014-2015

**Total Funds**: $20,000

**Improving clinical diagnosis of mild neurocognitive disorders**

**Funding Source**: National Health & Medical Research Council (NHMRC)

**Early Career Fellowship**

**Project ID**: RG123293

**Investigator/s**: Dr Nicole Kochan

**Duration**: 1 year: 2013-2014

**Total Funds**: $50,000

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

**Funding Source**: Alzheimer’s Australia NSW/RT

**Research Foundation Research Grant**

**Project ID**: RG123185-C

**Investigator/s**: Prof Lynn Chanowth

**Duration**: 1 year: 2013-2014

**Total Funds**: $28,009

**Sirtuin single nucleotide polymorphisms in brain ageing**

**Funding Source**: NHMRC Early Career Fellowship

**Project ID**: RO/12/2993

**Investigator/s**: Dr Nady Braidy

**Duration**: 4 years: 2013-2016

**Total Funds**: $149,792

** Amount per year**: $37,445.50

**Biomarkers of late-life depression and associated cognitive impairment**

**Funding Source**: Alzheimer’s Australia Dementia Research Foundation – Postgraduate Scholarship

**Project ID**: RG123530

**Investigator/s**: Ms Ruby Tjiang, Prof Perminder Sachdev

**Duration**: 2 years: 2013-2014

**Total Funds**: $100,000

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

Funding Source: NHMRC Program Grant
Project ID: RM06756
Investigator/s: Prof Perminder Sachdev, Prof Henry Brodaty, Prof Gavin Andrews
Duration: 5 years: 2010-2014*
Total Funds: $6,090,000

*Grant duration approved by NHMRC, 26 November 2014 - new end date 31 December 2015

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

Funding Source: NHMRC Project Grant
Project ID: RM07525
Investigator/s: Prof Perminder Sachdev, Prof Robyn Richmond, Dr Nicola Kochan, A/Prof Wei Wen, Dr John Crawford
Duration: 3 years: 2010-2014*

*Grant duration approved by NHMRC, 23 July 2014 – new end date 31 December 2014

Prevention and management of mental disorders in older Australians

Funding Source: NHMRC Capacity Building Grant
Project ID: RM06714
Investigator/s: Prof Perminder Sachdev, Prof Henry Brodaty, Prof Gavin Andrews, Prof Stephen Lord
Duration: 5 years: 2009-2013*
Total Funds: $2,382,525
Amount per year: $476,505

*Grant duration approved by NHMRC, 26 November 2014 - new end date 31 December 2015

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

Funding Source: NHMRC/ARC Strategic Award
Project ID: RM04226
Investigator/s: Prof Perminder Sachdev, Prof David Ames, Prof Peter Schofield, Prof GA (Tony) Broe, Dr Margie Wright, Dr Wei Wen, Dr Teresa Lee
Duration: 5 years: 2007-2011*
Total Funds: $2,000,000
Amount per year: $400,000

*Project acquitted and closed October 2014

Philanthropic

The Thomas Foundation Grant
Funding Source: The Thomas Foundation
Award: Prof Henry Brodaty, Prof Perminder Sachdev
Duration: 5 years: 2011-2015
Total Funds: $1,000,000

The Montefiore Chair of Health Brain Ageing at UNSW
Funding Source: The Sir Moses Montefiore Jewish Home
Award: Prof Henry Brodaty, Prof Perminder Sachdev
Duration: 5 years: 2011-2015
Total Funds: $665,000

Major Partner & Direct Donations 2014: $150,538

Event & Sponsorship 2014: $64,464

Appendix F: Statement of In-Kind Contributions

- ARA Restaurant
- Breathe Fire Specialised Training
- HWL Ebsworth Lawyers
- Intellectual Ventures
- Rockdale City Council
Appendix G: Statement of Financial Performance

**Notes to the Statement of Financial Performance**

**Total Funds**

<table>
<thead>
<tr>
<th>Year</th>
<th>Amounts</th>
</tr>
</thead>
<tbody>
<tr>
<td>2014</td>
<td>2,306,887</td>
</tr>
<tr>
<td>2013</td>
<td>2,771,444</td>
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**Costs**

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<tr>
<th>Category</th>
<th>2014</th>
<th>2013</th>
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</thead>
<tbody>
<tr>
<td>Faculty Funds</td>
<td>1,872,655</td>
<td>2,908,302</td>
</tr>
<tr>
<td>Research &amp; Development</td>
<td>222,061</td>
<td>402,298</td>
</tr>
<tr>
<td>Internal Expense</td>
<td>52,248</td>
<td>67,076</td>
</tr>
<tr>
<td>Repairs and Maintenance</td>
<td>4,086</td>
<td>1,470</td>
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<tr>
<td>Other Expenses</td>
<td>24,308</td>
<td>22,196</td>
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</table>

**Research Revenue**

<table>
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<th>Year</th>
<th>Amounts</th>
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<tbody>
<tr>
<td>2014</td>
<td>1,876,397</td>
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<tr>
<td>2013</td>
<td>2,503,977</td>
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**In-Kind Contributions**

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<th>Amounts</th>
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<td>2014</td>
<td>52,880</td>
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<tr>
<td>2013</td>
<td>76,000</td>
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**Funeral Services**

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<th>Amounts</th>
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<tr>
<td>2014</td>
<td>3</td>
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<tr>
<td>2013</td>
<td>15,000</td>
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**Sundry Other Revenue**

<table>
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<th>Year</th>
<th>Amounts</th>
</tr>
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<tbody>
<tr>
<td>2014</td>
<td>1,709</td>
</tr>
<tr>
<td>2013</td>
<td>3,513</td>
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</tbody>
</table>

**Notes**

1. Faculty Funds - Operating funds provided by the faculty are budget allocations, with no revenue transferred to CHeBA.

2. Fees - Other fees include fees for CHeBA's courses and other programs.

3. Research Revenue - Includes revenue from research grants and contracts.

4. Other Expenses - Includes costs associated with research activities and infrastructure.

5. Sundry Other Revenue - Includes miscellaneous revenue not categorized elsewhere.

**Journal Publications**


Appendix I: Conference Presentations


Appendix J: Workshops & Invited Lectures

International


Sachdev P. Neuroimaging for early diagnosis of Alzheimer’s disease. BCS Colloquium, Seoul National University, South Korea; 4 Jul 2014.

Sachdev P (Plenary Speaker). The centenarian subjects as a model of successful aging. XX Brazilian Congress of Gerontology and Geriatrics (CBGG). Belem, Para State, Brazil; 28 Apr – 3 May 2014.

Sachdev P (Plenary Speaker). What lessons have contributed to the understanding of aging and dementia? The Older Australian Twin Study. XX Brazilian Congress of Gerontology and Geriatrics (CBGG). Belem, Para State, Brazil; 28 Apr – 3 May 2014.

National


Local

