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Centre for Healthy Brain Ageing (CHeBA)
Annual Report 2018

research

positive ageing

big data

prevention

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CONTENTS

CO-DIRECTORS' REPORT

Dementia is the second leading cause of death of Australians, costs an estimated $15 billion annually, and affects over half of all residents in our residential aged care facilities. When we founded CHeBA six years ago, our vision was to achieve, through research, healthier brain ageing and better clinical care of age-related brain diseases, in particular dementia. In the intervening years, the impact of dementia has continued to grow. In 2016, dementia became the leading cause of death among Australian women, and the mortality rate for dementia had increased by the largest margin compared to other leading causes of death.

The need for a strong evidence-base to tackle dementia has never been greater.

Faced with this challenge, CHeBA further expanded its research activities in 2018, and continued to work to find strategies both to prevent dementia as well as improve the treatment and care of those already affected. This report summarises the achievements of our researchers, with several highlights that include:

- the work of Dr Nady Braidy in developing a world-first, improved method to measure a coenzyme found in all living cells, including brain cells;
- our international COSMIC consortium's discovery about the importance of using visual memory tests to improve identification of people at risk of developing Alzheimer's disease; and
- definitions of global prevalence of dementia in centenarians for the first time by the CHeBA-led ICC-Dementia consortium.

Thanks to the quality and innovation of our researchers, CHeBA secured several major, competitive grants. Our proposed nanotechnology approach to diagnosis and treatment won the inaugural $1 Million Dollar Innovation Challenge funded the Dementia Australia Research Foundation and the Yulgilbar Alzheimer's Research Program (YARP). We were granted about $650,000 by the NHMRC for our international, big data approach to identifying risk and protective factors for vascular cognitive disorders globally (the STROKOG consortium). Professor Brodaty's COGNISANCE team, and the SHARED team of which Professors Brodaty and Sachdev are part, were together awarded close to $1.5 million by the NHMRC & EU Joint Programme on Neurodegenerative Disease Research to improve dementia care and quality of life, as well as explore the role of socialisation in reducing dementia risk.

CHeBA continued its strong corporate and community partnerships in 2018, through our major philanthropic initiative, The Dementia Momentum. Through the remarkable generosity of our donors, we held the most successful Wipeout Dementia campaign yet in November. Spokesman for The Dementia Momentum, Mr Richard Grellman AM, officially launched a new campaign, Drive Out Dementia, with three events held in 2018 and more planned for 2019. The ongoing involvement of Richard Grellman has been invaluable in championing our cause and raising greater awareness within the corporate sector of the long-term implications of dementia for all Australians. The number of benefactors of CHeBA is large indeed, and we are grateful to each one for their generosity in supporting dementia research.

> “There is a new excitement in dementia research, and we expect that the long drought in new treatments will end soon.”

The funding we have secured this year will help drive new avenues of research in 2019 using cutting-edge technology and expanding on existing findings. Professor Sachdev and his team propose to use nanoparticles to move across the blood brain barrier and target dementia-specific molecules in the brain. Professor Brodaty and colleagues will begin developing international toolkits co-designed with clinicians and people with dementia to facilitate a positive quality of life.

The Australian Dementia Network (ADNet), which CHeBA strongly supports, is likely to make many strides in 2019, and we expect early stages of the development of a Dementia Registry and a network of Memory Clinics. Dementia trials are likely to be given a new lease of life. Professor Brodaty is a member of a team which will, with joint funding from NHMRC and Vietnam, develop a dementia plan for Vietnam. There is a new excitement in dementia research, and we anticipate that the long drought in new treatments will end soon.

As ever, we gratefully acknowledge the invaluable contribution and enthusiasm of our collaborators and supporters. We pay tribute to our dedicated team of researchers and support staff who continue to make the work of CHeBA successful and gratifying.

Sincerely,

Scientia Professor Henry Brodaty AO

Scientia Professor Perminder Sachdev AM

ABOUT THE CENTRE

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

OUR VISION

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

OUR MISSION

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

OUR AIMS

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

- Determine the pathways of normal and abnormal brain ageing in the community.
- Identify risk factors for and protective factors against abnormal brain ageing.
- Develop strategies for prevention of cognitive decline with ageing.
- Promote global collaborations to develop knowledge and further research into brain ageing.
- Understand the behavioural as well as the cognitive and functional manifestations of brain ageing.
- Translate relevant research findings into practice.
- Determine the prevalence of age-related neurodegenerative and cerebrovascular disorders.
- Identify biomarkers for brain disorders.
- Investigate the pathophysiology of brain diseases so that novel treatments can be discovered.
- Conduct treatment trials of novel drugs and non-pharmacological strategies.
- Conduct educational activities for a workforce involved in the care of the elderly, especially those with dementia.
- Design models of assessment and care using the latest research evidence.
- Develop research programs in special populations, e.g. young-onset dementia, dementia in intellectual disability.

OUR FUNCTIONS & GOALS

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

This will be achieved through:

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

SIGNIFICANT HIGHLIGHTS

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

Professor Perminder Sachdev AM

$1M DEMENTIA GRANT USING NANOTECHNOLOGY FOR DIAGNOSIS AND TREATMENT

CHeBA was an inaugural recipient of the $1 Million Dollar Innovation Grant for new research ideas that advance dementia research, awarded by the Dementia Australia Research Foundation and the Yulgilbar Alzheimer's Research Program (YARP).This research proposes to use nanoparticles to move across the blood brain barrier and target dementia-specific molecules in the brain such as amyloid and tau.

Professor Perminder Sachdev said this research would be a collaboration between clinical neuroscience and nanoscience and therefore has the potential to transform the diagnostics and therapeutics of neurodegenerative disorders.

"Of the many obstacles to achieving the goal of prevention and cure of Alzheimer's disease, we have identified two that can potentially be overcome with the latest developments in nanoscience. Firstly, the challenge of an easily available early diagnostic test can be met using nanoparticles with superparamagnetic properties as imaging agents, tagged with appropriate ligands, for magnetic resonance imaging and the newly emerging magnetic particle imaging.

"Secondly, nanoparticles can be harnessed as drug-delivery systems to deliver novel therapeutic agents directly to the site of pathology in the brain," explained Professor Sachdev.

Professor Perminder Sachdev AM

The successful CHeBA project is a collaboration between researchers at CHeBA, the Australian Centre for Nanomedicine, School of Chemistry UNSW, the Biological Resource Imaging Lab at UNSW, the Melbourne Dementia Research Centre and ARC Centre for Excellence in Convergent Bio-Nano Science and Technology, University of Melbourne.

> "Of the many obstacles to achieving the goal of prevention and cure of Alzheimer's disease, we have identified two that can potentially be overcome with the latest developments in nanoscience."
>
> Professor Perminder Sachdev AM

GRANT SUCCESS TO ADDRESS VASCULAR DEMENTIA

CHeBA was awarded a $649,205 grant from the National Health & Medical Research Council to support the Stroke and Cognition Consortium (STROKOG), which investigates risk and protective factors for vascular cognitive disorders globally.

Stroke is the second most common cause of death and disability around the world. Since gains in public health and advances in medicine have helped reduced stroke-related mortality, researchers are now paying attention to the effects of stroke on cognitive function.

While vascular dementia is the second most common type of dementia, many aspects of cognitive decline in relation to stroke remain only partly understood. Most research studies examining cognition in stroke patients have been small, and this limits the ability to determine with confidence (or precision) the factors that lead to cognitive disorders and dementia after stroke.

STROKOG brings together researchers from around the world, forming a collection of post-stroke studies with more than 16,000 participants from 18 countries and 30 studies.

Study Co-ordinator of STROKOG, Jessica Lo, explains that the consortium's geographical spread and representation from high, low and middle-income countries, involving different ethno-racial groups in diverse settings makes this consortium unique.

"By combining data from different studies and performing joint analyses on a 'mega'-dataset, this grant will allow us to address some of the most important questions in relation to the characteristics and determinants of vascular cognitive disorders, which in turn could help improve the diagnosis and treatment of cognitive disorders after stroke," said Ms Lo.

"This grant will allow us to address some of the most important questions in relation to the characteristics and determinants of vascular cognitive disorders."

Jessica Lo, STROKOG Study Co-ordinator

Support for STROKOG has largely been driven by CHeBA's major philanthropic initiative, The Dementia Momentum with significant five year funding support from the Vincent Fairfax Family Foundation (VFFF).

$1.5 MILLION TO ENHANCE SOCIAL CONNECTIONS AND IMPROVE QUALITY OF CARE FOR PEOPLE WITH DEMENTIA

Professor Henry Brodaty AO

CHeBA Co-Director Professor Henry Brodaty AO was awarded close to $1.5 million by the EU Joint Programme on Neurodegenerative Disease Research (JPND). The funding will support two projects: analysing socialisation and risk of dementia and improving quality of care for people diagnosed with neurodegenerative disease.

Current research suggests strong potential for improving quality of life for those living with neurodegenerative diseases such as Alzheimer's disease, with novel health and social care concepts and innovations focusing on the preservation of dignity, independence and social inclusion.

Professor Brodaty's Co-designing Dementia Diagnosis and Post-Diagnostic Care (COGNISANCE) team was selected for its ambitious, innovative and multi-disciplinary collaborative projects addressing health and social care at both the macro level of systems and infrastructures and the individual level of patients, carers and families.

"Despite many national guidelines for the management of dementia, people diagnosed with Alzheimer's, their families and carers often receive inadequate care," said Professor Brodaty.

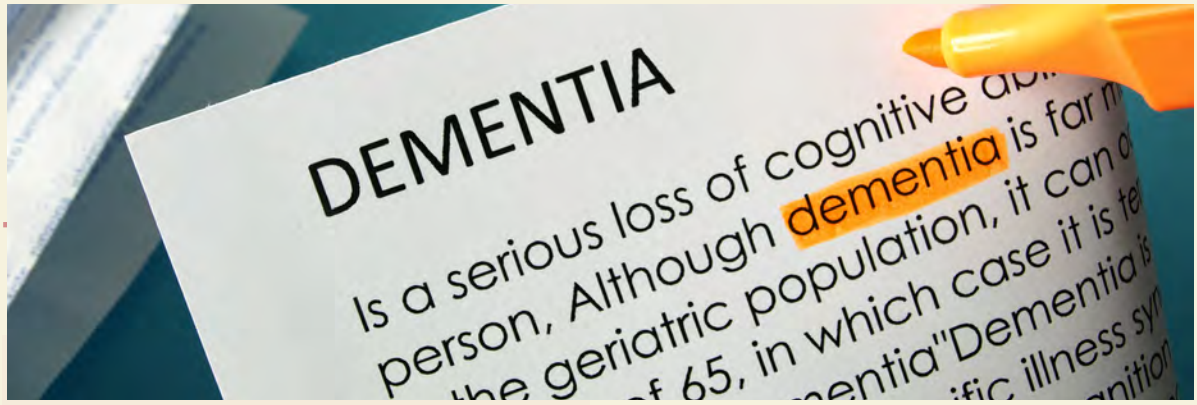
> "We will develop international toolkits co-designed with people with dementia and clinicians to facilitate high quality post-diagnostic care and a positive quality of life."
>
> Professor Henry Brodaty AO

"The first project will involve developing international toolkits co-designed with people with dementia and clinicians to facilitate high quality post-diagnostic care and a positive quality of life."

Professor Brodaty's second project aims to understand the link between socialisation and lower risk of dementia by analysing large global data sets and by developing interventions to enhance stronger social connections.

Partners involved in the COGNISANCE research are: Professor Perminder Sachdev, CHeBA, UNSW Sydney, Lee-Fay Low, University of Sydney, Australia, Isabelle Vedell, McGill University, Canada, Frans Verhey F, Maastricht University, The Netherlands, Greta Rait, University College London, United Kingdom, Louise Robinson, Newcastle University Institute for Ageing, United Kingdom, Joanna Rymaszewska, Wroclaw Medical University, Poland

LAUNCH OF ADNET



In July, CHeBA Co-Directors Professors Perminder Sachdev and Henry Brodaty announced their involvement in an Australian Dementia Network (ADNet), launched to monitor the diagnoses and care of dementia patients across Australia.

$18 million has been injected by the Federal Government into this world-first program, led jointly by Professors Perminder Sachdev and Henry Brodaty of CHeBA and Christopher Rowe of Austin Health, which is hoped to fast-track new developments in the treatment of Alzheimer's disease.

A national registry will also be launched, allowing those with dementia to participate in therapeutic trials.

Professor Sachdev said that this is a major boost to dementia research in Australia which will place it on par with developments occurring in Europe and North America, and help Australia join the world-wide push to develop novel treatments for Alzheimer's disease and other dementias.

ADNet will:

- Establish a national network of memory clinics to standardise assessment of cognitive disorders and improve specialist access for all Australians, through advanced imaging, genetics and lifestyle data;
- Register and prepare volunteers for participation in clinical trials and other research programs, by providing them with state of the art diagnosis and tracking their disease trajectory;
- Collate and compare data to chart dementia causes, progression and risks and potential new treatments, while supporting research participants and benchmarking clinical care;
- Ensure Australian and international data can be shared, providing unprecedented research access to global data and collaboration, to inform prevention, treatment and care.

ADNet will drive research and deliver improvements through five core teams - Registry, Clinics, Trials, Technology and Business - with close links to leading international programs in Europe and the USA.

ADNet is the largest single project funded to date through the Government's $200 million, five-year *Boosting Dementia Research Initiative* launched in 2014 by the National Health and Medical Research Council.

> "ADNet will lift the standard of Australian dementia diagnosis and care, with a coordinated and consistent approach."
>
> Aged Care Minister
> Ken Wyatt AM

LIVING TO 100 CONFERENCE

In September, CHeBA hosted the 2nd International 'Living to 100' Conference in Sydney to explore cutting edge research on longevity. The internationally acclaimed line up of speakers from Australia, Japan, Italy, Belgium, Sweden and the USA discussed findings from studies of exceptionally long-lived individuals, in particular centenarians (people aged 100 and above) and supercentenarians (people aged 110+).

"It was a valuable experience to bring together multidisciplinary experts from around the world to unravel the secrets of successful ageing," said CHeBA Co-Director Professor Perminder Sachdev.

Highlights included an interview panel of centenarians and near-centenarians, and a debate between world-leading researchers from Australian and Sweden about whether it is possible to live to 150.

Researchers presented on geographic 'hotspots' for centenarians, theories of ageing, factors for successful ageing (including diet, genetics, cognitive activity and exercise), the role of technology, as well as the demographic and economic implications for a long-lived population.

'Can we live to 150 years of age?' debate: (L-R) Prof Perminder Sachdev AM (Moderator), Prof Peter Schofield AM, Prof Ingmar Skoog & Prof Maria Fiatarone Singh.

"It was a valuable experience to bring together multidisciplinary experts from around the world to unravel the secrets of successful ageing."

Professor Perminder Sachdev AM

SPEAKERS

- Professor Heather Booth
- Professor Henry Brodaty AO
- Professor Ashley Bush
- Professor Julie Byles
- Dr Henry Cutler
- Dr Fatima El-Assaad
- Professor Maria Fiatarone Singh
- Professor Diane Gibson
- A/Professor Yasuyuki Gondo
- Professor Nobuyoshi Hirose
- Ngaire Hobbins
- Professor David Irving
- Dr Ugo Lucca
- A/Professor Jessica Mar
- Professor Peter Martin
- Dr Karen Mather
- Professor Brian Morris
- Professor Sharon Naismith
- Professor Michel Poulain
- Professor David Raubenheimer
- Professor Perminder Sachdev AM
- Dr Takashi Sasaki
- Professor Peter Schofield AM
- Sophie Scott
- Dr Claire Shepherd
- Professor Ingmar Skoog
- Adam Theobald
- Professor Michael Valenzuela
- Professor Toby Walsh
- Dr Lindsay Wu

PANEL OF CENTENARIANS & NEAR-CENTENARIANS

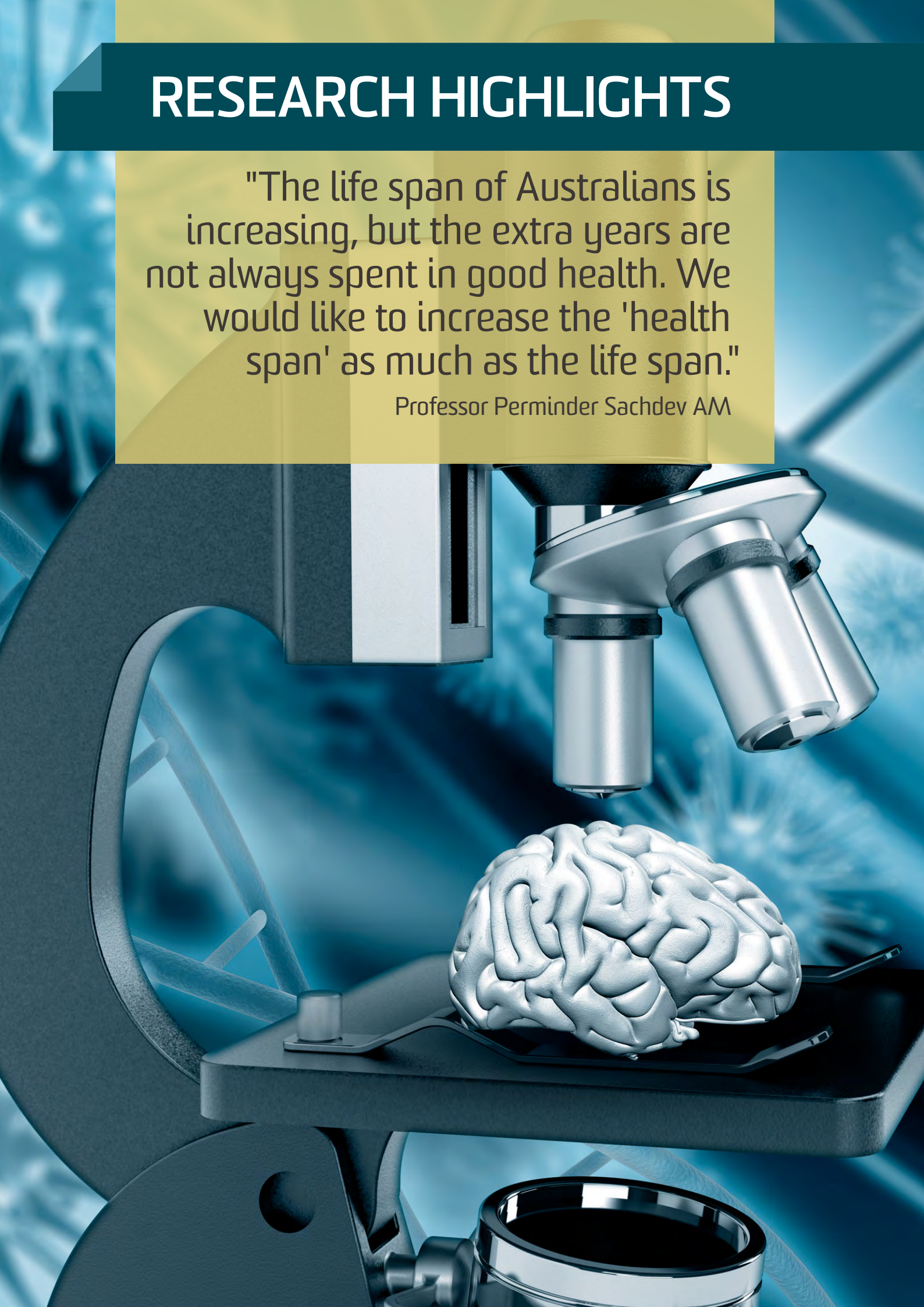
- Helena Goldstein (99)
- Michael Harvey (97)
- Eileen Kramer (103)
- Tom Sample (97)

SBS interviewing the panel of centenarians & near-centarians/ L-R: Michael Harvey (97), Eileen Kramer (103), Tom Sample (97) & Helena Goldstein (99).

RESEARCH HIGHLIGHTS

"The life span of Australians is increasing, but the extra years are not always spent in good health. We would like to increase the 'health span' as much as the life span."

Professor Perminder Sachdev AM



GOLD STANDARD MEASURE FOR AGEING

A collaborative study between researchers at CHeBA and the Mark Wainwright Analytical Centre developed a world-first, improved method to measure a coenzyme found in all living cells across biological samples, including brain cells and reproductive cells. The new 'gold standard' in the field of metabolomics may inform future understanding of the mechanisms of ageing. The findings were published in the journal *Metabolomics*.

Dr Nady Braidy

The coenzyme - nicotinamide adenine dinucleotide (NAD+) – has recently been shown not only to be a regulator of metabolism, but also is involved in numerous biological and pathophysiological processes including cancer, the stress response, inflammation and ageing.

"Recent discoveries have fuelled enthusiasm to examine both NAD+ anabolic pathways and the NAD+ metabolome in several model organisms," said Dr Nady Braidy, Co-Leader of CHeBA's Omics & Neurobiology of Ageing Group and senior author on the paper.

"These studies have provided renewed insights into the functional roles of NAD+ and its related metabolites and inspired the development of a sensitive, robust, reproducible and rapid method for concurrent quantitative determination of intracellular levels of NAD+ metabolome in certain cells using liquid chromatography coupled to mass spectrometry," he said.

Lead author Sonia Bustamante, from the Mark Wainwright Analytical Centre, said it was anticipated that the new method to quantify the NAD+ metabolome will help standardise NAD+ research across different laboratories. This is also expected to overcome challenges associated with translation of preclinical studies towards clinical practice making the new measure indispensable for targeted analysis.

"To the best of our knowledge, this is the first study to quantify the entire NAD+ metabolome in primary murine oocyte cultures", said co-author Professor Perminder Sachdev.

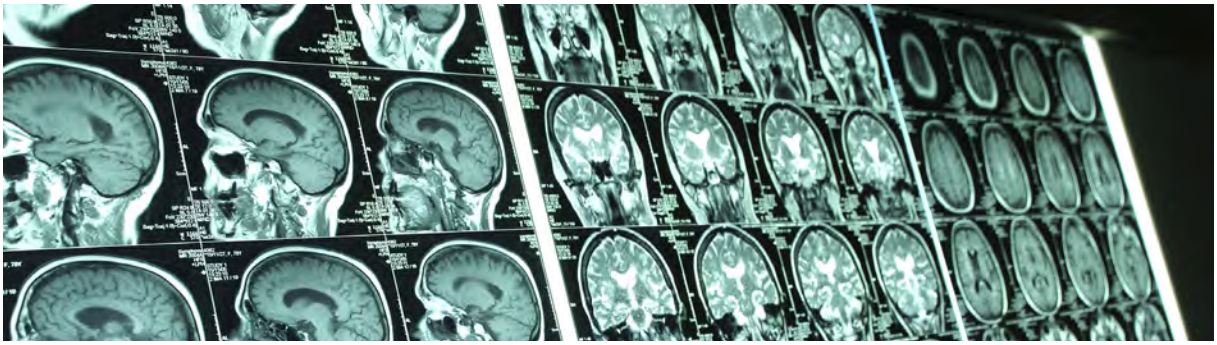
As chronic age-related oxidative stress is known to induce NAD+ depletion, our newly described testing process can be further used to characterise functional effects of changes to the NAD+ metabolome during ageing in several cells including those in ovaries and in the brain.

> "Not only will this research be of benefit in increasing our understanding of the mechanisms of ageing and memory, it will likely be highly relevant to improving fertility and cellular function as well."
>
> Dr Nady Braidy

"Not only will this research be of benefit in increasing our understanding of the mechanisms of ageing and memory, it will likely be highly relevant to improving fertility and cellular function as well," said Dr Braidy.

Publication: Bustamante et al., 'Quantifying the cellular NAD+ metabolome using a tandem liquid chromatography mass spectrometry approach', Metabolomics, 2018; 14: 15.

BRAIN ACTIVITY AT REST PROVIDES CLUES TO INTELLIGENCE



The ability of an adult to learn and to perform cognitive tests is directly linked to how active the brain is at rest, according to new research from CHeBA.

The study, published in *Brain Imaging and Behaviour,* found that how well an older adult performed on language recall, memory or executive function tests was directly related to the activity in specific brain regions while in a resting state, i.e. when they were not doing any specific tasks or thinking of anything in particular. The same brain regions have been shown to be activated when an individual is engaging in these cognitive activities.

CHeBA researchers used magnetic resonance imaging (MRI) images of the brain in 67 cognitively healthy adults aged between 73 to 90 years. The MRI images captured activity of the whole brain at rest when the participants were not thinking of anything in particular and had their eyes closed. They were also tested on their ability to perform three common neuropsychological tests, administered by trained psychology graduates.

> "We found that the human brain is already somewhat pre-determined to do well or perform poorly in testing."
> Professor Perminder Sachdev AM

"We found that the human brain is already somewhat pre-determined to do well or perform poorly in testing," said lead researcher Professor Perminder Sachdev. "Brains differ from each other in terms of resting state activity and it's not an even playing field. If there is activity in certain brain networks when the brain isn't doing anything, then that person is predisposed to do better than others on the tasks that rely on that network."

In the past, similar research had focused on specific brain regions, however this study examined 3D "voxel" images of the whole brain, thereby not constraining the results based on previous knowledge.

The results found that how well an individual did on language and executive function tests was linked with functional connectivity during rest in the frontal and temporal cortices. For memory retrieval, strong resting state activity was located in the inferior temporal cortices.

"The next stage in research would be to examine if this resting state activity of the brain can be modified by training. There is a possibility that training could boost the brain's intrinsic network, improving overall mental performance and possibly prevent cognitive decline or even dementia," Professor Sachdev said.

Publication: Zhang et al., 'The relationship between voxel-based metrics of resting state functional connectivity and cognitive performance in cognitively healthy elderly adults', Brain Imaging and Behaviour, 2018; 12(6): 1742–1758.

VISUAL MEMORY TESTS IDENTIFY RISK OF ALZHEIMER'S DISEASE

Research outcomes from an international consortium led by CHeBA have indicated that elderly people with suspected Mild Cognitive Impairment (MCI) should be tested with both verbal and visual memory tests to better identify those at greatest risk of developing Alzheimer's disease.

The study, published in *International Psychogeriatrics,* assessed 4,771 elderly participants across five community-based studies, each a member of the international COSMIC consortium and from different countries. All participants were classified as having normal cognition or MCI involving impairments in verbal memory, visual memory, or both, using international criteria and followed for an average of 2.48 years.

MCI can be an intermediate condition between normal cognitive ageing and Alzheimer's disease. MCI often causes memory impairments, which are usually assessed with tests of verbal memory that require someone to remember words from a list they are read. However, some people with MCI may perform well on verbal memory tests but not so well on tests of visual memory, such as remembering what shapes were shown to them on a card.

"Visual memory tests are not used in the clinic as often as verbal memory tests, which can mean visual memory impairments are not detected and someone with these misdiagnosed as not having MCI," said Dr Darren Lipnicki, Study Co-ordinator of COSMIC (Cohort Studies of Memory in an International Consortium).

"Our study found that people identified as having MCI involving visual memory impairments were as likely as those with MCI involving verbal memory impairments to later develop Alzheimer's disease," said Dr Lipnicki.

"The results highlight the importance of including both verbal and visual memory tests in neuropsychological assessments to more reliably identify those at risk of developing Alzheimer's disease," said co-author Professor Perminder Sachdev.

Established in 2012, COSMIC is one of four international consortia led by CHeBA to investigate risk and protective factors for dementia incidence and healthy brain ageing world-wide. Support for the consortia's research is driven by CHeBA's major philanthropic initiative, The Dementia Momentum.

Publication: Oltra-Cucarella et al., 'Visual memory tests enhance the identificatiobodn of amnestic MCI cases at greater risk of Alzheimer's disease', International Psychogeriatrics, 2018; DOI:10.1017/S104161021800145X

> "Our study found that people identified as having MCI involving visual memory impairments were as likely as those with MCI involving verbal memory impairments to later develop Alzheimer's disease."
>
> Dr Darren Lipnicki

BRAIN IMAGING STUDY REVEALS TURNING POINT IN AGE-RELATED SULCAL CHANGES

Researchers from CHeBA - in collaboration with international researchers from Beihang University, Capital Medical University Beijing and the University of Sydney - have identified significant, age-related decline over time in the brain structure of cognitively normal adults aged 70 to 90 years old. It is the largest study of its kind, examining longitudinal changes in the width and depth of grooves (sulci) in the folded surface of the brain. This research has laid a solid foundation for future cortical folding studies of neurocognitive disorders in the elderly. The findings were published online in the eminent journal, NeuroImage.

Leader of CHeBA's Neuroimaging Group and co-author, Associate Professor Wei Wen, said the findings indicate an accelerated atrophy of the brain cortex starting in the late 70s.

"We found significant decline in sulcal depth over time," said Associate Professor Wen. "Importantly, we also detected some turning points, which occurred between ages 75 to 80, with marked acceleration in the widening of the sulci."

The study examined 132 cognitively normal participants aged 70 to 90 years old over seven years using magnetic resonance imaging (MRI). The opening between grooves (sulcal width) and sulcal depth were measured for sixteen prominent sulci, including eight for each hemisphere.

The folded cortex of the human brain creates a larger surface area than the space of the skull could house if it were flattened, with two-thirds of its surface hidden in sulci. Previous research has identified that sulcal changes occur alongside brain atrophy, however patterns of change over time were unclear.

The present study identified accelerated widening and shallowing of sulci over time, including differences in rates of decline between the right and left brain hemisphere, as well as between different areas of the brain. The superior frontal sulcus showed the most rapid increase in fold opening and decrease in sulcal depth.

Co-author Dr Tao Liu, a former CHeBA PhD student and postdoctoral fellow now working at Beihang University in Beijing, said the study improved our understanding of structural changes occurring as part of normal ageing.

"These findings may help to provide a reference for studies of neurocognitive disorders and diseases in the elderly," said Dr Liu.

MAINTAIN YOUR BRAIN TRIAL COMMENCED

MAINTAIN YOUR BRAIN

"If successful, Maintain Your Brain will provide an intervention that is scalable for national and international use."

Professor Henry Brodaty AO

Maintain Your Brain (MYB) is the largest trial in the world to attempt to prevent cognitive decline and potentially dementia through an online intervention program. Participants, aged 55 to 77, are screened for modifiable dementia risk factors related to four modules that comprise the MYB intervention: physical activity, nutrition, cognitive training and mental health. A dress rehearsal of the main trial, the pilot study, started in November 2017 and finished in February 2018. Based on challenges and feedback during the pilot, the MYB digital platform was modified to extend the recruitment period, provide clearer instructions and a timeline for participants, and easily accessible help.

The MYB main trial recruited between June - October 2018. Of a total of 14,064 participants who consented to the trial, 6,236 participants were eligible and randomised into the trial. The first group started their first module in July 2018, while the second group commenced in October 2018. Recruitment has now closed, and all participants are currently completing their modules. MYB will run for 3 years and if successful, it will provide a model for not just effective intervention among older adults, but an intervention that is scalable for national and international use.

OUR GROUPS

"CHeBA is founded on the critical need for research to encompass diagnosis, cure and care of age-related brain diseases."

Professor Henry Brodaty AO

GROUP SNAPSHOT

Group Leader: Professor Perminder Sachdev

Group Leader: Professor Henry Brodaty

EPIDEMIOLOGY

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.

Group Leaders: Professor Perminder Sachdev, Professor Henry Brodaty.
Staff: Emeritus Professor Gavin Andrews, Dr Nicole Kochan, Dr Karen Mather, Dr John Crawford, Dr Anbu Thalamuthu, Dr Darren Lipnicki, Dr Yvonne Leung, Dr Steve Makkar, Dr Vibeke Catts, Jessica Lo.

BRAIN AGEING RESEARCH LABORATORY

Group Leader: Dr Nady Braidy

This interdisciplinary group was formed to apply state-of-the-art molecular biology techniques to the advancement of research in the areas of normal ageing, Alzheimer's Disease and other age-related neurodegenerative conditions. The Brain Ageing Research Laboratory in CHeBA was a sole recipient of a $1 million research grant from the The Yulgibar Foundation to develop nanoparticles as nanodiagnostics and nanotherapeutics in Alzheimer's disease. The group utilises human and murine brain cell cultures and postmortem tissue for understanding the brain and the ageing process.

Our current work is committed to discovering the fundamental causes and possible treatments for age-related neurodegenerative disorders such as Alzheimer's, and neurodevelopmental diseases, as well as on genetic and metabolic changes that take place as organisms grow old. Our cross-disciplinary and integrative approach using clinical samples and animal models will facilitate the detection of dementia-related changes in the preclinical stages and validate the efficacy of targeted novel early interventions for neurocognitive disorders. We also have the expertise to culture, propagate, differentiate, engineer and transplant in animal models the neural stem cells from various sources including skin-derived neuroprogenitors and human mesenchymal stem cells from bone marrow. In addition, we have expertise in the derivation of new human embryonic stem cell lines including their clonal propagation.

Group Leaders: Dr Nady Braidy, Professor Perminder Sachdev.
PhD Students: Fatemeh Khorshidi, Yue Liu, Marina Ulanova, Gurjeet Virk, Matthew Wong.

NOVEL CELLULAR APPROACH FOR EARLY DETECTION OF ALZHEIMER'S DISEASE

Dr Nady Braidy was awarded UNSW Sydney seed funding of $20,000 to continue his ground-breaking research in the field of stem cell transplantation.

The funding will involve working with CK Cell Technologies Pty Ltd, an Australian regenerative medicine company, to create the next generation of stem cell clones from Alzheimer's patients for disease modelling and developing diagnostics and future therapeutics.

Dr Braidy explains that the study of Alzheimer's disease is limited by lack of model systems that can reproduce the precise sequence and timing of cellular and molecular events.

"The recent advances in biomedicine have led to a growing interest in using stem cells as cellular carriers for disease modelling, drug discovery, drug toxicity, and regenerative medicine," said Dr Braidy.

"The screening of drug candidates for toxicity is a major cause of attrition in drug development that leads to high costs in drug development and reduced number of effective clinical candidates."

Group Leader:
Dr Karen Mather

GENETICS & EPIGENOMICS

The overall aim of this group is to identify the genetic and epigenetic factors associated with brain ageing and age-related decline and disease. To this end, we investigate these questions using data from the Sydney Memory and Ageing Study, the Older Australian Twins Study and the Sydney Centenarian Study. We have collected genotyping, epigenetic and gene expression data for many of our study participants. Our group has many collaborations with national and international research groups and consortia, as often large sample sizes are required to identify genetic/epigenetic factors that contribute to complex traits and disease. The findings of this work have facilitated the identification of novel genes and pathways that contribute to a wide range of traits, including brain structure and cognitive performance, leading to new insights into the underlying biology. Ultimately, we aim to translate these findings into diagnostic, preventative and/or treatment strategies to promote healthy ageing.

Group Leader: Dr Karen Mather.
Staff: Dr Anbupalam Thalamuthu, Dr Debjani Das,
Dr Sumangali Gobhidharan, Naga Mutyala, Sri Chandana Kanchibhotla.
Students: Heidi Foo, Jessica Lazarus, Wey-Lynn Liew, Dr Adith Mohan, Mary Revelas, Chloe Timms, Helen Wu.

Mary Revelas, CHeBA PhD Student

GENETIC VARIANTS LINKED TO EXCEPTIONAL LONGEVITY

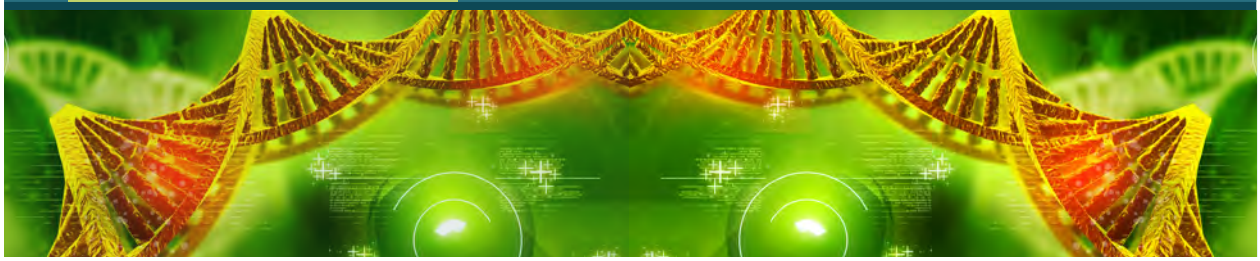
Five variants in the genetic code have been identified as significant for exceptional longevity in a study published in the journal *Mechanisms of Ageing and Development*. The study involved a review of existing findings and, for each variant identified, a meta-analysis was undertaken using data from at least three independent studies, including CHeBA's Sydney Centenarian Study.

Lead author and CHeBA PhD student Mary Revelas said polymorphisms, or variations in the genetic code, of five genes were identified as exceptional longevity variants in studies of people aged 85 and over versus controls: *ACE* rs4340, *APOE* ε2/3/4, *FOXO3A* rs2802292, *KLOTHO* KL-VS and *IL6* rs1800795.

"Our findings suggest that many genes of small influence play a role in exceptional longevity, which is consistent with results for other polygenic traits, or traits controlled by multiple genes, such as height," said Ms Revelas.

Senior author Dr Karen Mather said the findings provided insights for a range of future studies related to successful ageing.

Publication: Revelas et al., 'Review and meta-analysis of genetic polymorphisms associated with exceptional human longevity', Mechanisms of Ageing and Development, vol. 175, pp. 24 - 34, DOI:10.1016/j.mad.2018.06.002



NEUROIMAGING

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

Group Leader: Associate Professor Wei Wen. Staff: Dr Jiyang Jiang, Forrest Koch, Yue Liu. Students: Abdullah Alqarni, Heidi Foo.

Group Leader: Associate Professor Wei Wen

USE OF MULTIPLE MARKERS RECOMMENDED TO BETTER ESTIMATE BURDEN OF CEREBROVASCULAR DISEASE

A systematic review led by CHeBA PhD student, Dr Matt Paradise, found that only a small range of markers are used to identify cerebrovascular disease (CVD) burden. The study published in *Neurology* noted that validated composite indices using multi-modal neuroimaging measures, are needed to better reflect the true burden of the disease.

Dr Paradise said that despite the significance of CVD, there are no widely accepted criteria for quantifying the total burden of the disease, either using neuroimaging or neuropathologic measures.

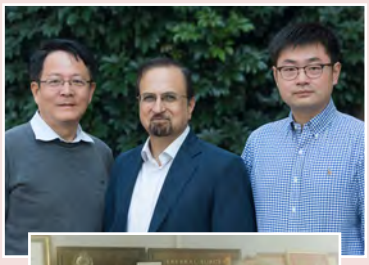
"There has been limited exploration of the properties of published indices and no comparison between indices," said Dr Paradise. "Better estimation of the burden of CVD could have multiple benefits in the diagnosis and prognosis of cognitive impairment and dementia."

The review, which examined twenty-five existing studies of neuroimaging and neuropathologic indices, found that the majority of imaging studies used a limited number of traditional individual markers of CVD, mainly from structural MRI scans. The studies also failed to utilise data from a range of other, more sensitive imaging types, such as diffusion tensor imaging (DTI).

"This review provided evidence that data from multiple imaging measures provide more information and are more reliable than using a single measure. It also highlighted current gaps in the field, so researchers can go on to construct better indices in the future, ultimately to benefit patients and their families," said Dr Paradise.

Publication: Paradise et al., 2018, 'Neuroimaging and neuropathology indices of cerebrovascular disease burden', Neurology, vol. 91, pp. 310 - 320, DOI:10.1212/WNL.0000000000005997

FULLY AUTOMATED SOFTWARE TO DETECT WHITE MATTER LESIONS



Dr Jiyang Jiang & Mr John Holden

Dr Jiyang Jiang and Associate Professor Wei Wen have developed an innovative piece of software which will promote research in cerebral small vessel disease and assist in the early identification of those at increased risk of stroke and vascular dementia. The findings have been published in the journals *Neuroimage* and *NeuroImage: Clinical*.

White matter lesions (WML), as seen on brain MRI, are a biomarker of cerebral small vessel disease (CSVD) which is common in older people. The accumulation of WML has been closely associated with various pathological processes, including stroke, cognitive decline and an increased risk of dementia. With an emerging interest in WML research and an increasing number of publicly available databases for neuroimaging, an urgent need had arisen for an efficient and effective tool to automatically detect and quantify WML.

The "UBO Detector" developed by Dr Jiyang Jiang and his colleagues at CHeBA is a fully automated pipeline for segmenting WML that has been successfully and rigorously tested on 2000 elderly brain scans.

"The pipeline takes T1-weighted and T2-weighted FLAIR scans as input. The acquisition of these two types of scans is very common in most research cohorts. The pipeline will generate comprehensive measures and distribution maps of WML," said Dr Jiang.

The software is publicly available for download at: https://cheba.unsw.edu.au/group/neuroimaging-pipeline

Publications: Jiang et al, 2018, 'The association of regional white matter lesions with cognition in a community-based cohort of older individuals', NeuroImage: Clinical, vol. 19, pp. 14 - 21, DOI:10.1016/j.nicl.2018.03.035 and Jiang et al, 2018, 'UBO Detector – A cluster-based, fully automated pipeline for extracting white matter hyperintensities', NeuroImage, vol. 174, pp. 539 - 549, DOI:10.1016/j.neuroimage.2018.03.050

Funded by the John Holden Family Foundation.

Group Leader:
Dr Nicole Kochan

Group Leader:
Dr Teresa Lee

NEUROPSYCHOLOGY

The Neuropsychology group aims to advance our understanding of the cognitive changes associated with normal ageing, mild neurocognitive syndromes and dementia. We have established strong collaborative links with other researchers in CHeBA, and are actively involved in research investigating the associations between cognition with brain structure and function, genetics and environmental factors, medical comorbidities, inflammatory markers and falls in the older adult population. We are developing normative data for a range of cognitive tests and evaluating computerised neuropsychological assessment to improve the diagnostic accuracy of mild neurocognitive disorders and dementia.

Group Leaders: Dr Nicole Kochan, Dr Teresa Lee.
Staff: Dr John Crawford, Karen Allison, Dr Karen Croot, Dr Adam Bentvelzen, Min Yee Ong, Matilda Rossie.
Students: PhD candidate: Dr Rebecca Koncz, Annette Spooner; Fourth year medical students (Independent Learning Projects 2019): Dansen Cho, Ashwini Kumar, Alice Yan; Neuroscience Honours student: Zara Page.

COGSCAN - STUDY OF COMPUTER-ADMINISTERED NEUROPSYCHOLOGICAL TESTS IN SENIORS

CogSCAN

CHeBA is excited to announce the launch of the first independent, systematic evaluation of four prominent and widely used computerised cognitive assessment instruments in healthy older adults and in people with mild cognitive impairment and dementia. With dementia a major health problem in Australia, early diagnosis is critical for interventions yet many older adults do not receive a timely or accurate diagnosis. CogScan, led by Dr Nicole Kochan, will move the field of computerised neuropsychological assessments forward and has the potential to revolutionise cognitive assessment of older adults with suspected cognitive decline.

Karen Allison: CogSCAN Study Coordinator

NEUROPSYCHIATRY

Group Leader: Professor Perminder Sachdev

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

Group Leader: Professor Perminder Sachdev.
Staff: Dr Adith Mohan, Dr Rebecca Koncz, Dr Matt Paradise.

PROTEOMICS

Group Leader: Dr Anne Poljak

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

Group Leader: Dr Anne Poljak, Professor Perminder Sachdev.
Staff: Dr Tharusha Jayasena, Maboobeh Hosseini, Dr Fei Song.
PhD Students: Gurjeet Virk (Scientia PhD candidate).

CONSORTIA HIGHLIGHTS

Researchers at CHeBA are studying the process of human ageing to determine the factors that influence the trajectory of healthy ageing and age-related cognitive decline, including dementia. At CHeBA, we are taking a lead in this line of investigation by making it international. International research consortia provide opportunities for researchers to share and compare data from existing studies, allowing systematic examination of brain ageing on a far greater scale.

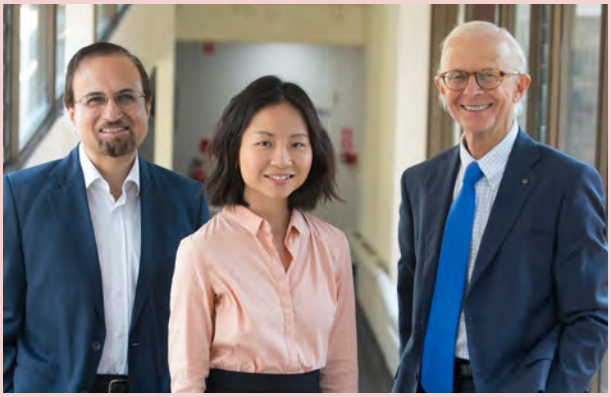
ICC-DEMENTIA

ICC-Dementia is a work group of the International Consortium of Centenarian (ICC) studies. It aims to determine the global prevalence of dementia and identify common risk factors for dementia across centenarian cohorts from around the world through data sharing and harmonisation.

In 2018, ICC-Dementia had received data shared by 18 brain ageing studies from 11 countries. We combined and analysed data of over 4000 culturally and ethnically diverse centenarians and near-centenarians, which made our study the largest analysis of global dementia prevalence in the oldest-old to date. We estimated a global dementia prevalence to be close to 52%. Risk of dementia was higher in women and it increases significantly with age, from 32% before reaching 100, 60% between 100 to 104 years old, to 73% beyond 105 years old. Education is a protective factor against dementia and cognitive impairment. We also found large differences in dementia prevalence across studies, which might be due to the variations in sampling strategies, sample size, and possibly also differences in culture, social resources and model of care in each country. Analyses are continuing to understand this phenomenon. These results were presented in national and international conferences including the Australian Dementia Forum (NHMRC) and featured in Alzheimer's Association International Conference (AAIC 2018) press release.

In 2018 CHeBA hosted the first Australian ICC Collaborators' Meeting (see page 25), where chief investigators and their team from eight international brain ageing studies came and presented their recent work, including Prof Peter Martin from the Georgia Centenarian Study and Prof Yasuyuki Gondo from the Tokyo Centenarian Study.

For a full list of studies involved, see: https://cheba.unsw.edu.au/consortia/icc-dementia/studies



CHeBA's consortia are largely funded by The Dementia Momentum initiative, with the Vincent Fairfax Family Foundation providing a $500,000 contribution over five years to fund Ms Jessica Lo's co-ordinating role.

"The Dementia Momentum is a great initiative which brings together researchers and the community," said Ms Lo. "It allows the community to invest in bringing about positive, significant social change."

> "I think it's our collaborative and international effort that makes CHeBA unique." Jessica Lo

Having been in the role for three years, Ms Lo said that CHeBA's innovative push for creating international-scale, big datasets is a key motivator. "At CHeBA we work collaboratively by setting up a number of international consortiums to address universal issues such as healthy ageing and age-related diseases," says Ms Lo.

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

Jessica Lo is funded by the Vincent Fairfax Family Foundation who encourage philanthropic support for The Dementia Momentum.

COSMIC

COSMIC (Cohort Studies of Memory in an International Consortium) is an international consortium to combine data from population-based longitudinal cohorts studies to identify common risk factors for dementia and cognitive decline.

Currently there are 37 international studies participating in COSMIC.

For a full list of studies involved, see: https://cheba.unsw.edu.au/consortia/icc-dementia/studies

In 2018, a number of new studies joined, including:

- Epidemiology of Dementia in Central Africa (EPIDEMCA) - Central African Republic and Republic of Congo
- Identification and Intervention for Dementia in Elderly Africans (IDEA) Study – Tanzania
- Indianapolis Ibadan Dementia Project – Nigeria and USA
- I-Lan Longitudinal Aging Study (ILAS) – Taiwan
- Marikina Memory and Aging Project (MMAP) – The Philippines
- Monongahela-Youghiogheny Healthy Aging Team (MYHAT) – USA
- Puerto Rican Elderly: Health Conditions study (PREHCO) – Puerto Rico
- Gothenburg H70 Birth Cohort Studies – Sweden

The major highlights for COSMIC in 2018 include:

1. MOUs were signed with 8 new studies.
2. 7 new projects were started, led by either CHeBA researchers or international workgroups:
    a. Risk factor clustering and incident cognitive decline;
    b. Depression in the pre-clinical phase of AD: trajectories and determinants;
    c. Risk of AD associated with nullipara, and with number of children;
    d. Decline in verbal and visual memory in mild cognitive impairment: predictors of AD and associations with biomarkers;
    e. Relationship between body mass index and cognitive decline;
    f. Relationship between education, apolipoprotein epsilon 4 (APOE*4) and cognitive impairment;
    g. Apolipoprotein E4 and cognitive decline: the moderating roles of sex, age, and ethnicity;
3. Findings (from our largest project *Determinants of cognitive performance and decline in diverse ethno-regional groups: The COSMIC collaboration*): overall sample comprised 48,522 individuals from 20 cohorts across 15 countries. We analysed two cognitive outcomes: scores for the Mini-Mental state Examination, and global cognition scores derived from tests of memory, language, attention, and executive functioning. For at least one cognitive outcome, age, APOE*4 carriage, depression, diabetes, current smoking, and stroke history were independently associated with poorer cognitive performance, and higher levels of education and more physical activity were associated with better performance. Age, APOE*4 carriage and diabetes were independently associated with faster cognitive decline. Some different effects between Asians and Whites were observed, including stronger associations for Asians between ever smoking and poorer cognition, and between diabetes and cognitive decline.
4. PhD awarded: Javier Oltra-Cucarella from the University of Alicante, Spain was awarded his PhD by publication, which included a COSMIC project.
5. Publications:
    a. Visual memory tests enhance the identification of amnestic MCI cases at greater risk of Alzheimer's disease. *Oltra-Cucarella J, Sánchez-SanSegundo M, Lipnicki DM, Crawford JD, Lipton RB, Katz MJ, Zammit AR, Scarmeas N, Dardiotis E, Kosmidis MH, Guaita A, Vaccaro R, Kim KW, Han JW, Kochan NA, Brodaty H, Pérez-Vicente JA, Cabello-Rodríguez L, Sachdev PS, Ferrer-Cascales R; Cohort Studies of Memory in an International Consortium (COSMIC). Int Psychogeriatr. 2018 Oct 25:1-10. doi: 10.1017/S1041610218001450X. [Epub ahead of print]*
    b. Differential effects of completed and incomplete pregnancies on the risk of Alzheimer disease. *Jang H, Bae JB, Dardiotis E, Scarmeas N, Sachdev PS, Lipnicki DM, Han JW, Kim TH, Kwak KP, Kim BJ, Kim SG, Kim JL, Moon SW, Park JH, Ryu SH, Youn JC, Lee DY, Lee DW, Lee SB, Lee JJ, Jhoo JH, Yannakoulia M, Kosmidis MH, Hadjigeorgiou GM, Sakka P, Kim KW. Neurology. 2018 Aug 14;91(7):e643-e651. doi: 10.1212/WNL.0000000000006000. Epub 2018 Jul 18.*
6. Conference presentations: COSMIC project papers and posters were presented at the Australia Dementia Forum, Sydney, and the Alzheimer's Association International Conference (AAIC), Chicago.

7. COSMIC collaborator meeting pre-AAIC, Chicago: 30 members from 11 countries met for a day to discuss topics that included current and future projects, and collaboration with IALSA on workshops and networking.

STROKOG

STROKOG is a consortium of longitudinal studies of cognitive disorders following stroke, TIA or small vessel disease. Developed under the auspices of VASCOG (Society for the Study of Vascular Cognitive and Behavioural Disorders), it is the first international effort to harmonise work on post-stroke dementia.

Currently there are 30 international studies participating in STROKOG, which include the following countries: Australia, China, Finland, France, Germany, Hong Kong, Ireland, Korea, Nigeria, Poland, Singapore, South Africa, Sweden, The Netherlands, Scotland, Ireland, United Kingdom and the USA.

In 2018, the following new studies joined STROKOG:

- INSIST-Cog, Australia
- PODCAST, United Kingdom

In 2018, CHeBA researchers completed the project on the profile of and risk factors of post-stroke cognitive impairment in diverse ethno-regional groups. We found that diabetes, a history of past stroke, and to a lesser degree, hypertension, smoking and atrial fibrillation are related to poorer cognitive function at 1-6 months after stroke. The paper for this project is currently being reviewed by a high-impact journal.

In 2019, CHeBA researchers will be focusing the next project on cognitive decline in stroke survivors in diverse ethno-regional groups.

CHeBA presented at the 10th International Conference of The International Society of Vascular Behavioural and Cognitive (VASCOG) in Hong Kong in November 2018, the Australian Dementia Forum in Sydney in June 2018, and at an ISTAART (Alzheimer's Association) webinar in February 2018. A collaborator from the UK and a PhD student from the UK are making good progress with their projects using STROKOG data and will be presenting at European conferences in 2019. We also held a STROKOG meeting/symposium with STROKOG members and other conference delegates at VASCOG 2018 in Hong Kong. STROKOG had a high profile at the conference and attracted interests from researchers from around the world.

Additionally, CHeBA received a $649,205 grant from NHMRC to support STROKOG. This grant will allow STROKOG to hire a data manager and a post-doctorial researcher and it is anticipated that STROKOG can expand their efforst and output in the coming years.

For a full list of studies involved, see: https://cheba.unsw.edu.au/consortia/strokog/studies

AGEDEP

The AGEDEP consortium was established in 2018 to address the global unmet health priority of understanding the aetiology and pathophysiology of late-life depression through collaboration, innovation and partnership by pooling data and knowledge. The aim is to include studies with data collected across one or more of the domains including genomic, epigenomic, biomarkers, psychological and environmental determinants and their interactions.

AGEDEP has been promoted at national and international conferences, including the World Congress of Psychiatric Genetics, Society for Mental Health Research and Biological Psychiatry Australia.

CHeBA contributes to the consortium with data from 3 ongoing, longitudinal studies: the Older Australian Twins Study, the Sydney Memory and Ageing Study and the Sydney Centenarian Study.

A survey for future participating groups/institutions has been developed and will be sent in early 2019 to national and international researchers to join AGEDEP.

INTERNATIONAL EXPERTS IN CENTENARIAN STUDIES CONVENE IN SYDNEY

In September, CHeBA hosted the International Centenarian Consortium (ICC) Annual 2018 Conference in the Blue Mountains, which focused on brain health and its determinants well into late life, and the centenarian as a living model of this.

Leading experts in centenarian studies from around the world convened with an objective of further spearheading an international effort to promote successful ageing. There were representatives from Italy, Sweden, the USA, Portugal, Singapore, China and Japan.

Convenor of the meeting, CHeBA Co-Director Professor Perminder Sachdev, said that these collaborative meetings are critical to examining demographic change and its impact on society now and in the future.

“Longevity beyond 100 is no longer rare but it remains an exception,” said Professor Sachdev. “It is an exciting time to engage with other international experts to discover the determinants of such longevity, with the expectation that it will help support positive ageing internationally.”

The next annual meeting will be held in Switzerland in May 2019.

"Longevity beyond 100 is no longer rare but it remains an exception."
Professor Perminder Sachdev AM

AAIC CONFERENCE

A world first study defining the global prevalence of dementia in people aged 95-110 was reported at the 2018 Alzheimer's Association International Conference in Chicago on 22 July attended by 5900 scientists and clinicians from around the world.

Dementia prevalence, risk factors and cognitive and functional impairment was examined across 4,121 participants in 17 centenarian studies across 11 countries, led by CHeBA's International Centenarian Consortium for Dementia (ICC-Dementia).

Using statistical predictive models, ICC-Dementia Study Co-ordinator Dr Yvonne Leung and colleagues found that prevalence of dementia, cognitive impairment and functional impairment increased with age (from 95-99 to ≥ 105 years) in all societies. Women in this age group had a higher risk of dementia and cognitive impairment compared to men.

The risk of dementia, cognitive and functional impairment varied significantly between countries, suggesting cultural and lifestyle factors play a role in remaining physically and cognitively healthy as we age. Participants with higher levels of education expressed lower prevalence of dementia and cognitive impairment than those with fewer years of education.

"This is the first study to define the global prevalence of dementia in this advanced age group using a set of common diagnostic criteria," said Dr Leung. "These data, and this type of research, may help identify protective factors to reduce the risk of dementia, and provide insights into longevity and brain health."

> "It was a privilege for CHeBA to be represented so strongly at this unique, multi-disciplinary event with a collective goal to change the future of Alzheimer's disease."
>
> Professor Perminder Sachdev AM

Other highlights from CHeBA at this year's AAIC included:

- an invited plenary presentation on psychosocial dementia research from Professor Henry Brodaty
- a one-day pre-conference on CHeBA's COSMIC consortium
- an invited speech by Study Co-ordinator of CHeBA's CogScan Study Dr Nicole Kochan on methods of harmonising data, which is crucial to enabling research groups to collaborate and share data
- Dr Adith Mohan's speech on the genomic mechanisms of age-related changes in the brain
- Dr Steve Makkar's presentation on outcomes from CHeBA's COSMIC consortia, including his research on the relationship between BMI and cognition
- poster presentations by Dr Megan Heffernan, Dr Darren Lipnicki, Dr Rebecca Koncz, Dr Steve Makkar and Gurjeet Virkon on a range of topics including the Maintain Your Brain study, as well as the relationship between apolioprotein E and cognitive decline and the moderating effects of age, sex and ethnicity.

PHD COMPLETIONS

DR RUBY TSANG

Thesis: Nature and nurture: Insights from genetic, environmental and epigenomic studies of late-life depression

"My research focused on understanding the biological and environmental factors that contribute to late-life depression. In examining the relative contributions of genetic and environmental contributions to late-life depression and co-occurring conditions, it was observed that late-life depression shares genetic influences with anxiety but not hypertension. Next, I reviewed the literature on genetic association studies of late-life depression, which revealed there was limited research on this topic with a general lack of replication. I also assessed the effects of early-life trauma, which found childhood emotional abuse and exposure to Holocaust trauma predicted late-life depression. Finally, an epigenome-wide association study of late-life depression was conducted, and 69 differentially methylated probes were identified, and the genes associated with the top-ranked probes were enriched for a range of neurodevelopmental processes."

Dr Tsang was supported by an Alzheimer's Australia Dementia Research Viertel PhD Scholarship. She is now a postdoctoral research assistant at Dementias Platform UK (DPUK), Department of Psychiatry, University of Oxford.

FIRST CLASS HONOURS

Medical student, Adrian Cheng, spent the past year completing an honours project which examined the psychological health of centenarians and near-centenarians. Supervised and mentored by Professor Henry Brodaty, Mr Cheng, who achieved first class honours and is now completing an exchange program in Political Sciences at the prestigious Sciences Po in Paris, compared levels of psychological distress and degree of life satisfaction in Sydney Centenarian Study participants to a younger CHeBA cohort. He also explored protective factors for maintaining good psychological health as people reach very advanced ages.

Despite showing higher levels of psychological distress than younger age groups, near-centenarians and centenarians were more satisfied with their overall lives. A major finding from this study was that social support was a significant predictor of psychological health. Friends and family help provide the very old with meaningful experiences and are an integral component of happiness in old age. These findings suggest potential targets for future interventional studies to improve the psychological health of near-centenarians and centenarians.

"Professor Henry Brodaty has been a brilliant mentor. He has taught me clinical and research skills that will be invaluable for my future career as a doctor."

LONGITUDINAL STUDIES

"We are finding there are a number of things one could do to possibly prevent dementia."

Professor Perminder Sachdev AM

SYDNEY CENTENARIAN STUDY

The Sydney Centenarian Study (SCS) was launched in 2007 and to date has included 426 Sydney residents aged 95 and above. The project examines the cognition, physical health, psychological health, functional independence, nutrition, brain structure and genetics of Australia's oldest old. Centenarians and near-centenarians are seen as exemplars of successful ageing, and the study is elucidating factors that are important to longevity and maintenance of physical and cognitive health. Participants are interviewed at baseline and every subsequent six months. Each assessment covers; medical history, medications, cognitive performance, subjective memory complaints, psychological distress, falls, physical activity, mental activity, social integration and diet. Participants also complete a brief physical exam. 64% of participants have provided a blood sample for genetics and proteomics analysis; 10% of participants have undergone structural brain imaging (MRI). An informant (i.e. someone that knows the participant well) is interviewed after each assessment to corroborate the information provided by the participant as well as comment on their degree of functional independence.

HIGHLIGHTS:

- We performed analyses with the baseline data collected from 343 participants recruited from seven local government areas in Sydney. Results indicated that dementia prevalence was 25.53% among men and 40.95% among women. Centenarians had the highest prevalence of 47.22%, while participants aged 95-96.99 and 97-99.99 showed a prevalence of 28.42% and 46.73% respectively.
- Risk of dementia increased with age and decreased with more years of education. However, we did not find any significant sex differences after other sociodemographic factors and clinical statuses were considered.
- Participants with non-medicated hypertension had a significantly higher risk of having dementia compared with those without hypertension or those on medication for hypertension.
- Men showed significantly better performance than women on language and visuo-spatial related cognitive tests and less cognitive decline. However, they performed worse than women on tests of psychomotor speed. Years of education was associated with better performance in a number of cognitive tests and less cognitive decline.

Study Coordinator of the Sydney Centenarian Study, **Adam Theobald**, is proud to be involved in the international effort to unlock the secrets of ageing. According to Mr Theobald, who was a guest speaker at the Living to 100 Conference in September, the study seeks to understand how our oldest Australians can maintain physical and cognitive health at advanced ages, delay or avoid dementia, support independent living as well as have meaningful social engagement and a high quality of life.

"I have personally witnessed both ends of the spectrum of ageing," says Mr Theobald, who watched his grandmother endure a long and difficult battle with dementia but whose grandfather remains vital and spirited aged 96.

"Through these experiences I have developed a strong personal and professional investment in the study," he says.

"The opportunity to work with and learn from our centenarian participants is a privilege. Our team is eternally grateful for the generosity of these extraordinary individuals, who give up so much of their time and energy to support our research. Everybody who has lived into their late 90s is a success story and each have a fascinating tale to tell. I look forward to many more years of learning from our current participants and to welcoming new centenarians into our study."

OLDER AUSTRALIAN TWINS STUDY

Commenced in 2007 as a collaboration between CHeBA, the National Ageing Research Institute (NARI) and the Queensland Institute of Medical Research (QIMR), the Older Australian Twins Study (OATS) has assessed a total of 727 participants on up to four occasions – totalling over 1600 assessments in the past decade. The main objective of OATS is to identify genetic and environmental factors that contribute to healthy ageing, especially healthy brain ageing. Studying twins provide a unique opportunity to do so, as identical twins have the same genetic code, whereas non-identical twins share 50% of their genetic code (in a similar fashion to other siblings). Using special data analysis techniques, this genetic difference between identical and non-identical twin pairs allows us to determine the relative contribution of genes and environment on specific outcomes. The assessment that twins undergo as part of the OATS study involves many questionnaires on their life experiences, current lifestyle and diet, physical and mental health, brain scans, blood sample analysis and providing DNA for genetics analysis. In 2018, the administration of the OATS study was consolidated to the CHeBA, UNSW Sydney, study site.

OATS gratefully acknowledges the contribution of our participants, Twins Research Australia who mediates the initial contact to many of our participants, the funding received from the National Health and Medical Research Council, and the contribution of our project staff and many collaborators in Australia and beyond. Over its lifetime, OATS has contributed to 41 scientific publications, with 7 published in 2018. Currently, 11 Higher Degree students are utilising OATS data for their studies.

HIGHLIGHTS:

- In 2018, we analysed data for the amyloid imaging project which investigates the deposition of amyloid plaques in the brain using positron emission tomography (PET) scans in 207 individuals. The presence of plaques predicts memory decline and are one of the hallmark features of Alzheimer's Disease (AD). The assessment also included analysis of blood chemistry, a structural MRI brain scan, and analysis of genes and their expression. Preliminary analysis of the PET imaging data from this study was presented at VasCog, the annual conference for the International Society of Vascular Behavioural and Cognitive Disorders in Hong Kong in September 2018.
- Ms Helen Wu, a PhD student, is looking at a small sub-sample of monozygotic twins, where PET scans revealed one twin has a high burden of amyloid and the other does not. Helen is investigating gene expression in blood samples, with a specific focus on microRNA. MicroRNAs are an example of epigenetics, and is one way in which the environment influences gene expression. In monozygotic twins, who are genetically identical, changes in microRNA levels may be related to the differences in amyloid burden in the brain and it is hoped Helen's study will provide insight into the pathobiology of AD.
- This year we also published a study showing that language ability, measured using three neuropsychological tests, naming (BNT), letter fluency (FAS), and semantic fluency (ANIMALS), is influenced by genes to varying extent, and is strongly influenced by general global cognitive function and by level of education achieved. The heritability of ability differed between sexes, and was higher in women than men across the three tests.
- The unique contribution of sex will be further explored by the IGEMS (Interplay of Genes and Environment across Multiple Studies) consortia, which in 2018 received funding from the NIH to collate and analyse data from 47,632 twins collected across 9 twin studies, including OATS. Analysis of such large numbers of participants will be informative in elucidating the contributions of protective factors, such as sex, educational attainment, physical and social activity, and risk factors, such as vascular disease and depression/anxiety, to the development and progression of dementias.

- OATS contribute to multiple other large international studies, which in 2018 have published studies that identified genes associated with general cognitive function and with changes in brain structure, both of which in turn are important predictors of risk of dementias.
- The OATS team is working towards an online project, aiming to give the study access to more participants, particularly those living in non-metropolitan areas. We have piloted the online questionnaires and we are modifying delivery to make it the best possible experience for our research volunteers. We currently have 424 enrolled participants, who we will contact in early 2019 to seek their participation in this next phase of assessment. Beyond that, we hope to recruit additional participants to boost our sample size to approximately 1000 participants.

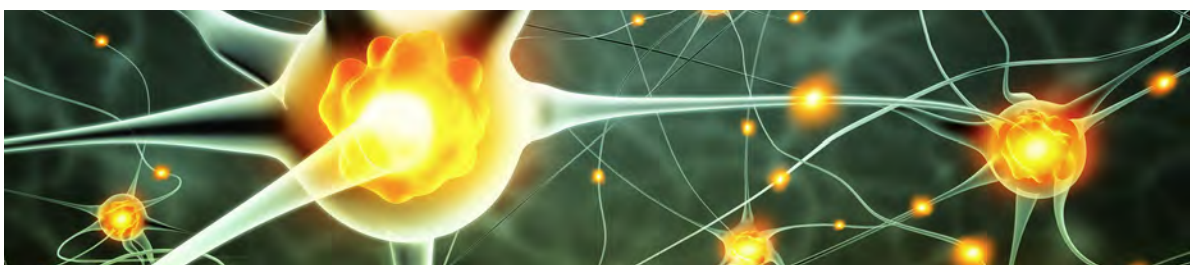
Older Australian Twins Study (OATS) Coordinator, **Dr Vibeke Catts**, is passionate about the contribution science and medical research can make to the health of everyone in our society. She was delighted to join the OATS team in 2017, as twins provide a "natural experiment" that can provide unique insights into the contributions of lifestyle factors and genetics to well-being, disease risk and longevity.

"It is interesting to note that many of the lifestyle factors that appear to strongly influence health in older age are those that also make our busy everyday working lives easier to manage. Maintaining a balanced diet and doing physical activity contributes to good heart and vascular health, which is so important for health across the lifespan," says Dr Catts.

Additionally, despite many OATS participants experiencing more health problems with advancing age, it's delightful to observe their ability to maintain a sense of purpose and enjoyment by finding pleasure and joy in social interaction and intellectual stimulation, something many of us often neglect in the hustle and bustle of modern life. Dr Catts has been very touched to observe the unique bond between twins, and also humbled to experience the generosity of our OATS participants in contributing many hours of their time to our research.

SYDNEY MEMORY AND AGEING STUDY

The Sydney Memory and Ageing Study (MAS) began in 2005 with 1037 participants aged 70 to 90-years old living in Sydney's Eastern Suburbs. Nearly 14 years later MAS continues to track the physical, emotional and cognitive health of 410 participants and 381 of their friends and relatives. This makes MAS one of Australia's largest and longest running longitudinal studies of ageing and cognitive health. The main objective of MAS is to investigate rates and predictors of health and cognitive decline in a well-characterised, community-based older population. We are especially interested in when and why normally functioning older adults who show some signs of memory or cognitive decline either progress to dementia or improve. Since 2005, MAS has carried out over 4,488 cognitive and health assessments, has conducted 1,230 MRI scans, and has analysed 2,218 blood samples donated by our participants. Because of our participants' generosity, our study has amassed an enormous amount of data that has led to the publication of over 135 scientific papers – 7 of which were published this year – in respected, international medical journals with another 40 manuscripts already in preparation for 2019. As a significant contributor to several large-scale international collaborations, MAS is also helping researchers worldwide as they refine measures of early diagnosis, prognosis and biomarkers associated with neurogenerative diseases like Alzheimer's. Currently, there are 15 higher degree students and postdoctoral fellows who are using MAS data as part of their research.



HIGHLIGHTS:

- In 2018, MAS published the first study examining cross-sectional and longitudinal relationships between obesity and aspects of quality of life in elderly adults in Australia. We found that obesity was predictive of, and associated with, lower quality of life in elderly Australians. Additional risk factors such as age, performance on a brief cognitive screen (MMSE), apolipoprotein ε4 status and recruitment setting emerged.
- Subjective cognitive decline (SCD) is the personal experience of cognitive failure in the absence of objective impairment on cognitive tests. In collaboration with researchers at the Alzheimer's Center in Amsterdam, MAS found that SCD preceded Alzheimer's and other dementias. That is, the subjective experience of decline may be a prodrome for dementia.
- MAS also published papers that examined the relationship between cerebral microbleeds (CMB) and dementia, uncovered genetic loci that influence general cognitive function, produced a topology of structural brain networks in MCI and dementia patients and confirmed the genetic loci associated with blood measures that are related to cardiovascular diseases and some cancers.
- In collaboration with multiple large international studies (or consortia) MAS contributed to papers that investigated the impact of reproductive experiences on risks of cognitive decline in elderly women, mapped the genetic architecture of subcortical brain structures across 40,000 brains, explored whether verbal and visual memory impairments precede Alzheimer's disease and MCI, and uncovered 7 loci associated with brain ventricular volume.
- MAS is currently conducting its 7th wave of testing – or 12-year follow-up interviews from baseline – with over 400 participants still active in the study. Our 7th wave of testing will reintroduce our comprehensive neuropsychological test battery and optional bloods donation component. Because of this, Wave 7 promises to bring in a tremendous amount of new data that will help us better understand various aspects of ageing including memory and cognition, physical and emotional health, lifestyle factors, genetics and mortality.

Memory and Ageing Study Coordinator, **Dr Katya Numbers**, is a strong advocate for positive ageing. According to Dr Numbers, growing older provides a sense of broader perspective and often encourages people to focus their efforts and energy towards bettering society. In addition to spending more time with loved ones and pursuing personal dreams, older adults have more time to volunteer their time – and CHeBA's MAS participants do just that. "I have witnessed firsthand how uniquely generous elderly adults are. MAS participants have spent countless hours being interviewed by our team and have also volunteered to have their blood drawn, have MRIs conducted or have agreed to donate their brain to science," says Dr Numbers, who has a PhD in Cognitive Science and a Master of Science in Cognitive Psychology. Dr Numbers' research focuses on understanding stigmas around, and perceptions of, older adults' memory abilities.

"I am constantly amazed and inspired by the foresight and compassion that our participants have for future generations," says Dr Numbers.

"Because of them, I look forward to growing old and having the opportunity to give back to the global community one day just as they have."

BRAIN BANK DONATION PROGRAM

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

In 2018, 5 new brains were donated to the CHeBA Brain Donation Program.

Over the last decade, CHeBA's research activities and collaborations have evolved to impressive heights. In order to meet the increasing demand for coordination and management across our many projects, CHeBA is pleased to announce the appointment of a Research Manager, **Dr Kristan Kang**. Dr Kang has worked as the Centre's Data Manager for this period and played the primary role in implementing our Brain Donation Program and the newly established Research Bank. In recent years he has become a key liaison with UNSW's Division of Research and been responsible for training and supporting our study coordinators. Dr Kang's promotion to Research Manager is both an acknowledgement of CHeBA's growth and the central role he plays in our research activities.

OUR COMMUNITY

"Such extraordinary support from our community members encourages us to expand upon our research objectives and our striving toward better clinical care."

Professor Henry Brodaty AO

THE DEMENTIA MOMENTUM

SPOKESMAN'S REPORT

From 2012-2017, dementia received just 6% of the total National Health & Medical Research Council (NHMRC) funding allocated to the government's National Health Priority Areas. With limited public resourcing available, it is incumbent on us all to play a role in facing the challenge posed by dementia.

When we launched The Dementia Momentum in March 2015, there were 342,000 Australians with dementia. Just a few years on that statistic has increased by close to 100,000 to more than 430,000 people affected by this insidious disease. My wife, Suellen, remains one of them.

Back then, dementia was not the single greatest disability in older Australians – it now is. The reality is that Alzheimer's disease and other dementias continue to become an ever-burgeoning social and economic issue, without a cure or definitive answers on how it can be addressed. The question of how we confront dementia, the greatest public health challenge in Australia, was the focus of the third anniversary of The Dementia Momentum in March, once again hosted by in-kind partner KPMG. This year we took a different approach to the event with a panel style interview led by Ita Buttrose AO OBE, allowing our donors and supporters to hear my own story and engage with CHeBA's internationally leading Professors, Henry Brodaty and Perminder Sachdev. What emerged from the discussion was the overwhelming need to drive more investment to research, which continues to lag behind funding of other diseases both in Australia and internationally.

With dementia currently estimated to cost Australia more than $15 billion – which is predicted to increase to more than $40 billion by the middle of the century – the undeniable need is to advance critical and promising research. Which is expensive. Which means more funding.

Although CHeBA had significant grant success in 2018 for projects that fall under The Dementia Momentum, there remains a necessity for increased numbers of committed philanthropic partners. The vision of this initiative was to raise $10 million over 5 years to dramatically advance CHeBA's research into risk and protective factors using large-scale "big data" harnessed through international consortia. It is my pleasure to announce that between philanthropic and grant success we have generated $7.5 million toward this goal, putting CHeBA in an excellent position to make a world-wide difference to prevention, earlier diagnosis and earlier and more effective interventions. With this need to significantly advance research in mind, The Dementia Momentum expanded its outreach events in 2018 and it was a privilege to have an increased involvement in my role this year. In February, we officially launched a new campaign, **Drive Out Dementia**, with support from the indefatigable Phil Cave and Judy Harris, both Platinum Members since the initiative's inception. Drive Out Dementia has brought together a new group of people focused on corporate social responsibility and, with the support of Luke O'Neill, we hosted three events in March, May and October.

Wipeout Dementia exceeded our expectations in 2018, beating the optimistic fundraising target set by nearly 20%. The November property industry event was the most successful to date since the campaign's launch in 2015, raising over $155,000 and nearly doubling the numbers of donors from the previous year, including supporters from over 13 countries. Colliers International Residential once again demonstrated unwavering support, hosting the pre-event and generously donating auction proceeds from their annual property developers' lunch.

This year's success drives hope for more industry support for future events and expansion of the campaign in the coming years. We are adopting a new approach for the May 2019 Wipeout Dementia, with an inter-generational surfing event to promote increased awareness around the importance of physical activity throughout life.

My hope is that in the final year of this initiative we can fulfil our goal and raise the final $2.5 million for The Dementia Momentum by philanthropic means, and start turning the tide on these frightening statistics. Throughout 2018, the condition of my wife Suellen, whose journey with young-onset Alzheimer's disease inspired the Wipeout Dementia campaign, has continued to deteriorate. I am optimistic about 2019 and the medical and research advances that appear closer than ever before.

Richard Grellman AM
Chairman, IPH Limited & FBR Limited

THE DEMENTIA MOMENTUM THREE YEAR ANNIVERSARY AT KPMG

The Dementia Momentum's three year anniversary event was hosted by in-kind partner KPMG and focused on the question: "How can we confront dementia, the greatest public health challenge in Australia?" CHeBA's Maintain Your Brain study patron, Ita Buttrose AO OBE, chaired the discussion between CHeBA's Co-Directors and Spokesman of The Dementia Momentum which social and economic costs of dementia for Australia.

Pictured L-R: Professor Perminder Sachdev AM, John Teer, Ita Buttrose AO OBE, Professor Henry Brodaty AO, Richard Grellman AM

The population with dementia stands to have tripled by 2050, and its impact on the Australian economy is set to double to 2% of GDP. According to CHeBA's Co-Directors Professor Brodaty and Professor Perminder Sachdev, identification of risk factors is crucial for changing the future of dementia. Despite estimates suggesting the cost of dementia globally to be US$818 billion, research funding into risk and protective factors lags substantially, which means that despite advances in technology there remains too few researchers working toward significant change.

The panel at The Dementia Momentum's three year anniversary event.

"Even if a therapeutic treatment is discovered, it won't help the millions of people like Suellen who already have Alzheimer's disease and those with other types of dementia," said Professor Brodaty.

"We need a quantum leap in investment in research to meet these challenges."

> "We need a quantum leap in investment in research to meet the challenges of dementia."
>
> Professor Henry Brodaty AO

MEMBERS OF THE DEMENTIA MOMENTUM

DIAMOND MEMBERS

John Holden Family Foundation

Vincent Fairfax Family Foundation

PLATINUM MEMBERS

Colliers International

Sachdev Foundation

Judy Harris & Phil Cave AM

The Yulgilbar Foundation

GOLD MEMBERS

morgans

Peter & Yvonne Halas

Henroth Investments Pty Ltd

SILVER MEMBERS

IPH Limited

Roger & Merrilyn Layton

BRONZE MEMBERS

Flight Centre – The Airfare Experts

Cunninghams

Kennards Hire

Sandler

RayWhite Commercial

Genworth

Keri Chittenden

Jan Surnicky

Sue Edwards

Paul Cave AM & Carol Cave

TEAL MEMBERS

AMP

Alceon

The Mansfield Family

Pamela Madafiglio

Brenda & Stephen Lennard

Ann & John Cunningham

Watson Mangioni

realestate.com.au

Aoyuan – building a healthy lifestyle

The Howarth Foundation

MAJOR IN KIND SUPPORTERS

Aria.

brandmatters.

Charter Hall

Hurley

HWL Ebsworth Lawyers

KPMG

Queenscliff Surf Life Saving Club

Bucket List

FRIENDS OF THE DEMENTIA MOMENTUM

Abacus Funds Management Limited
Abey-Perera Family Foundation
ACES Air Conditioning
Actinogen Medical
Agentbox
Mr Terry Agnew
Allan Hall Chartered Accountants
Alliance Project Group
The Alps Wine Shop & Bar
Mr Tony & Mrs Katrina Anderson
Aoyuan Property Group (Australia) Pty Ltd
Argentum
Atdec
Mr John Atkin
Avenor Pty Ltd
Baillie Lodges
Barana Group
Bathe
Mr Ian Bennett
Mrs Julianne Blain
Mr Andrew & Mrs Alison Blattman
Mr Andrew Bloore
Breakwater Advisory
Justin Breheny
Mrs Karoline & Professor Henry Brodaty AO
Mrs Barbara Brown
Ms Tanya Buchanan
Mr Paul Cave AM
Charter Hall Holdings
Chiat Kwong Ching of Oxley Holdings
City Freeholds Pty Ltd
Dr Margaret & Dr Ian Clark
Mrs Camille & Mr Chris Clarke
Mr Peter & Mrs Belinda Clemesha
Mr Paul Coady
Construction Services & Infrastructure Pty Ltd
Coral Technologies Pty Ltd
R. Bruce Corlett AM
Mr Tim Crommelin
Mr Chum Darvall AM
Derwent Executive
Design Confidence
Mr Richie Dolan
The Done Group
Mr Nick Douglas-Morris
Mrs Heidi & Mr Craig Douglass
EG
Brett Eichhorn
Mrs Lynnette Ellerman
EP&T Global
Mr Peter Evans
FDC Construction & Fitout
Finlease
Ford Civil
Mr Ian & Mrs Kathy Freestone
Jamie Fullagar
Mr Reno Gambi
Ms Kirsty Gerahty
Mr David Gillespie
Mrs Louise Gillespie
Mr Robert Gillespie
Mr Kym Godson
Mr Peter Granger
Mr Brian Greig
Mr David & Mrs Penny Griffith
Mr Mark Gross
Group Homes Australia
Halfords IP
Hall Chadwick Melbourne Chartered Accountants
Mrs Dale & Mr John Harkness
Mr Robert Hartman
Mr Matthew Hayson
Dr R.O. Hellyer
Mrs Kelly Hobbs
Mr John Hughes
Mr Mark & Mrs Sophie Hutchinson
Mr & Mrs Greg and Lana Hynd
Iglu Pty Limited
Mr Rodney Inder
Insurance House
Mr Kenichi Ishiyama
Mr Brian & Mrs Susan Jackson
Mr Doug Jackson
Mr Andrew Jerogin
Mr Chris Jessop
JT Consultancy
KBT Overnight Express Pty Ltd
Vince Kernahan
Mr Rob Kift
Fred Khoury
Mr Guy Lake
LCI Consultants
Lindsay Bennelong Developments
Mr Hao Liu
Mr Jan Lech
Mr John L'Estrange
Mr David Levi
Mr Simon & Mrs Vicki Liddy
Mr Sam & Mrs Barbara Linz
Ms Robin Low
m3property
m3property Queensland
Mr Ian MacDonald
Mr Douglas MacDougal
Mr Michael Madigan
The Manly Daily
Mr Glenn Maris
Mr Peter Mason
Mr Simon Matison
Mrs Michelle & Mr Tony McGrath
McGrath Estate Agents — Neutral Bay
Mr Robert McGregor
Andrew McKirdy
Mr Chris Meehan
Mrs Christine and Mr David Michaelis
Ms Nancy Milne
Mr Arthur Milner
Minderoo Foundation
Morgans Foundation
Mr Nigel Mukhi
Mr Donovan Murphy
Mrs Reiko Murphy

Mr Derek Nelson
Ms Georgette Nicholas
Mrs Colleen Nichols
Mrs Trish O'Brien
Mr Adrian O'Connor
Oxley
Donny Painting
Parkview Group
Mr Graeme Pettigrew
Mr Paul Pierlot
Dr Sally Pitkin
Mr Don & Mrs Anne Potter
Mr Douglas Potter
Profectus Build
ProGood
Mr Simon Ranson
Mrs Angela Raymond
Mr Craig Rodgers
Mr Mark Rohr
The Rotary Club of Rose Bay
Roxy-Pacific Investments Pty Ltd
Mr Bill Ryan
David Scardoni
Mr Ari Schachna
Schiavello Construction
Ms Dagmar Schmidmaier AM
Sense Projects
Shape Australia Pty Ltd
Mr Ken Sheridan
Sherkane
SkiJapan
Mrs Jacqueline Smith
Mr James Smith
Somerville Electric
Sothertons Melbourne
Sparke Helmore Lawyers
Star & Associates
Susan Rothwell Architects
Sydney Airport
TDM Foundation
The Directors of LCI
The Gap State High School
ThreadCare
TOGA Group
Ms Gayle Tollifson
Urban Space Group
Vodafone Australia
Mrs Sally White OAM
Mr Sam Wicks
William Alexander Accountants
Andrew Wilson
Wilson Asset Management
Winten Property Group
Mrs Ali Wood & Mr Brian Holder
Wordsearch Communications Pty Ltd
Mr David G. Young
Mr Geoff Zuber

Riding a research wave

Jim O'Rourke

Pro surfer Austin Ware and Richard Grellman with Wipeout Dementia surf event competitors at Queenscliff. Picture: Troy Snook

Surfing challenge to help wipeout dementia

MEDICAL experts advise people to become physically active from an early age — and stay active — to help reduce the chances of getting dementia.

So this Saturday's Wipeout Dementia surfing challenge at Queenscliff is a great reminder to start exercising and to raise money for research into the condition.

The organiser, the Centre for Healthy Brain Ageing (CHeBA) at the University of NSW, needs money to support its Dementia Momentum initiative, which aims to increase awareness about Alzhemer's disease and other dementias.

Three teams of local surfers, mostly senior execs and business people, are hoping to raise $100,000 for research into dementia — the second leading cause of death in Australia — through being sponsored in a fun tag-team format.

Each surfer has set a target of $5000.

Last Saturday surf coach and former pro surfer Austin Ware had challenge participants in the surf to give las- minute tips and put them through rigourous exercises.

A recent analysis showed that physically inactive people had an 80 per cent increased risk of dementia.

Mr Ware, of Balgowlah, was with Wipeout Dementia ambassador Richard Grellman, the former chairman of the Association of Surfing Professionals, whose wife Suellen has advanced young onset Alzheimer's disease.

Mr Grellman said money raised would go towards advances in understanding the causes, preventive measures, treatment and care of people with "this terrible disease".

Mr Ware, whose mother was diagnosed with early onset Alzheimer's in her early 50s, will be a surf judge at Queenscliff on Saturday, from 8.30am.

"I wanted to help, especially with my surfing background, to raise money for those with the disease and those who have to help care for them," he said.

Another ambassador, 1978 World Surfing Champion Wayne "Rabbit" Bartholomew, will be competing.

To sponsor a surfer up go to https://cheba2.everydayhero.com/au/wipeout-dementia-may-2018-2

Many Wipeout Dementia surfers have kindly shared their stories with media to assist in raising awareness about this fundraising campaign and the significance of physical activity in relation to brain health in late life. Thank you to Austin Ware and Rodney Jamieson who shared their journeys with media in 2018.

WIPEOUT DEMENTIA

With people aged 65 and over set to comprise over 20% of the population within the next decade and dementia now the single greatest cause of disability in this demographic, senior executives across Sydney once again joined forces at Queenscliff in May and at Bondi Beach for the property industry event in November. The two events - raised over $240,000 for key dementia research at CHeBA, making it the most successful year to date in Wipeout Dementia history.

The surfing event, which supports The Dementia Momentum initiative at CHeBA, also aims to highlight the global social and economic impact of dementia.

A number of the surfers who participated in the property industry event in November, which raised $155,000, have family members with Alzheimer's disease or another dementia, known only too well by Ambassador Richard Grellman AM whose wife Suellen has advanced young onset Alzheimer's disease.

Director of AWM Commercial Furniture & Joinery and second time surfer in Wipeout Dementia, **Anthony Scotts**, has witnessed first-hand the devastating impact that dementia has on the individual and extended family - with both his father being diagnosed some 20 years ago and passing away earlier this year and, more recently, another family member being diagnosed aged just 62. One of 8 children, Mr Scotts and his siblings are hopeful for better support of people with young onset Alzheimer's disease.

"My sibling became very socially withdrawn and struggled with short-term memory," said Mr Scotts.

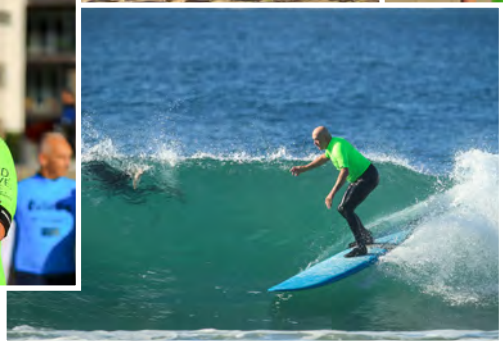
"The rest of our family have been discouraged by the level of support available for young onset Alzheimer's disease," he said.

"It's certainly the reason I got on board Wipeout Dementia and an important cause I want to support," said Mr Scotts.

In 2017, Director and Founder of AN+A, **Patrick Nicholas**, lost his father - Graeme Nicholas - to vascular dementia.

"My dad, Graeme, loved Bondi Beach and the surf and led a very active life. When he was first diagnosed with vascular dementia we were lucky in that we managed to get him moved from the Central Coast to Surry Hills near the office and had some great contact as a family over his last few years. As hard as it was to experience his changing condition to an eventual complete decline, we were extremely impressed with the care and medical attention dad received," said Mr Nicholas.

> "There is a critical need for partnerships between research and business in order for us to tackle the extraordinary challenge posed by dementia."
>
> Richard Grellman AM



"In saying that, this event and fundraiser is all about research and awareness and I wonder what we would have done differently 10 years ago with our father knowing what I've now learned," he said.

Another first-time participant, **Rodney Jamieson**, of FDC Construction & Fitout bore witness to his loving Nan experiencing 'sundowners' dementia in the late stages of her life.

"Two years after my Grandfather had passed my Nan started having visions of him daily at 5pm with another woman," says Mr Jamieson.

"After 67 years of a beautiful marriage together her 'sundowning' was extraordinarily traumatic for her and for all of us," he said. "It broke my heart to watch my Nan decline with dementia and for such a cruel end to her life."

Fellow first-time participant, **Craig Shelsher**, Director at Custance Associates shares a similar story of his father's brother, whose cognitive decline has advanced rapidly following his diagnosis three years ago aged just 71.

"My father and his brother forged a very successful construction business together," he said.

"My Uncle is now at a point where he does not recognise family members," says Mr Shelsher.

Personal stories such as these inspire CHeBA's academics to continue to expand their research across the full spectrum of the disease beyond drug treatments, to include early diagnosis and prevention strategies in mid-life to reduce modifiable risk factors associated with dementia.

Eight Wipeout Dementia events have run since 2015 and seek to promote awareness about the modifiable risk factors of Alzheimer's disease and other dementias while driving research funds to harness global research to prevent dementia.

Reigning champions at both events prevailed on the day, with Cunninghams Cruisers (captained by **John Cunningham**) taking the title in May and Cliff's Carvers (captained by **Craig Rodgers** of Charter Hall) taking home the trophy in November. A custom Gerry Lopez 'Gnarly Award' for highest fundraiser was taken by **Mark Gross**, Executive Director Corporate Advisory of sponsor Morgans, who raised over $12,500 in the event and has raised close to $40,000 over four events.

The November highest fundraiser award was taken by **Steve Watson**, Captain of Watto's Wavehunters and Managing Director of Steve Watson & Partners who raised over $14,000 for CHeBA. Special thanks go to runner up **Patrick Nicholas** with over $13,000 raised and **Joel Ducey** and **Rodney Jamieson** who both raised over $10,000. All three runners up took

home a competition DHD board for their extraordinary efforts.

Watto's Wavehunters stole the glory of highest fundraising team raising more than $55,000 for the cause and receive an opportunity to celebrate together thanks to in-kind supporter The Bucket List.

A number of other awards were announced at the events including the prestigious peer-vote 'Player's Player' which went to **Morgan Hill** in May and, in November, to **Steve Watson** whose father has just recently been confined to a nursing home with dementia.

"Watching the decline of a vibrant and intelligent man who taught me to embrace life as a grand adventure has been difficult over the last few years," said Mr Watson.

"The decision to move him to full time care was inevitable but still feels terrible. Raising money for dementia research is something tangible I can do to help others facing this in the future," he said.

Wipeout Dementia was created by CHeBA's Heidi Douglass. In 2019 CHeBA will host its first ever inter-generational Wipeout Dementia event at Queenscliff.

Morgans and Kennards Hire were the major sponsors for Wipeout Dementia in 2018. Cunninghams, Colliers International Residential, Ray White Commercial and Aoyuan International were secondary sponsors.

Hurley, Queenscliff Surf Lifesaving Club, The Bucket List and Scentre Group have provided significant in-kind support.

Judging was conducted by Global Surf Tag.

Photography by Sprout Daily.

WIPEOUT DEMENTIA 2018 PARTICIPANTS

Tony Abbott
Scott Anderson
Wayne 'Rabbit' Bartholomew (Ambassador)
Darren Beasley
Phil Butt
Tony Camphin
Chris Clarke
Ali Clemesha
Peter Clemesha (Team Captain, November)
John Cunningham (Team Captain, May)
Pip de Rohan
Joel Ducey
Brett Eichhorn
Matthew Faddy (Wave of the Day, November)
Benjamin Freeman (Best Wipeout, May)
Ian Freestone
Rob Gillespie (Team Captain, May)
Ben Grellman
Richard Grellman (Team Captain, May; Wave of the Day, May)
Mark Gross (Gnarly Award, May)
Morgan Hill (Player's Player, May)
Rodney Jamieson
Andy Kennard
Alexandra Kent
Vince Kernahan
Peter Kleijn (Best Wipeout, November)
Badier Kubis
Stephen Lennard
Simon Liddy
Darren Mansfield
Brad Miles
Jeff Moxham
Geoff Nesbitt
Stephen Newey
Brett Newman
Patrick Nicholas
Iain Pretty
Karl Riedel
Anthony Roberts
Clive Rodell
Craig Rodgers (Team Captain, November)
Adam Russell
Jeremy Saxton
David Scardoni
Anthony Scotts
George Sharpe
Craig Shelsher
Heath Sims
Martin Taylor
Chris Tootell
Philip Vivian (Team Captain, November; Best Wipeout, November)
Steve Watson (Team Captain, November; Gnarly Award, November; Player's Player, November)
Phillip Wicks
Sam Wicks
Ian Wright
Duncan Young

ENDURING SUPPORT FROM COLLIERS INTERNATIONAL RESIDENTIAL

Colliers International Residential raised over $70,000 for the Wipeout Dementia campaign at their annual Residential Developer's charity event held on Friday, 7 September 2018.

"This cause has become an important one for the entire team at Colliers," said Managing Director Peter Chittenden. "I'm extremely proud of my staff and grateful to our corporate sponsors for getting behind Wipeout Dementia and raising over $200,000 in just a few years."

Spokesman for The Dementia Momentum initiative and Ambassador and inspiration behind the Wipeout Dementia campaign, Mr Richard Grellman AM, spoke at the property luncheon and extended his thanks to the team at Colliers International for their enduring support of CHeBA's research into dementia.

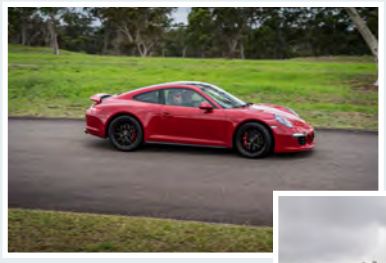
Along with keynote speaker Mark Bouris and MC Peter Chittenden, more than 350 people attended the VIP luncheon held in the Grand Ballroom at Luna Park. These guests included Colliers' representatives, sponsors and the industry's most prominent residential developers.

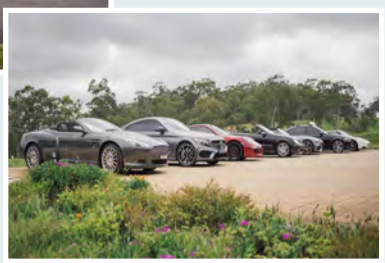
Colliers also hosted the launch event for the November 2018 Bondi Beach Wipeout Dementia at their George Street, Sydney offices.

> "Improved understanding of the disease and care requirements is both an ethical and business imperative."
>
> Peter Chittenden

DRIVE OUT DEMENTIA

Spokesman for The Dementia Momentum initiative, **Richard Grellman AM**, hosted three Drive Out Dementia events throughout 2018 to raise awareness and funds for CHeBA's research. Drive Out Dementia is an elite one-day event where motoring enthusiasts have the opportunity to test their luxury vehicles on a purpose-built 5km private road in the name of dementia research.





THE AMAZING RACE

Community supporter Ashleigh Brown and her team of friends organised an 'Amazing Race' fundraiser st Shellharbour North Beach, raising more than $1,000 for The Dementia Momentum. The Race itself was hosted by Kieran Sernig and his trainers with teams required to find clues between locations around Shellharbour village all in the name of CHeBA's research.

PUBLIC FORUMS

AGEING WITH PURPOSE

An engaged and enthusiastic audience filled the auditorium at The Juniors on Wednesday, 31st October 2018, for the annual Aged Care Psychiatry Service, South Eastern Sydney Local Health District's healthy ageing forum.

With 15% of the population now aged over 65, the theme of the 2018 public event was **Ageing With Purpose** which enticed over 580 registrants and had media icon and former Australian of the Year Ita Buttrose AO OBE as keynote speaker. Other speakers were leading researchers in the area of purposeful ageing including Professor Henry Brodaty AO, Associate Professor Chanaka Wijeratne and Dr Karen Croot.

The event, supported by the Centre for Healthy Brain Ageing (CHeBA), NSW Health, Dementia Centre for Research Collaboration, The Juniors and the Waverley Council, sought to promote meaningful ageing. A highlight of the free event was a delightful and inspiring panel discussion chaired by Ita Buttrose with Australian celebrities Diana "Bubbles" Fisher OAM, Robina Beard OAM and 96 year old Bill Bishop; a study participant in CHeBA's Sydney Centenarian Study.

The educational presentations focused on *Being me: understanding and managing mood in late life* from Associate Professor Wijeratne, *Being heard in late life* from Psychologist and CHeBA Research Officer Dr Karen Croot and *Being visible in late life* from Professor Henry Brodaty.

Ita Buttrose emboldened the attendees to focus on the many pluses with ageing.

"Older people know what it's like to be young but young people don't know what it is like to be old," she said.
Professor Brodaty supported Ita Buttrose's statements and reminded all attendees that it is never to late to create meaning in one's life through family, volunteering, socialising, spirituality, religion and personal development.

"The future is an ageing society which gives us distinct electoral power. Politicians need to take note," said Professor Brodaty.

All presentations from the Forum can be accessed at: https://www.seslhd.health.nsw.gov.au/ageing-purpose-2018

Representatives from the Benevolent Society, Little Bay Coast Centre for Seniors, Holdsworth Community and Junction Neighbourhood Centre gave information about the services they provide to the community to encourage activity and purpose for seniors, while opportunities were made available to join CHeBA's Sydney Centenarian Study for people aged 95 and over or CHeBA's CogSCAN Study for people aged 60+. For more information contact h.douglass@unsw.edu.au.

WAR MEMORIAL HOSPITAL SEMINAR

Professor Henry Brodaty delivered a public talk at the annual Uniting War Memorial Hospital seminar on 5 September 2018. With community education a priority focus for CHeBA, this talk provided updated information on prevention of dementia.

YOUR BRAIN MATTERS

Professor Henry Brodaty was a keynote speaker at "Your Brain Matters" on 11 April 2018 hosted by Hunters Hill Council, Lane Cove Council and Dementia Australia, as part of the 2018 NSW Seniors Festival. Former CEO of Dementia Australia, The Hon. John Watkins AM, was a fellow keynote speaker. The discussion focused on the importance of staying curious, creative and connected as we age.

This event was funded by the NSW Government in association with Hunter's Hill Council.

Professor Henry Brodaty AO

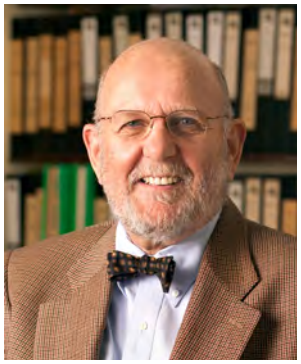
BEECROFT MEN'S PROBUS CLUB

Professor Perminder Sachdev was the invited speaker at Beecroft Men's Probus Club meeting on 22 October 2018 on *Living to 100*. Both genes and the environment/lifestyle are important to live to an exceptional old age, and indeed become a centenarian. Professor Sachdev gave a presentation outlining how – despite the fact that we cannot do much about our genes - we can strive to optimise our physical, cognitive and social activity, and take care of our health and nutrition from an early age to achieve this objective. Even if we do not reach 100, we would have a long and healthy life well into a very old age.

We extend our thanks to President Robin Graham for incorporating positive ageing into their program.

Professor Perminder Sachdev AM

AUSTRALIAN MENTAL HEALTH PRIZE



Professor Gavin Andrews AO

CHeBA Co-Directors Professor Henry Brodaty and Professor Perminder Sachdev, both members of the Australian Mental Health Prize Committee, congratulated two outstanding winners of the prestigious prize. The 2018 dual winners were Janne McMahon OAM, who is an extraordinary mental health consumer advocate, particularly in area of Borderline Personality Disorder, and Emeritus Professor Gavin Andrews AO, an incredibly respected innovator, clinician, teacher and researcher who retired earlier this year after a career in mental health spanning 60 years. The prize recognises the major contributions from both professionals and community advocates in mental health care.

BRUSHES WITH LIFE ART EXHIBITION

Michelle McEwing & Professor Henry Brodaty AO

In 1964, 34 year old Sydney-based painter Naomi Lewis was a proud finalist of the Archibald Prize. 50 years later in 2013, and with a history of her distinctive free-form art hanging throughout many Australian buildings including the Qantas first class lounges, The Hyatt in Canberra and St Vincent's Hospital, this talented artist was diagnosed with vascular dementia.

In 2017, the artist - Naomi Lewis - passed away, leaving behind a rich body of work which furnished an exhibition in her honour at the Workshop Arts Centre in Willoughby from 11 to 28 April.

Proceeds from the sale have been donated to research at CHeBA.

"Clearly this cause is an important one for me," said Michelle McEwing, daughter of Naomi Lewis and coordinator of the art show held at the Ewart Gallery, Workshop Arts Centre in Willoughby.

"Mum's great passions were her family, her community and painting. She would have wanted her final show to benefit a charity."

The opening of the art show was attended by family and friends of Naomi Lewis as well as representatives from CHeBA - including Co-Director Professor Henry Brodaty and Communications & Projects Officer Heidi Douglass - and executives from Group Homes Australia, where Naomi was fortunate enough to live during her final months.

Michelle McEwing's support of CHeBA has continued following her mother's artshow with the inclusion of a gift to CHeBA in her own Will.

"Such extraordinary support from community members like Michelle McEwing encourages us to expand upon our research objectives and our striving toward better clinical care," said CHeBA's Co-Director Professor Henry Brodaty.

> "Such extraordinary support from community members like Michelle McEwing encourages us to expand upon our research objectives and our striving toward better clinical care."
> Professor Henry Brodaty AO

VISITING LECTURES

We were delighted to host two highly acclaimed international visiting lecturers in 2018.

PROFESSOR DIETER WILLBOLD

Professor Dieter Willbold studied biochemistry in Tübingen (Germany), Bayreuth (Germany) and Boulder (Colorado, USA). He completed his PhD in 1994 at the University of Bayreuth, followed by post-doctoral work in Bayreuth and the Sackler School of MedicineTel-Aviv University. He headed a junior research group at the Institute for Molecular Biotechnology in Jena and in 2001 Willbold became an associate Professor at the Heinrich-Heine-University of Düsseldorf. Since 2004, he is full professor at the Institute of Physical Biology in Düsseldorf and director of the Institute of Complex Systems in the Research Centre Jülich. His main interests are protein ligand interactions, structural biology, neurodegeneration and autophagy.

Talk Title: Aβ oligomer elimination, cognition enhancement and deceleration of neurodegeneration in tg AD mouse models by an orally available compound

Date of Visiting Lecture: 5 April 2018

DR RACHEL WHITMER

Dr. Whitmer leads a laboratory of population-based science in brain aging at the University of California, Davis. Her group focuses on three major themes: 1) Ethnoracial disparities and diversity in cognitive aging and dementia outcomes; 2) Early-life contributions to brain health and dementia risk; and 3) Metabolic and vascular influences on brain aging. Her group utilizes lifecourse methods to address these themes. Dr. Whitmer is Principal Investigator of several studies, among them the SOLID (Study of Longevity in Diabetes), a cohort study of 1200 individuals with diabetes mellitus; KHANDLE (Kaiser Healthy Aging and Diverse Life Experiences), a multiethnic cohort of 1,800 elderly individuals; and Kaiser STAR (Study of Healthy Aging in African Americans), a cohort of 700 African Americans age 50 and older. The primary objective of her research program is to identify and understand risk and protective factors for cognitive and brain aging in populations at high risk for dementia, including ethnic minority groups and those with chronic disease such as diabetes mellitus.

Talk Title: Epidemiology of Dementia in Real World Settings: Clues from Health Over the Lifecourse

Date of Visiting Lecture: 25 May 2018

MAJOR SUPPORTERS

GOVERNMENT & PARTNERS

Australian Government
NHMRC National Institute for Dementia Research

Australian Government
Australian Research Council

UNSW SYDNEY

NHMRC

DCRC Dementia Collaborative Research Centres

NeuRA Discover. Conquer. Cure.

FOUNDATIONS & MAJOR DONORS

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Sachdev Foundation

Roger & Merrilyn Layton

IN-KIND

KPMG Aria. HWL EBSWORTH LAWYERS

INVESTIGATING VASCULAR RISK FACTORS TO PREVENT DEMENTIA

Dr Matt Paradise is the 2018 recipient of the Josh Woolfson Memorial Scholarship which supports research looking at modifiable risk factors of Alzheimer's disease to identify and target at-risk groups and individuals and develop intervention strategies for risk reduction.

This award was generously donated to CHeBA by Ms Liz Woolfson in honour of her late husband Mr Josh Woolfson who had Alzheimer's disease.

Dr Paradise will use this PhD scholarship to further his research into the quantification of vascular burden in the brain with the hope of determining ways to control vascular risk factors and ultimately prevent dementia.

Dr Paradise said he was privileged to be the recipient of the Josh Woolfson Memorial Scholarship and was encouraged that the importance of dementia research was being recognised by the community with such awards.

"There is increasing recognition of the role of vascular risk factors in both Alzheimer's and vascular dementia. This is all the more important with the failure to find effective drug treatments for Alzheimer's disease and other dementias."

"We know that we can prevent dementia by controlling vascular risk factors so by investigating this area further, we will be able to develop better markers of vascular damage in the brain and consequently improve diagnosis and prognosis," he said.

"Intervention in early cognitive deficits provides us with the greatest potential for treatment and amelioration of symptoms," he said.

> "This award allows me to concentrate more on my research career and goals to make a significant impact on dementia research."
>
> Dr Matt Paradise

DONORS 2018

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Group Homes Australia

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Anita Hochman

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JA Hurley

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Catherine Kalokerinos

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Vince Kernahan

Fred Khoury

L

Beth Laughton

Estate of the Late Naomi Lewis

Barbara & Sam Linz

Baillie Lodges

Robin Low

M

m3property

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Henk Sjoerdsma

Murray Smith

Susan Rothwell Architects

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Nabeel Tahir (in memory of Phullan Bibi)

ThreadCare

Zoe Thurner

Simon Turnill

V

Vincent Fairfax Family Foundation

Vodafone Australia

W

Rhyees Wedes

Justin White

Sally White OAM

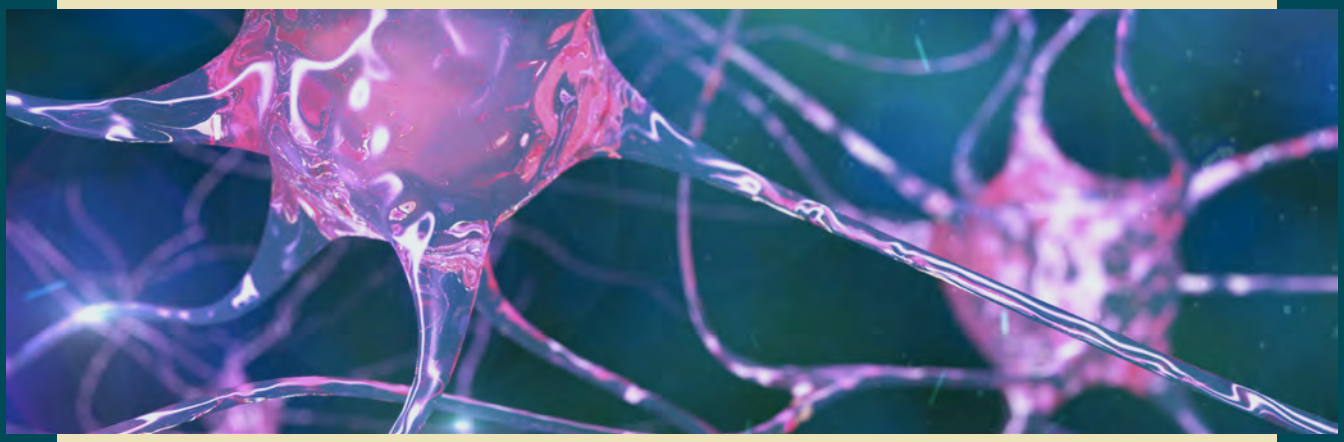
Andrew Wilson

Winten Property Group

Y

The Yulgibar Foundation

SACHDEV FOUNDATION SUPPORTS KEY CENTENARIAN RESEARCH



CHeBA gratefully acknowledges and thanks the Sachdev Foundation for their ongoing support, which includes funding support for the whole genome sequencing of centenarians and to undertake studies investigating the epigenetics of exceptional longevity.

Life expectancy in most societies has increased steadily in the last century due to medical improvements and other advances, with many individuals living beyond 80 years of age in developed countries. As ageing is associated with frailty and a number of diseases, an ageing population poses an increasing medical, social and economic burden on society. However, many exceptionally long-lived individuals, such as centenarians, have delayed morbidity or have escaped age-related diseases. Thus, centenarians represent a unique human paradigm for studies to identify the determinants of exceptional longevity and healthy ageing.

The funding from the Sachdev Foundation has allowed us to generate whole genome sequencing data, which will form a cornerstone of future work examining successful ageing and exceptional longevity . This work is facilitating our growing reputation as leaders in genetic research investigating successful ageing and longevity, both nationally and internationally.

The Sachdev Foundation funding has also allowed an increased focus on research into epigenetics and exceptional longevity, which is leading us to ask unique questions and to develop more international collaborations.

The results from this research may ultimately lead to strategies designed to improve the health of older adults.

Dr Karen Mather is the lead investigator in the research undertaken with the funding provided by the Sachdev Foundation. Dr Mather is a Senior Research Fellow at the Centre for Healthy Brain Ageing (CHeBA), investigating the genetic and epigenetic factors associated with ageing, age-related disorders and exceptional longevity. To date, she has published over 65 peer-reviewed manuscripts, including papers in high-ranking journals, such as Nature. She has received over $3.4 million dollars in competitive funding from granting bodies such as the NHMRC. Dr Mather's leads the Genetics and Epigenomics Group and she supervises four PhD students and undergraduate medicine students.

Dr Mather collaborates with national and international researchers and consortia to answer important questions regarding human ageing. Through this research, she aims to translate her findings into strategies to promote health in our ageing population.

CHeBA COLLABORATORS

INDUSTRY

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

SOCIETIES/PROFESSIONAL ASSOCIATIONS

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

NATIONAL

Commonwealth

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

Western Australia

- Edith Cowan University, Perth
- Murdoch University, Perth

Tasmania

- University of Tasmania, Hobart

ACT

- Australian National University, Canberra

New South Wales

- NSW Department of Health Older People Mental Health Working Group
- University of Newcastle, Newcastle
- University of New England, Armidale
- University of Wollongong, Wollongong

Sydney

- Academic Department for Old Age Psychiatry (ADFOAP), Prince of Wales Hospital
- Australasian Research Institute, Sydney Adventist Hospital
- Australian Catholic University
- Bankstown-Lidcombe Hospital
- Bioanalytical Mass Spectrometry Facility, Mark Wainwright Analytical Centre, UNSW Sydney
- Black Dog Institute
- Centre of Excellence in Population Ageing Research (CEPAR), UNSW Sydney
- Clinical Research Unit for Anxiety and Depression (CRUfAD), UNSW Sydney
- Garvan Institute of Medical Research
- Macquarie University
- National Drug & Alcohol Research Centre (NDARC), UNSW Sydney
- Neuropsychiatric Institute (NPI), Prince of Wales Hospital
- Neuroscience Research Australia (NeuRA)
- Notre Dame University
- School of Biotechnology and Biomolecular Sciences (BABS), UNSW Sydney
- School of Medical Sciences (SOMS), UNSW Sydney
- School of Psychology, UNSW Sydney
- St Vincent's Centre for Applied Medical Research
- St Vincent's Hospital
- University of Sydney
- University of Technology (UTS) Sydney
- Western Sydney University (WSU)

IGEMS (INTERPLAY OF GENES AND ENVIRONMENT ACROSS MULTIPLE STUDIES)

OATS is a partner in the IGEMS (Interplay of Genes and Environment across Multiple Studies) consortia, which seeks to clarify risk and protective factors for Alzheimer's disease and related dementias using data from twin studies.

In 2018 IGEMS received substantial funding from the NIH to collate and analyse data from 47,632 twins collected across 9 twin studies (involving three Scandinavian twin registries, four twin studies in the USA, and OATS).

The depth and breadth of data collected as part of the OATS study will be invaluable in elucidating the contributions of protective factors, such as sex, educational attainment, physical and social activity, and risk factors, such as vascular disease and depression/anxiety, to the development and progression of dementias.

South Australia

Adelaide

- Flinders University
- University of Adelaide

Victoria

Melbourne

- The Florey Institute of Neuroscience and Mental Health
- La Trobe University
- Monash University
- Royal Melbourne Hospital
- University of Melbourne
- Department of Molecular Imaging & Therapy Austin Health
- Twins Research Australia

Queensland

Brisbane

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

INTERNATIONAL

Africa

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

Asia-Pacific

- Beihang University, China
- Beijing Normal University, China
- Department of Neurology, Tianjin Huanhu Hospital, China
- Capital Medical University, China
- Chinese Academy of Sciences, China
- Peking University, China
- Renji Hospital, China
- Shanghai Jiaotong University, China
- Wenzhou University, Wenzhou, China
- Institut de Recherche pour le Développement (IRD), Tahiti, French Polynesia
- Institut Louis Malardé, Tahiti, French Polynesia
- Chinese University of Hong Kong, Hong Kong
- Hong Kong Polytechnic University, Hong Kong
- The University of Hong Kong, Hong Kong
- CSI Holdsworth Memorial Hospital, India
- Atma Jaya Catholic University, Indonesia
- Keio University, Japan
- Kyushu University, Japan
- Osaka University, Japan
- National Center for Geriatrics and Gerontology, Japan
- Tohoku University, Japan
- University of Macau, Macau
- Universiti Kebangsaan, Malaysia
- Universiti Putra Malaysia, Malaysia
- Department of Neuropsychiatry, Gyeonggi Provincial Hospital for the Elderly, Republic of Korea
- Hallym University, Republic of Korea
- Seoul National University, Republic of Korea
- Changi General Hospital, Singapore
- National Neuroscience Institute, Singapore
- National University, Singapore
- National University Health System, Singapore
- Mahidol University, Thailand
- Taipei Veterans General Hospital. No. 201, Taiwan
- St. Luke's Medical Center, Philippines

Middle East

- Baqiyatallah University of Medical Sciences, Iran
- Bushehr University of Medical Sciences, Iran
- Tabriz University of Medical Sciences, Iran
- Tehran University of Medical Sciences, Iran
- Sultan Qaboos University, Oman
- Nigde Omer Halisdemir University, Nigde, Turkey
- Suleyman Demirel University, Turkey

Europe

- Innsbruck Medical University, Austria
- University of Helsinki, Finland
- CHU Amiens-Picardie, France
- French National Institute of Health and Medical Research (INSERM), France
- Institut Pasteur de Lille, France
- Lille University Hospital, France
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- Leiden University, Germany
- Ludwig Maximilians University Munich, Germany
- Max Planck Institute of Psychiatry, Germany
- Neuroscience Network Düsseldorf, Heinrich Heine University, Germany
- University of Leipzig, Germany
- University of Marburg, Germany
- University of Athens, Greece
- Golgi-Cenci Foundation, Italy
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UK

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- Newcastle University, England
- University College London, England
- University of Bradford, England
- University of Leeds, England
- Royal College of Surgeons in Ireland, Ireland
- University of Aberdeen, Scotland
- University of Edinburgh, Scotland
- Swansea University, Wales

The Americas

- Instituto Rene´ Rachou da Fundaçaõ Oswaldo Cruz, Brazil
- University of São Paulo, Brazil
- Dalhousie University, Canada
- McGill University, Canada
- Simon Fraser University, Canada
- Université de Montréal, Canada
- Pontificia Universidad Católica de Chile, Chile
- Medical University of Havana, Cuba
- Stanford University, USA
- University of California, USA
- University of California, Irvine, USA
- University of Southern California, USA
- University of Colorado, USA
- James A Haley VA Hospital, Florida, USA
- University of Georgia, USA
- Northwestern University, USA
- Johns Hopkins Medicine, USA
- Mayo Clinic, USA
- University of Minnesota, USA
- Boston University, USA
- Harvard University, USA
- Iowa State University, USA
- Oregon Health and Science University, USA
- Washington University, USA
- Cleveland Clinic, Nevada, USA
- Columbia University, USA
- Fordham University, USA
- Gertrude H. Sergievsky Center, New York, USA
- Yeshiva University, USA
- University of Pittsburgh, USA
- American Institutes for Research, USA
- Pennsylvania State University, USA
- Wayne State University, USA
- University of Alabama, USA

CHeBA CONSORTIA COLLABORATIONS

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

- BRIDGET (Brain Imaging, Cognition, Dementia and Next Generation Genomics: a Transdisciplinary Approach to Search for Risk and Protective Factors of Neuro-degenerative Disease)
- CHARGE (Cohorts for Heart and Aging Research in Genetic Epidemiology)
- DIAN (Dominantly Inherited Alzheimer Network)
- EADB (European Alzheimer's Disease DNA BioBank)
- ENIGMA (Enhancing Neuro Imaging Genetics through Meta-Analysis)
- EuroDiscoTWIN (European Discordant Twin Study)
- IALSA (Integrative Analysis of Longitudinal Studies on Aging and Dementia)
- IGEMS (Consortium on Interplay of Genes and Environment across Multiple Studies)
- PERADES (Defining Genetic, Polygenic and Environmental Risk for Alzheimer's disease).

CHeBA PROJECTS

"CHeBA is in an excellent position to make a worldwide difference to prevention, earlier diagnosis, and earlier and more effective interventions."

Professor Perminder Sachdev AM

CURRENT PROJECTS

A study of the effect of acute physical illness requiring hospitalisation on the long-term cognitive trajectory of the Sydney Memory and Aging Study (MAS)

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

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

Aims:

- Observe the effect of acute physical illness requiring hospitalisation on cognitive and functional trajectory over several years in longitudinal cohort studies of cognitive ageing.
- Examine whether variables describing the nature of the illness and hospitalisation influence the level of decline in cognition and function over time.
- Explore whether a number of risk-factor variables, such as APOE4 carrier status or mild cognitive impairment (MCI), act as moderator variables to increase the effect of acute physical illness requiring hospitalisation on cognitive and functional decline.

Findings:

- We have conducted a systematic review of peer reviewed papers investigating the effect of acute illness hospitalisation on cognition from Medline, Embase, Psycinfo and CINAHL, screening about 400 titles and abstracts. We synthesized results from 40 papers. Most papers were prone to bias as a result of have no baseline cognition data or appropriate comparison groups. However, 8 large studies used community cognition data and most of these showed cognitive decline associated with acute hospitalisations. 8 studies were able to be pooled statistically and the meta-analysis also supported this finding that acute hospitalisation increased cognitive decline in subsequent years.
- The MAS data will be analysed using latent growth modelling to observe changes in cognitive trajectory over the 4 waves in relation to intervening hospitalisations, as well as undergoing survival analysis to assess the risk of conversion to dementia or MCI the association of this with hospitalisations at W6 from prior to W1 up to W4.

Funding: Australian Society of Anaesthetists, DCRC-ABC.

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

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

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

Aims:

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

Findings: To build on our previous findings relating to the Sydney MAS cohort (Poljak et al., *Current Alzheimer Research* 2016 Vol 13 issue 3, pp 243- 255 and Poljak et al., *Expert Review of Neurotherapeutics* 2017, 17(1), 3-5), where we found lower levels of plasma Aβ in MCI and AD relative to normal controls, we are using a meta-analysis approach to explore biomarker levels in early onset AD. An early stage Scientia awarded PhD candidate, Gurjeet Kaur, has prepared a manuscript of our findings which will be submitted for peer review this year. We will also explore publicly available data on late onset AD, as described in the aims.

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

Apolipoprotein E4 and cognitive decline: the moderating roles of sex, age, and ethnicity

CHeBA staff: Steve Makkar, Darren Lipnicki, John Crawford, Anbupalam Thalamuthu, Nicole Kochan, Henry Brodaty, Perminder Sachdev.

Other investigators: Contributing COSMIC study leaders and associates: Representing cohorts from around 15 countries.

Aim:

- Examine if carriage of the Apolipoprotein E ε4 (APOE*4) allele is associated with decline of general cognitive functions and memory in late adulthood, and if this effect is dose-dependent.
- Investigate if the effect of APOE*4 on general cognitive and/or memory decline is moderated by:
  - Age
  - Sex
  - Vascular risk factors
- Examine if the effect of APOE*4 on general cognitive and/or memory decline differs between ethnicities, namely Asians and Whites.

Findings: APOE*4 carriage was related to faster general cognitive decline in women and men, and faster memory decline in men. However, carriage of two versus one APOE*4 alleles was associated with faster general cognitive and memory decline in men only. Significant effects in men were specific to the older-aged (i.e., 80-year-old) participants. Furthermore, the negative effects of carrying two versus one APOE*4 allele on general cognitive decline worsened with age in men more than women. Increasing numbers of vascular risk factors worsened the effects of APOE*4 carriage on general cognitive decline in *younger-aged* participants, with the effect being significant in women. In contrast, increasing numbers of vascular risk factors decreased the effects of APOE*4 carriage on general cognitive decline in older-aged participants, with the effect being significant in men. Regarding ethnoregional differences, in older-aged participants, APOE*4 had a stronger effect on memory decline in Asians versus Whites. Also, increasing numbers of vascular risk factors attenuated the effects of *APOE*4* on MMSE decline in Asians, but not Whites.

Funding: Direct donations to The Dementia Momentum Fund, NIH grant, NHMRC grant

Apolipoproteins in plasma (particularly APOA1, APOD, APOJ and APOH)

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

Other investigators: Dr Julia Muenchhoff (CHeBA Hon. Research Fellow), Professor John Attia (University of Newcastle), Professor Mark Duncan (University of Colorado), Professor Ralph Martins (Edith Cowan University), Associate Professor Mark McEvoy (University of Newcastle), Associate Professor Peter W. Schofield (University of Newcastle), Dr Tamar Ziehm (visiting research fellow from Forschungszentrum Jülich, Germany), Professor Dieter Willbold (collaborating researcher from Forschungszentrum Jülich, Germany), Professor Gideon Caplan.

Aims:

- Determine if apolipoprotein changes observed in MCI and AD plasma, relative to normal controls, would be reproducible across independent cohorts of similar design.
- Identify which of the apolipoproteins change with age and/or are dysregulated in MCI and AD.
- Correlate plasma apolipoprotein changes with cognitive domain scores and brain volumetrics.
- Study the mechanisms of action, expression changes with age, and dysregulation in neurodegenerative diseases of ageing, including animal models for apolipoproteins APOA1, APOD, APOJ and APOH.
- Interactions between APOH and Aß peptides, and binding partners of APOH in plasma and cerebrospinal fluid (CSF).

Findings: ApoH has some binding affinity for Aβ42 and has a variety of protein binding partners in plasma and CSF. The work is ongoing, with a manuscript in preparation.

Funding: NHMRC, Rebecca L. Cooper Medical Research Foundation, Alzheimer's Australia Rosemary Foundation, Sachdev Foundation, UNSW Faculty of Medicine FRG and Early Career Researcher Grants, Australian Research Council Discovery Early Career Research Fellowship to Dr Nady Braidy

Brain ageing and transcriptomics

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

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

Aims:

- Identify transcriptomic changes in the ageing brain.

Findings: For this ongoing project, over 60 samples from two brain regions have been collected from national and international brain banks, ranging in age from 35 to 105 years. RNA extraction and sequencing on these brain samples will be undertaken in early 2019. Analyses are also being undertaken looking at age-related changes in brain expression from 10 brain regions using publicly available data, this work is being written up for publication by PhD student, Adith Mohan.

Funding: NHMRC, Thomas Foundation

Brain proteomics: Differential expression of the proteome in AD brain

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

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

Aims:

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

Findings: Using differential detergent fractionation followed by mass spectrometric (proteomic) analysis we identified ~2000 proteins in brain tissue extracts, of which dysregulated expression was identified in a variety of protein families, including antioxidant proteins, metabolic enzymes and mitochondrial proteins, many of which were downregulated in AD. By contrast several proteins involved in cell cycle regulation, neuronal remodeling or structural roles, were upregulated in AD relative to controls. We used this data to explore protein expression at the tissue level using immunohistochemistry, and observed upregulation of Translocase of outer mitochondrial membrane (TOMM70) and Solute Carrier Family 25 Member 11 (SLC25A11) in AD occipital lobe. We speculate that such upregulation may reflect a protective response to the burden of pathology, and are currently preparing a manuscript for peer review.

Funding: NHMRC, Rebecca L. Cooper Medical Research Foundation

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

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

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

Aims:

- Identify rare and common genetic variants influencing brain structure in older adults.
- Explore the determinants of brain ageing from a life-course perspective, including genomic, epigenomic and environmental factors.
- Examine whether identified genes predict decline in memory performance and an increased risk of Alzheimer's disease.

Findings: This work comprises a number of ongoing collaborative genetic and epigenetic projects, with a current focus on neuroimaging traits. In 2018, CHeBA researchers attended the third Annual BRIDGET Meeting in Graz, Austria and another meeting focussing on whole genome sequencing analyses in Bordeaux, France. Planned analyses include seeking to identify genetic variants associated with a composite measure of brain ageing based on MRI imaging using whole genome sequencing.

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

Cerebrovascular disease (CVD) lesion detection – using machine learning methods

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

Other investigators: Dr Pierre Lafaye de Micheaux, School of Mathematics and Statistics, UNSW; Dr Audrey Poterie, Melbourne School of Population and Global Health, University of Melbourne; Associate Professor Tao Liu (Beihang University, China) (CHeBA Hon. Research Fellow).

Aim: Cerebral white matter hyperintensity (WMH), cerebral microbleeds (CMB), lacunes and dilated perivascular spaces (PVS) are some of the most common CVD lesions. At present, they are usually detected and quantified manually (visual rating) by the neuroradiologist. Automated detection and quantification of CVD related lesions will help to elucidate the mechanisms of CVD burdens and neuro-degenerative diseases such as Alzheimer's disease as they often appear in the MRI scans of AD brains. The broad aim of this project is to design novel computer algorithms using machine learning methods for their automated detection and quantification. Different lesions are visualised with MRI scans of different modalities, e.g. WMH, lacunes, PVS in FLAIR (fluid attenuation inversion recovery) and T1-weighted scans and CMB in SWI (susceptibility-weighted imaging) scans. We have so far completed our work on WMH and are now focusing on lacunes. Therefore, our first aim will be using machine learning methods to accurately detect lacunes in the T1-weighted and FLAIR scans.

Progress: This work started in February 2018 as an honours student project. We are aiming to create a new module for this specific task for our pipeline. The first step will be to complete our algorithm-building. Our pilot work shows high sensitivity and reasonable reliability compared with visual rating results and provides the ability to characterise lacunar infarcts on a per-occurrence, volumetric basis. We hope that automated detection of lacunes, using our improved machine learning methods, will allow for efficient processing of large datasets, as well as novel explorations investigating the clinical implications of volumetric and morphologic characteristics likely to be highly relevant to the clinical setting.

Funding: NHMRC

CogSCAN: Evaluation of computerised cognitive tests in healthy older adults, and in patients with mild cognitive impairment and mild dementia

CHeBA staff: Nicole Kochan, Perminder Sachdev, Henry Brodaty, John Crawford, Brian Draper, Teresa Lee, Karen Croot (Neuropsychology Research Officer), Karen Allison (Study Coordinator), Min Yee Ong (Research Assistant), Matilda Rossie (Research Assistant).

Other investigators: Professor Julie Henry (University of Queensland), Professor David Bunce (University of Leeds), Professor Jacqueline Close (Neuroscience Research Australia).

Aim: To systematically evaluate four computerised neuropsychological assessments in terms of suitability, reliability and validity for assessing cognitive function in community-living older adults without cognitive impairment, and in adults diagnosed with mild cognitive impairment and dementia.

Findings: The study protocol was presented at the Australian Dementia Forum in June 2018 and data collection commenced in late 2018. More than 80 participants have been interviewed for the study, and more than 20 participants have visited UNSW Sydney to complete computerised cognitive testing and traditional pen-and-paper assessments.

Funding: NHMRC Boosting Dementia Research Grant

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

CHeBA staff: Lynn Chenoweth, Henry Brodaty.

Other investigators: Tracey Clarke, Jacki Wesson (Montefiore Home), Janet Cook (DCRC/CHeBA, UNSW).

Aim: Develop and pilot test an education program to promote collaboration and positive relationships between family and direct care staff for the purpose of improving the quality of residential care services.

Findings: 12 staff trainers facilitated the targeted relationship development education program with 49 direct care staff and 38 family members from two aged care homes. The education program was informed by data obtained with the Person-Centred Environment and Care Assessment Tool (PCECAT) and evidence-based resources developed by the Australian Institute for Primary Care and Ageing, La Trobe University, Australia. Organisational factors of with an influence on family-staff relationships were assessed with the Staff and Family Relationship Audit. Direct care staff and family attitudes about the importance of family-staff relationships were assessed with the Family and Staff Relationship Assessment Tool (FASRAT). Pre/post-intervention data on changes in family-staff relationships were obtained with the Family and Staff Relationship Implementation Tool (FASRIT) and changes in care quality were obtained the Combined Assessment of Residential Environments (CARE). Participant feedback was obtained at 8-month follow-up through

six separate staff focus groups and 20 one-on-one family interviews. There were significant improvements in FASRIT score percentages for family (p=0.001) and staff (p=0.001) post-intervention, and in staff median ratings of CARE 'safety' items (p=0.014), and family median ratings of CARE 'significance' items (p=0.020) at post-test. While existing organisational structures supported positive family/staff relationships, improvements were recommended by study participants in communication policies and procedures, care delivery information sharing and decision-making and in educating staff on how to build strong relationships with families.

Funding: Montefiore Home

Cross-validation of a cognitive risk score to identify post-stroke patients requiring comprehensive cognitive assessment

CHeBA staff: Perminder Sachdev, Jessica Lo.

Other investigators: Dr Olivier Godefroy (Amiens University Hospital) and other STROKOG collaborators.

Aims: A strategy based on a cognitive risk score to identity patients eligible for comprehensive cognitive assessments was developed in the GRECOGVASC cohort in France. The aim for this project is to cross-validate this score in the STROKOG population.

Findings: Project proposal was approved by the RSC and data was sent to Dr Godefroy for analysis.

Funding: Vincent Fairfax Family Foundation

Decline in verbal and visual memory in mild cognitive impairment: predictors of AD and associations with biomarkers

CHeBA staff: Darren Lipnicki, Perminder Sachdev, Nicole Kochan, Wei Wen, Henry Brodaty.

Other investigators:

- Dr Javier Oltra Cucarella (workgroup leader), Dr Rosario Ferrer Cascales, Dr Miriam Sanchez Sansegundo: University of Alicante, Spain; Dr Juan Carlo Arango Lasprilla, Dr Jesus M. Cortes: Biocruces Health Research Institute, Spain.
- Contributing COSMIC study leaders and associates: Representing cohorts from around 4 countries.

Aim: This study will expand upon an earlier COSMIC project to use a Reliable Change Index to quantify cognitive decline separately for verbal memory and visual memory. The risk of AD for individuals with amnestic mild cognitive impairment (aMCI) who are visual memory decliners will be compared against those who are verbal memory decliners. Whether decline on visual or verbal memory tests outperforms biomarkers (APOE status and grey matter volumes) for predicting risk of AD will also be investigated. A secondary aspect of the study will use MRI data to investigate any differences in brain connectivity between individuals with aMCI who decline in verbal memory tests, visual memory tests, or both (in collaboration with researchers at the IBERBASKE Research Institute).

Findings: Data collection underway.

Funding: Direct donations to The Dementia Momentum Fund, NIH grant, NHMRC grant

Deprescribing guidelines for people with dementia: cholinesterase inhibitors and memantine

CHeBA staff: Lynn Chenoweth.

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

Aims:

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

Findings: The guideline was produced following a systematic review using the GRADE process to assess the quality of the evidence and to convert the evidence into recommendations. The Guideline is registered on the NHMRC guideline register (https://www.clinicalguidelines.gov.au/portal/2588/evidence-based-clinical-practice-guideline-deprescribing-cholinesterase-inhibitors-and).

Recommendations:

The Guidelines recommend that medication decisions should be based on the goals, values and preferences of the person with dementia and/or their family/carer. Discussion of the potential benefits and harms of both continuation and discontinuation, as well as the level of evidence and uncertainties of the benefits and harms, are essential to this conversation.

1. For individuals taking a **cholinesterase inhibitor** (donepezil, rivastigmine or galantamine) for Alzheimer's disease, dementia of Parkinson's disease, Lewy body dementia or vascular dementia for greater than 12 months, we recommend trial discontinuation if:

cognition and/or function has significantly worsened over the past six months (or less, as per the individual); no benefit (improvement, stabilisation or decreased rate of decline) was seen at any time during treatment; and the individual has severe/end-stage dementia (characteristics of this stage include dependence in most activities of daily living, inability to respond to their environment and/or limited life expectancy) *(Strength of recommendation: Strong; Level of evidence: Low)*.

2. For individuals taking a **cholinesterase inhibitor** (donepezil, rivastigmine or galantamine) for an indication other than Alzheimer's disease, dementia of Parkinson's disease, Lewy body dementia or vascular dementia, we recommend trial discontinuation *(Strength of recommendation: Strong; Level of evidence: Low)*.

3. For individuals taking **memantine** for Alzheimer's disease, dementia of Parkinson's disease or Lewy body dementia for greater than 12 months, we recommend trial discontinuation if: cognition and/or function has significantly worsened over the past six months (or less, as per the individual); no benefit (improvement, stabilisation or decreased rate of decline) was seen at any time during treatment; and the individual has severe/end-stage dementia (characteristics of this stage include dependence in most activities of daily living, inability to respond to their environment and/or limited life expectancy). *(Strength of recommendation: Strong; Level of evidence: Very Low)*.

4. For individuals taking **memantine** for indications other than Alzheimer's disease, dementia of Parkinson's disease or Lewy body dementia, we recommend trial discontinuation *(Strength of recommendation: Strong; Level of evidence: Very Low)*.

Practice points:

1. Deprescribing of cholinesterase inhibitors and/or memantine should be a **trial discontinuation**, with close periodic monitoring (such as every four weeks) and re-initiation of the medication if the individual evidences clear worsening of condition after withdrawal.

2. The dose of the cholinesterase inhibitors and/or memantine should be tapered prior to discontinuation by halving the dose (or by stepping down through available dose formulations) every four weeks to the lowest available dose, followed by discontinuation.

3. Other situations in which trial deprescribing of cholinesterase inhibitors and/or memantine can be considered include a decision by a person with dementia and/or their family/carer to discontinue the medication, a person with dementia's refusal or inability to take the medication, non-adherence that cannot be resolved, drug–drug or drug–disease interactions that make treatment risky, severe agitation/psychomotor restlessness and non-dementia terminal illness.

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

Depression in the pre-clinical phase of AD: trajectories and determinants

CHeBA staff: Simone Reppermund, Darren Lipnicki, Perminder Sachdev, Nicole Kochan, Henry Brodaty.

Other investigators:

- Karen Ritchie (workgroup co-leader), Isabelle Carriere, Sophie Carles: INSERM, France.
- Contributing COSMIC study leaders and associates: Representing cohorts from around 10 countries.

Aims:

- Characterise the trajectory of depressive symptoms within the pre-clinical period leading up to the diagnosis of AD, and determine its clinical correlates (notably cardiovascular disease, diabetes, hypertension, head trauma).
- Assess the longitudinal association between depressive symptoms and cognitive decline taking into account findings from the first aim.

Findings: Data collection currently underway.

Funding: Direct donations to The Dementia Momentum Fund, NIH grant, NHMRC grant

Determinants of cognitive performance and decline in diverse ethno-regional groups: The COSMIC collaboration

CHeBA staff: Darren Lipnicki, John Crawford, Steve Makkar, Anbupalam Thalamuthu, Nicole Kochan, Henry Brodaty, Perminder Sachdev.

Other investigators: Study leaders and associates from 19 COSMIC member studies in addition to Sydney MAS representing 15 countries.

Aim: Investigate how cognitive performance and decline is affected in different ethno-regional groups by various risk factors: sex, educational attainment, apolipoprotein E4 allele (APOE*4) status, body mass index, general health, current anxiety, current and past depression, hypertension, blood and pulse pressure, diabetes, high cholesterol, peripheral vascular disease, atrial fibrillation, cardiovascular disease, stroke, smoking, alcohol use, and physical activity.

Findings: The overall sample comprised 48,522 individuals (58.4% women) aged 54–105 (mean = 72.7) years at baseline. We analysed two cognitive outcomes: scores for the Mini-Mental state Examination, and global cognition scores derived from tests of memory, language, attention, and executive functioning. For at least one cognitive outcome, age, APOE*4 carriage, depression, diabetes, current smoking, and stroke history were independently associated with poorer cognitive performance, and higher levels of education and more physical activity were associated with better performance. Age, APOE*4 carriage and diabetes were independently associated with faster cognitive decline. Some different effects between Asians and Whites were observed, including stronger associations for Asians between ever smoking and poorer cognition, and between diabetes and cognitive decline.

Funding: Direct donations to The Dementia Momentum Fund, NHMRC grant

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

CHeBA staff: Anne Poljak (conjoint), Nady Braidy, Perminder Sachdev, Matthew Wong (PhD student), Yue Liu (MSc candidate), Maboobeh Hosseini (MSc candidate – to enrol in 2019).

Other investigators: Dr Russ Pickford (BMSF, UNSW), Dr Fatemeh Vafaee (BABS, UNSW), Professor Daniel Chan (Department of Aged Care and Rehabilitation, Bankstown-Lidcombe Hospital).

Aims:

- Identify lipid biomarkers in plasma to assist in diagnosis of MCI and/or Alzheimer's disease (AD).
- Explore the possibility that plasma lipids are correlated with brain volumetric and cognitive changes.
- Compare plasma lipidomics profiles across dementia subtypes (AD, vascular dementia) and stroke.
- Compare fatty acid levels in control vs AD, using plasma from MAS and OATS subjects.

Findings: Three manuscripts are in preparation; *(a)* a comparative methods paper, *(b)* lipidomics across age groups paper, *(c)* plasma lipidomics differences between APOE2 ***vs*** E4 carriers. For a fourth study data processing is in progress to compare mono- and dizygotic twins.

Funding: NHMRC, Australian Research Council Discovery Early Career Research Fellowship to Dr Nady Braidy, Australian Postgraduate Award PhD Scholarship to Matthew Wong

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

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

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

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

Findings: This large international consortium plans to undertake genetic studies examining Alzheimer's disease and related phenotypes. CHeBA will contribute genetic data to a series of planned genetic studies, including the largest genome-wide association study (GWAS) on Alzheimer's disease to date and GWAS on other related measures, including amyloid imaging.

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

Epigenetic and genetic factors and AD development

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

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

Aim: Improving our understanding of the relationships between DNA methylation, microRNAs (miRNAs), genome variation and gene expression in Alzheimer's disease (AD).

Findings: This work uses samples and data from CHeBA studies and the Australian Imaging Biomarker and Lifestyle Study (AIBL).

Cognitively normal controls and individuals diagnosed with mild cognitive impairment and AD were selected from AIBL for miRNA analysis. Blood RNA was extracted and small RNA sequencing completed. Analyses indicated a number of miRNAs that may be useful as candidate biomarkers for AD.

Identical twins discordant for an early marker of AD, brain amyloid burden, were selected for miRNA and mRNA gene expression studies. Blood RNA was extracted and gene expression (miRNA, mRNA) assays performed. A number of dysregulated miRNAs were observed and will serve as candidates for future studies.

This work is currently being written up as part of Helen Wu's PhD thesis.

Funding: The Mason Foundation, Henroth Investments, NHMRC, Thomas Foundation, Yulgilbar Foundation Alzheimer's Research Program Grant

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

CHeBA staff: Lynn Chenoweth.

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

Aims:

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

Findings: Final data collection was completed and analysed for the EPIC trial and for some of the trial sub-studies. Articles were submitted to international refereed journals. The main DCM-EPIC trial results were published in *Trials. 18:300 DOI 10.1186/s13063-016-1416-z*. The DCM-EPIC Trial Monograph was published in the *National Institute for Health Research – Health Technology Assessment (NIHR-HTA) Repository,* UK. Accepted papers include *Process evaluation of the implementation of Dementia Care MappingTM in a cluster randomised controlled trial in long care* (by JAMDA in December 2018) and *Health economic analysis of Dementia Care MappingTM in a cluster randomised controlled trial in long care* (by Lancet Psychiatry in December 2018). A number of trial sub-study articles are currently under review. The main trial results and sub-study results were presented at 2018 international conferences, including the AAIC.

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

External validation of dementia risk models in stroke-survivors

CHeBA staff: Perminder Sachdev, Jessica Lo.

Other investigators: Dr Eugene Tang (Newcastle University, UK; PhD student) and other STROKOG collaborators.

Aims: Use the STROKOG data resource to externally validate currently published dementia risk prediction models; and if model validation is found to be poor, develop new models for predicting risk of dementia in persons with stroke.

Findings: Analysis in progress. Dr Tang was able to validate several risk dementia models in a number of STROKOG studies in 2018. Since studies have contributed new data, Dr Tang will repeat the analyses in the year ahead.

External validation of risk scores for cognitive impairment five years after stroke

CHeBA staff: Perminder Sachdev, Jessica Lo.

Other investigators: Marion Fahey (King's College London, PhD student) (until November 2018) and Dr Clare Flach (King's College London) and other STROKOG collaborators.

Aims: A patient specific tool which predicts cognitive impairment to a high level of accuracy was derived using a UK cohort. The aim of this project is to use the STROKOG data resource to externally validate our cognitive decline model; and, if model validation is found to be poor, update the model to maximise external validity.

Findings: Project proposal was approved by the RSC and data was requested and sent to Ms Fahey who left the university in 2018. Dr Clare Flach from the same research group will take up this project in 2019.

Funding: Vincent Fairfax Family Foundation

Genetic and environmental contributions of amyloid deposition using amyloid-PET imaging in the Older Australian Twins Study cohort

CHeBA staff: Perminder Sachdev, Rebecca Koncz (PhD student), Wei Wen, Anbupalam Thalamuthu, Teresa Lee, Vibeke Catts, Suzy Forrester, , Kristan Kang, Karen Mather, Anne Poljak (conjoint).

Other investigators: Professor Christopher Rowe (Austin Hospital, Victoria), Associate Professor Victor Villemagne (University of Melbourne), Professor David Ames (National Ageing Research Institute), Dr Eva Wegner (Prince of Wales Hospital, NSW).

Aims:

- Determine the heritability of amyloid deposition in the brain using amyloid PET imaging in the Older Australian Twins Study (OATS) cohort, as a potential endophenotype of Alzheimer's disease.
- Determine the genetic and environmental risk (and protective) factors associated with amyloid deposition in older individuals.
- Investigate the relationship between amyloid burden and aspects of cognitive function.

Findings:

- With the recruitment, assessment and scanning for the OATS amyloid PET imaging project completed in 2017 (total n=207; PiB-PET n=58; NAV-PET: VIC - n=69, NSW n=80), this year the team has been cleaning, collating and running preliminary analyses on the data.
- So far, the analysis suggests moderate heritability for global amyloid burden (h2= 0.43), with a range of 0.18–0.54 across cortical regions of interest. This suggests that amyloid deposition is under strong environmental influences.
- One potentially important contributor to amyloid deposition is cerebral small vessel disease (SVD), as these two pathologies have been noted to commonly co-occur. However, our preliminary analysis suggests the genetic and environmental correlations between global amyloid burden and markers of SVD are negligible.
- Sachdev, Koncz, Thalamuthu et al. presented data on the co-occurrence between amyloid deposition and SVD in poster format at the 2018 VasCog International Conference, Hong Kong.

Funding: NHMRC.

Genetic and epigenetic markers of late-life depression

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

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

Aims:

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

- Identify differentially methylated regions of the genome associated with depression in late-life.

Findings: Heritability has been estimated using twins from the Older Australian Twins Study cohort, with depression in late life under moderate to high genetic influence. There was also a significant genetic correlation observed between depression and anxiety. This work has been written up for publication. Suggestive differentially methylated regions were also identified using the twin sample but require replication in independent and larger cohorts. This work formed the basis of a PhD thesis by Ruby Tsang, which has now been successfully completed.

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

Genetic influence on human hippocampal atrophy

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

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

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

Findings: We have computed over 1000 MRI scans including over 500 participants from MAS aged between 70 to 95.3 years of age The voxel-wise topographic pattern of change was compared with the genetic relationship of maximal shared genetic influence, obtained from an independent sample of over 320 twins aged between 65 and 72. We found that the pattern of genetic correlations for the surface of the hippocampus largely corresponded to hippocampal atrophy in the ageing brain. The patterns of heritability and genetic correlations of the right and left hippocampi were similar, but not bilaterally symmetrical on the vertex level. We had our hypothesis for this project that ageing-related changes in hippocampus would be strongly influenced by their genetic organization. Our work indicated that individual differences in hippocampus in the ageing process had a genetic factor. We are still exploring the pattern of atrophy. A journal manuscript is currently in preparation.

Funding: NHMRC

Genetic influence on the spatial distribution and density of white matter fibre tracts between brain regions

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

Other investigators: Dr Pierre Lafaye de Micheaux, School of Mathematics and Statistics, UNSW; Professor David Ames, National Ageing Research Institute; Royal Melbourne Hospital; Associate Professor Margaret J. Wright, Queensland Brain Institute, University of Queensland.

Aims: The relationship between genetics, brain structure, and function has long been explored. Genetic influence on, including heritability of some of the diffusion properties measured by using diffusion weighted imaging, such as FA (fractional anisotropy), MD (mean diffusivity), AD (axial diffusivity) and RD (radial diffusivity) have also been reported in the previous research literature. However, some important, biologically relevant aspects of white matter fibre tract geometry, such as the spatial distribution and density of a tract buddle has not been investigated. We aim to explore these characteristics of white matter fibre buddles using the diffusion tensor scans of a cohort of older twins (OATS). We will first establish a mathematical model which will effectively describe the geometry of a fibre buddle and further extract the main features of the buddle and then apply our approach/model to the OATS cohort.

Findings: We have established a mathematical model which summarises and analytically represents the geometry of the density, shape and flow of brain fibre tracts. We have made a journal submission of the paper which describes the maths model. Computations of the scans are to start in mid-2019.

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

Genetics and epigenetics of longevity

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

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

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

Findings: Meta-analyses examining commonly studied genetic polymorphisms with exceptional longevity have been completed, including using data from the Sydney Centenarian Study. Several variants in genes linked to cardiovascular health were significantly associated with exceptional longevity. This work has been now been published by PhD student, Mary Revelas (Reveals et al., *Mech Ageing Devpt,* 2018). Polygenic risk scores for a particular trait can be estimated using the results of previous genome-wide association studies. As expected, high polygenic risk scores for exceptional longevity were associated with longevity in our samples from the Sydney Centenarian Study. However, polygenic risk scores for cardiovascular factors and disease (e.g. low density lipoproteins, stroke) were not significantly associated with longevity. This work has now been submitted for publication by Mary Revelas.

Funding: Sachdev Foundation, NHMRC, Thomas Foundation

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

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

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

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

Findings: Genetic variants located in a locus on chromosome 19, containing the GDF-15 gene, were significantly associated with GDF-15 blood concentration in Sydney MAS and three other international cohorts. A manuscript was written by postdoctoral fellow, Jiyang Jiang, and has now been published (Jiang et al., *Frontiers in Genetics,* 2018).

Funding: NHMRC, Thomas Foundation

Genetics of white matter hyperintensities

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

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

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

Findings: WMH are regions of hyperintensity in the white matter, which are observed on neuroimaging scans. High burden of WMH is associated with negative health outcomes, including dementia and disability. WMH can be sub-classified into two categories based on their location in the brain, deep and periventricular WMHs. This genome-wide association study uses WMH and genetic data from over 24,000 participants from around the world and has identified a number of genetic variants significantly associated with deep and periventricular WMHs. The results confirm that these two sub-classifications of WMH have distinct but also overlapping aetiology. This work is currently being written up for publication.

Funding: NHMRC, Thomas Foundation

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

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

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

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

Findings: A number of other genetic and epigenetic projects are underway and we have contributed data/results to these studies during 2018, including examining copy number variants and neuroimaging traits.

Funding: NHMRC, Thomas Foundation

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

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

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

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

Findings: CHeBA studies (Sydney MAS, OATS) have contributed to a number of projects on a variety of phenotypes using not only genetic data but also epigenetic data (e.g. DNA methylation). A study of over 300,000 individuals identified 148 independent genetic loci for general cognitive function. This work was published in Nature Communications in 2018 by Davies et al. In another CHARGE Consortium study, seven significant genetic variants were identified for lateral ventricle volume. This study used a sample of over 23,000 participants from the CHARGE consortium (Vojinovic et al., *Nature Communications*, 2018).

Funding: NHMRC, Thomas Foundation

Heritability of gene expression

CHeBA staff: Karen Mather, Anbupalam Thalamuthu, Sri Chandana Kanchibhotla, Perminder Sachdev.

Other key investigators: Professor Bernhard Baune (University of Adelaide), Liliana Ciobanu (University of Adelaide).

Aim: To estimate the heritability of gene expression.

Findings: This work examines gene expression microarray data from the Older Australian Twins Study to analyse the contribution of genetics and environment to expression levels. The results suggest that there are heritable transcripts (n=128), with a mean heritability of 74%, as well as non-heritable gene transcripts, suggesting that genetics as well as environmental factors are important in the regulation of gene expression. This work is currently being written up for publication.

Funding: NHMRC

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

CHeBA staff: Perminder Sachdev, Henry Brodaty, Yvonne Leung, John Crawford, Nicole Kochan.

Other investigators: Study leaders and their colleague from among 18 ICC-Dementia member cohorts.

Aims:

- Determine the prevalence of dementia, cognitive and functional impairments in people over the age of 95 years across countries and ethnic groups using common diagnostic criteria.
- Identify and examine commonality and differences in risk and protective factors for dementia and cognitive impairment between international cohorts.
- Identify and examine biological markers of cognitive disorders common to the different cohorts.

Findings: We combined data received from 18 centenarian studies across 11 countries using a harmonisation protocol we developed. In total, we collected sociodemographic and neuropsychological data from over 4000 centenarians and near centenarians (aged 95+) from around the world, which made our study the largest analysis of global dementia prevalence in the oldest-old to date. We estimated a global dementia prevalence to be close to 52% based on results from the population-based studies. Risk of dementia was higher in women and it increases significantly with age, from 32% before reaching 100, 60% between 100 to 104 years old, to 73% beyond 105 years old. More years of education were significantly associated with lower risk of dementia, from a prevalence of 53% in people who had attained primary school education or less, to 31% in those who had attained higher education beyond high school. Our study found large differences in

dementia prevalence across studies, which might be due to the variations in sampling strategies, sample size, and possibly also differences in culture, social resources and model of care in each country. Further analysis currently being undertaken to understand this phenomenon.

Funding: Direct donations to The Dementia Momentum

Identifying expression quantitative trait loci (eQTLS) in older adults

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

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

Aim: Identify genetic variants associated with gene expression

Findings: Cis and trans SNPs controlling the expression level of genes (eQTLs) have been identified using association tests controlling for age, sex, batch effects and cell counts in the Sydney MAS cohort. . This analysis will be extended to the OATS cohort, which will be used as a replication cohort for the significant eQTLs identified in Sydney MAS. Other publicly available eQTL databases will also be used for replication of the results. The eQTL analysis will help determine the function of SNPs that are associated with age-related phenotypes. This work will be written up by PhD candidate, Liliana Ciobanu.

Funding: NHMRC

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

CHeBA staff: Maboobeh Hosseini (Biobank Officer), Kristan Kang, Anne Poljak (conjoint), Karen Mather, Henry Brodaty, Perminder Sachdev.

Aims:

- Inventory and aliquot samples for ready distribution to researchers.
- Improve the safety of sample storage by aliquoting and transferring samples into -80^{o}C and vapour phase storage.
- Setup of a biobanking subcommittee and preparation of a Biobank Ethics submission.

Findings: Aliquoting of MAS samples (all waves which have plasma) has been completed, and . OATS samples aliquoting is currently in progress (W1 completed). Biobanking is an ongoing project for remaining stored CHeBA blood samples, as well as new samples coming for additional waves of existing projects, or any new projects.

Funding: NHMRC and UNSW MREII 2015

Improving clinical diagnosis of mild neurocognitive disorders using neuropsychological assessment

CHeBA staff: Nicole Kochan, Perminder Sachdev, Henry Brodaty, John Crawford, Adam Bentvelzen.

Other investigators: Claudia Woolf (University of Sydney).

Aims:

- Establish Australian normative data for neuropsychological measures used in the assessment of cognition.
- Improve usability of neuropsychological test performance in persons from culturally and linguistically diverse (CALD) backgrounds by investigating the influence of cultural, linguistic and educational factors.

Findings:

- Psychometric and normative data have been acquired for the Telephone Interview for Cognitive Status – Modified (TICS-M), a popular telephone-based cognitive screening instrument. Data were drawn from the Sydney Memory and Ageing Study from 617 participants, aged 71-91 years. An online normative data calculator has been developed and will be made available for clinical and research use. A publication of this work is being prepared for submission.
- Normative data tables for another commonly used cognitive screening test – *The Addenbrooke's Cognitive Examination – Revised (ACE-R)* have been developed using data collected from the Sydney Centenarian Study. These normative scores are drawn from an extraordinary group of individuals, aged 95-104 years of age who remain cognitively well (non-demented). We expect the ACE-R

normative data will be useful in clinical practice to evaluate cognitive function in the oldest-old. The paper is being written up for publication.

Funding: DCRC – Assessment and Better Care, UNSW Sydney

Longitudinal course of post-stroke cognitive impairment across ethno-racial groups and geographic regions: an individual participant data meta-analysis from the STROKOG consortium

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

Other investigators: STROKOG collaborators.

Aims:

- examine the longitudinal course of post-stroke cognitive function in a diverse group of international post-stroke cohorts;
- investigate how rates of cognitive decline varied among STROKOG international studies by stroke subtype, gender, educational attainment, and ethno-racial groups.

Findings: Project proposal was approved by the RSC in late 2018. Data request began in Dec 2018. Currently awaiting data and will begin data cleaning and harmonization in the first part of 2019.

Funding: Vincent Fairfax Family Foundation

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

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

Other investigators: Dr Julia Muenchhoff (CHeBA Hon. Research Fellow), Dr Sonia Bustamante (BMSF, UNSW), Dr Donald Thomas (NMR Facility, UNSW).

Aims:

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

Findings: Using quantitative stable isotope dilution GC/MS we observed a significant age-dependent increase in the levels of D-serine, L-serine and glycine in the hippocampus of *O. degus* and APPsw/Tg2576 mice, together with a decline in L-alanine, and L-threonine. In human plasma, L-alanine, methylserine, glycine, D-serine and L-serine were higher in AD vs control plasma. We have a manuscript in draft reporting these results.

Funding: Thomas Foundation

Maintain Your Brain

CHeBA staff: Henry Brodaty, Perminder Sachdev, Gavin Andrews, Megan Heffernan (Coordinator), Tiffany Chau, Juan Carlo San Jose.

Other investigators:

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

Aims:

- Determine the efficacy of a multi-modal targeted intervention delivered on the internet to reduce the rate of cognitive decline in non-demented community-dwelling persons aged 55-77 years and in the long-term to delay the onset of dementia.
- Examine the cost-effectiveness of the program with a view to making this a national and potentially a globally suitable program.

Findings: Validation of outcomes measures study and pilot study are completed and undertaking analyses. Main trial commenced on June 2018.

Funding: NHMRC Dementia Team Research Grant

MINDSED: The effects of sedentary behaviour on cognitive function and cognitive decline in older persons without dementia

CHeBA staff: Darren Lipnicki, Perminder Sachdev.

Other investigators:

- Workgroup from the Radboud Medical Center (The Netherlands): Dr René Melis, Carlijn Maasakkers.
- Contributing COSMIC study leaders and associates: Representing cohorts from five countries.

Aim: Determine if sedentary behaviour is associated with poorer cognition, or predicts future poorer cognition, in older persons without dementia.

Findings: Across the five population cohorts examined, no negative association between total undifferentiated sedentary time and global cognition was found, cross-sectionally nor longitudinally. There is reason to believe that specific types of sedentary behaviour may differentially influence cognition depending on what a person is doing while sitting.

Funding: Direct donations to The Dementia Momentum Fund, NIH grant, NHMRC grant

Nursing competencies in care of the older person

CHeBA staff: Lynn Chenoweth.

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

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

Findings: The Nursing Aged Care Competencies (NACC) group consisted of 80 senior registered nurses working in the partner organisations. The e-Delphi included volunteer nurses working across 10 countries (90% in Australia). Participation rate ranged from 409 in round 1 to 139 in round 5: registered nurses (57%), nurse managers (30%) and nurse academics (13%). Over half of the participants had postgraduate qualifications (56%). A final set of core competencies generated a 98% (SD ±2) level of agreement: 1. Living Well for Older People across Communities and Groups; 2. Maximising Health Outcomes; 3. Communicating Effectively; 4. Facilitating Transitions in Care; 5. Facilitating Choices; 6. Partnering with Family Carers; 7. Promoting Psychological Well-being and Mental Health; 8. Providing Evidence-Based Dementia Care; 9. Providing Optimal Pain Management; 10. Providing Palliative Care; 11. Enabling Access to Technology. Participants also agreed that the domains of practice within the Geriatric Nursing (GerNurs) Competencies described two levels of practice for registered nurses working with older people and their families in nursing home and community care settings: essential and enhanced (60-88% levels of agreement). A final round of face-to face consultations is occurring with an expert panel from relevant government, professional and peak body organisations and aged care nurse academics. A pilot study of the GerNurs Competencies and supporting guidelines is currently in process across the NACC organisations, due for completion in May 2019. The pilot study findings will inform the final GerNurs Competencies, which will be presented to influential nursing organisations for their endorsement. Once approved, the GerNurs Competencies and supporting guidelines will be available on an accessible central website for use by individuals to monitor their professional development, and for the use of aged care organisations to support implementation of their strategic plans.

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

Olfactory ability and language test performance in Indonesian and Australian cohorts

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

Other investigators: Workgroup from the Atma Jaya Catholic University, Indonesia: Dr Yuda Turana, Dr Yvonne Handajani, Dr Tara Sani, Dr Josephine Widayanti, Ika Suswanti.

Aim: Investigate associations between olfactory ability and language function and Mini-Mental State Examination (MMSE) scores in Indonesian and White Australian cohorts.

Findings: In both Indonesians and White Australians, poor olfactory ability was associated with older age, less education, and lower MMSE and language test scores. Poor olfactory ability was associated with lower levels of low density lipoprotein cholesterol only among Indonesians, and with having diabetes or higher depression scale scores only among White Australians. Being female was associated with better olfaction in White Australians. Interventions for olfactory dysfunction might need to be tailored to specific ethno-regional groups. The role of language ability in OI test performance may be independent of race/ethnicity.

Funding: Direct donations to The Dementia Momentum Fund, NIH grant, NHMRC grant

Oxidative stress in AD

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

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

Aims:

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

Findings: Oxidative stress is a frequently reported feature of Alzheimer's brain, however less is known about AD plasma, though we and others have identified lower levels of antioxidants and vitamin binding proteins. We used stable isotope dilution GC/MS to quantify the ortho and meta isomers of tyrosine in AD relative to control plasma. These are specific markers of oxidative damage to proteins and we found higher levels in AD subjects vs normal controls in a small cross-sectional study. We are planning to extend this work to MCI subjects.

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

Personality and Total Health (PATH) Through Life project

CHeBA staff: Perminder Sachdev, Wei Wen, Anne Poljak.

Other key investigators: Australian National University: Associate Professor Nicholas Cherbuin, Professor Kaarin Anstey, Dr Moyra Mortby, Dr Erin Walsh, Dr Marnie Shaw, Dr Sid Chopra; Dr Elizabeth Luders (UCLA).

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

Findings:

Some salient findings from 2018 are listed below:

- On brain MRI, cortical sulci were examined in detail. On average, sulci were wider in old age participants compared to middle age participants. Differences in sulcal width were generally higher in males than females. Differences in the width of the superior frontal and central sulci were significantly associated with differences in the volume of adjacent local gyri, while age-related differences in the width of lateral and superior temporal sulci were associated with differences in whole brain cortical volume. These findings suggest that sulcal characteristics provide unique information about changes in local and global brain structure in aging (Jin et al, *Front Aging Neurosci*).
- The relationship between diabetes, BMI and bran volume was examined. Diabetes was most strongly associated with brain volumes. We found evidence of protective reserve from higher brain volumes and that a combination of high BMI and higher blood glucose was particularly concerning for individuals with lower brain volumes (Walsh et al, *Eur J Neurol*).
- Diabetes and brain structure and function: Type 2 diabetes is associated with smaller right putamen volume and lower Purdue Pegboard scores after controlling for age, sex and intracranial volume. These findings add to the evidence suggesting that higher blood glucose levels, especially type 2 diabetes, may impair brain structure and function (Zhang et al, *Psychiatry Res Neuroimaging*).
- Myelin content of the brain's white matte and neuropsychological function: We found that estimated myelin content of the bilateral anterior limb of the internal capsule and left splenium of the corpus callosum were significant predictors of processing speed, even after controlling for socio-demographic, health and genetic variables and correcting for multiple comparisons. We also found significant differences in estimated myelin content between middle-age and older participants in all six white matter tracts. The present results indicate that myelin content, estimated in vivo using a neuroimaging approach in healthy older adults, is sufficiently precise to predict variability in processing speed in behavioural measures (Chopra et al, *Neuroimage*).

Funding: NHMRC (administered by ANU)

Plasma proteomics biomarkers

CHeBA staff: Anne Poljak (conjoint), Tharusha Jayasena, Fei Song, Nicole Kochan, Julian Trollor (conjoint), Henry Brodaty, Perminder Sachdev, Gurjeet Kaur Virk (PhD student).

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

Aims:

- Determine if proteomic changes observed in MCI and AD plasma, relative to normal controls, would be reproducible across independent cohorts of similar design.
- Identify specific plasma proteins and protein families that are dysregulated in MCI and AD and validate these using ELISA assays and/or western blotting.
- Correlate the effects of plasma proteome changes with cognitive domain scores and brain volumetrics.
- Investigate the plasma proteome in Dominantly Inherited Alzheimer's Disease (DIAN) samples, using iTRAQ and improved plasma fractionation methodology.

Findings: To date our iTRAQ proteomics studies have identified differential expression in a number of protein family groups, including complement components, apolipoproteins, inflammation related proteins, coagulation pathways and vitamin carrier proteins. However our analysis to date has been hampered by rather low coverage of the plasma proteome, which has been limited so far to 100-150 proteins. We have recently adopted a new methodology, involving fractionation of the plasma proteins, which now provides coverage in the range of 1000-2000 proteins, including a number of proteins with high expression in the brain. We have a manuscript in progress describing the method, and more importantly the new technique provides a better tool to identify brain specific biomarkers. Our intention is to use the approach in the near future to explore the brain specific plasma proteome using Sydney MAS, DIAN and AIBL cohorts. A new Scientia funded PhD candidate, Gurjeet Kaur, is currently engaged on this project.

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

Prediction of the onset of dementia in older individuals using machine learning techniques

CHeBA staff: Perminder Sachdev, Henry Brodaty.

Other investigators: Annette Spooner (PhD student), Professor Arcot Sowmya (Computer Science & Engineering, UNSW), Professor Claude Sammut (Computer Science & Engineering, UNSW).

Aim: Develop techniques in artificial intelligence and machine learning to identify patterns in the data from the Sydney Memory and Ageing Study (MAS) and the Older Australian Twins Study (OATS) that could identify a set of biomarkers to predict the onset of dementia in its early stages.

Findings: The MAS and OATS datasets present significant challenges to machine learning. New methods are needed that can effectively analyse censored survival data that are heterogeneous, high-dimensional, longitudinal and contain missing values, in order to uncover new information about the onset of dementia, and in particular Alzheimer's disease. Existing techniques that address some of these challenges have been investigated and are currently being benchmarked, before the development of new techniques begins.

Funding: Australian Government RTP Scholarship

Relationship between body mass index and cognitive decline

CHeBA staff: Steve Makkar, Darren Lipnicki, John Crawford, Anbupalam Thalamuthu, Nicole Kochan, Henry Brodaty, Perminder Sachdev.

Other investigators: Contributing COSMIC study leaders and associates: Representing cohorts from around 15 countries.

Aim: Examine the association between body mass index (BMI) and the rate of prospective decline on general cognition and memory. Investigate whether this association:

- Differs between sexes.
- Is moderated by (baseline) age.
- Differs depending on carriage or non-carriage of the Apolipoprotein epsilon 4 (APOE*4).

- Is influenced by vascular risk factors.
- Differs between ethnicities, namely Whites and Asians.

Findings: Specific to older-aged (i.e., 80-year old) elderly female adults, higher BMI was associated with attenuated decline of general cognition, and obese (i.e., BMI≥30 kg/m^2) participants displayed a significantly slower rate of general cognitive decline compared to lower-normal participants. Between-sex comparisons indicated that both effects were significantly larger in women than men. BMI was not associated with cognitive decline in men overall. The association between BMI and decline of either general cognition or memory did not differ between APOE*4 carriers and non-carriers. The analysis of vascular risk factors indicated that the relationship between higher BMI and slower MMSE decline observed in older women was significantly weakened by the presence of vascular risk factors. Also, in this group, vascular risk factors counteracted the reduction in memory decline at higher BMI cut-points. In terms of ethnoregional differences:

- There was a stronger association between higher BMI and attenuation of memory decline, and a larger protective effect of obesity against MMSE decline in older Asian women versus White women.
- Although BMI was unrelated to cognitive decline in men as a whole, we found different effects of upper-normal weight (i.e., 23≤BMI<25 kg/m^2) on MMSE decline in older Asian and White men. Namely, upper-normal weight was more strongly related to MMSE decline in Asians compared to Whites.
- Overweight men (25≤BMI<30 kg/m^2) also displayed a significantly slower rate of MMSE decline than lower-normal weight men among Whites, but not Asians.

Funding: Direct donations to The Dementia Momentum Fund, NIH grant, NHMRC grant

Relationship between education, apolipoprotein epsilon 4 (APOE*4) and cognitive impairment

CHeBA staff: Steve Makkar, Darren Lipnicki, John Crawford, Anbupalam Thalamuthu, Nicole Kochan, Henry Brodaty, Perminder Sachdev

Other investigators: Contributing COSMIC study leaders and associates: Representing cohorts from around 15 countries.

Aim:

Examine whether years of education is associated with a reduced risk of cognitive impairment.

- Further explore the nature of this relationship, namely:
  - Whether the association between education and attenuated risk of cognitive impairment is nonlinear.
  - By treating education as categorical, to identify the maximum level of educational attainment that provides protection against cognitive impairment.
- Explore whether the protective effects of education against cognitive impairment are moderated by sex and age.
- To clarify the nature of ethnoregional differences in the relationship between education and the risk of cognitive decline.
- To determine whether education can reduce the risk of cognitive decline associated with carriage of the APOE*4 allele, and if these effects are moderated by sex, age, and ethnicity.

Findings: Education was associated with a reduced risk of cognitive impairment. This association, however, was non-linear, indicating that at very high levels of education, the reduction in the risk of cognitive impairment was less pronounced. Categorical analyses of education indicated that a middle level of education (i.e., about 8-11 years, typically signifying the completion of ***middle*** school or intermediate high school) significantly attenuated cognitive impairment risk relative to primary education (up to 5-7 years of education). These protective effects of middle education weakened with older age at baseline, and a trend for the effect to be larger in women than men. High school education did not provide significant additional protection against cognitive impairment risk relative to middle education. In terms of ethnoregional differences, compared to Whites, there was a larger protective effect of high school (versus primary) education in Asians, and a larger protective effect of middle (versus primary) education in Blacks. Middle education reduced the risk of cognitive impairment in non-APOE*4 carriers, but not among APOE*4 carriers, both overall, and in White participants specifically. In Asians, however, both high school and middle education reduced the risk of cognitive impairment in APOE*4 carriers, compared to primary education. In Blacks also, middle school reduced cognitive impairment risk among APOE*4 carriers.

Funding: Direct donations to The Dementia Momentum Fund, NIH grant, NHMRC grant

Risk of AD associated with nullipara, and with number of children

CHeBA staff: Darren Lipnicki, Perminder Sachdev.

Other investigators:

- Dr Jong Bin Bae (workgroup leader), Professor Ki-Woong Kim: South Korea.
- Contributing COSMIC study leaders and associates: Representing cohorts from around 8 countries.

Aim: This study will expand upon an earlier COSMIC project to determine the risk of AD for women who never give birth, and the risk of AD associated with the number of children mothered or fathered.

Findings: Preliminary findings with more cohorts/countries support previous findings of five or more births being associated with an increased risk of AD, but no effect of nullipara on risk of AD. Analyses investigating effects of number of children are underway.

Funding: Direct donations to The Dementia Momentum Fund, NIH grant, NHMRC grant

Risk factor clustering and incident cognitive decline

CHeBA staff: Darren Lipnicki, Perminder Sachdev, Nicole Kochan, Steve Makkar, John Crawford, Henry Brodaty.

Other investigators:

- Dr Ruth Peters (workgroup leader), Dr Kim Kiely, Dr Moyra Mortby, Professor Kaarin Anstey: NeuRA/UNSW Sydney.
- Contributing COSMIC study leaders and associates: Representing cohorts from around 15 countries.

Aim: (1) To assess the presence of risk factor clusters (baseline risk factors for dementia and cognitive decline) in the COSMIC data sets (specific risk factors to include where available are smoking, low physical activity, sedentary lifestyle, poor diet, excess alcohol consumption, midlife obesity, high blood pressure, midlife high cholesterol and diabetes and depression); (2) If clusters are present, to evaluate the association of such clusters with incident dementia/cognitive decline/change in cognitive functioning over follow up. Two additional aims, if feasible, are (1) to look at whether possession of one or more APOE E4 alleles changes the prevalence or pattern of clustering and their relationship with cognitive outcome, and (2) evaluate the impact of clustering and patterns of clusters on imaging measures.

Findings: Preliminary analyses currently underway.

Funding: Direct donations to The Dementia Momentum Fund, NIH grant, NHMRC grant

Social engagement and variance in cognitive function

CHeBA staff*:* Anne-Nicole Casey (Postdoctoral researcher), Ross Penninkilampi (5th Year UNSW Doctor of Medicine candidate), Nicole Kochan, Perminder Sachdev, Henry Brodaty.

Other investigators*:* Professor Maria Fiatarone Singh (University of Sydney, Faculty of Health Sciences and Sydney Medical School, Sydney), Dr Zhixin Liu (Statistical consultant, UNSW Stats Central).

Aim: Conduct a systematic review and meta-analysis of literature investigating associations between social engagement and dementia risk. Investigate cross-sectional and longitudinal associations between social engagement and health-related quality of life with cognition using data from the Sydney Memory and Ageing (MAS) study.

Findings:

- Updated systematic review and meta-analysis of literature investigating associations between social engagement and dementia risk included 31 cohort and 2 case-control studies comprising 2,370,452 participants. Poor social engagement indices were associated with increased dementia risk, including having a poor social network and poor social support. There was a trend toward Loneliness as a risk factor for dementia, but no significant association. In long-term studies (≥10 years), good social engagement was modestly protective against dementia. Findings encourage interventions targeting social isolation and disengagement for dementia prevention.
- Analysis of baseline data from the Sydney Memory and Ageing Study indicated that a person's age, the number of years of education that they had received, experiencing depression, and the number of face-to-face contacts with friends and family that a person experienced per month predicted differences in specific areas of their cognitive function. After accounting for all other variables, reporting less than one face-to-face contact each month predicted lower Executive function. Reporting between one and four face-to-face contacts per month predicted decreases in Processing Speed and Language ability. Reporting fewer than five regular face-to-face contacts predicated lower overall cognitive function. Findings suggest that the type, frequency and number of social encounters

that older adults experience are associated with their cognitive functioning. However we still need to determine whether having fewer face-to-face contacts is a cause, or a consequence, of impaired cognition.

- Ongoing research will use longitudinal data from the Sydney Memory and Ageing Study to investigate the possibility of longer-term associations between social engagement and health-related quality of life and cognitive function over time.

Funding: Thomas Foundation

Social Orientation of Care in Aged Living (SOCIAL) Study: Meaningful relationships for people expressing dementia-associated neuropsychiatric symptoms in residential care

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

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

Aim: Identify the occurrence of and factors associated with meaningful relationships among people expressing dementia-associated neuropsychiatric symptoms in residential care.

Findings: Analysis at systems, situation and person levels is still in progress. Initial findings suggest that at the systems level, staff allocation in terms of role types and paid hours per staff per 24-hour day; care home organisation culture, processes and physical layout; the extent of dementia care training; and the interpretation and practice of 'quality of care' have an association with meaningful relationships in care. At the situation level, staff's number and type of interactions with residents coupled with the type and number of residents' emotional responses to the way staff and others interact with them, as well as a comparison of the care residences' functional and personhood network structures similarly suggest an association with meaningful relationships. At the person level, the residents' psychological rather than physical co-morbidities infer more of an association. Neither the Neuropsychiatric Inventory results nor the Barthel Index of Activities of Daily Living scores indicate an association. The frequency of family and friends' visits to residents and their connections with staff and visiting personnel suggest an association. Further analysis continues.

Funding: TBA

Stroke recovery associated with cognitive impairment: A population-based study

CHeBA staff: Perminder Sachdev, Jessica Lo.

Other investigators: Dr Clare Flach (King's College London) and other STROKOG collaborators

Aims: To determine how cognitive impairment in the first three months after stroke is associated with physical, mental, social and care needs up to five years post-stroke.

Findings: Analyses completed in 2018 with paper to be drafted in 2019. Abstract submitted to a European conference. Individuals who are cognitively impaired three months after stroke are at significantly increased risk of depression and disability in long-term follow-up.

Funding: Vincent Fairfax Family Foundation

Superparamagnetic iron oxide nanoparticles (SPIONs) as contrast agents for MRI of neurodegenerative pathology

CHeBA staff: Perminder Sachdev, Wei Wen, Nady Braidy.

Other investigators: Professor Richard Tilley (ARC Centre for Excellence in Convergent Bio-Nano Science and Technology (CBNS), UNSW), Scientia Professor Justin Gooding (CBNS, UNSW), Dr Andre Bongers (Biological Resources Imaging Laboratory (BRIL)/ National Imaging Facility, UNSW).

Aims:

- Develop and test a series of novel SPIONs that can penetrate the blood-brain barrier (BBB) and provide a superparamagnetic signal for MRI with limited toxicity. If successful, these can be used as vehicles for specific ligands to penetrate the brain and bind to amyloid and other abnormal brain proteins, which can then be imaged with MRI. The SPIONs, developed by Professor Tilley in the School of Chemistry, UNSW Sydney, have already been subjected to characterisation studies to determine their size, morphology, structure, and chemistry.
- Demonstrate BBB permeability of the nanoparticles.
- Examine neuronal and glial cell toxicity of the nanoparticles.
- Investigate cellular internalisation and membrane transport of the nanoparticles.

- Examine the paramagnetic properties of the nanoparticles using MRI.

Findings:

- In previous work our group has demonstrated the feasibility to coat specially designed nanoparticles with DMSA and Ab antibodies. The preliminary data from MRI relaxometry measurements demonstrate that that coated and tagged NP retained sufficient T2 relaxivity to enable detection in MRI.
- We also showed that these nanoparticles can cross the endothelial/astrocyte BBB model with little or no toxicity reported.
- Our preliminary data has shown that our nanopraticles can bind to Aβ plaques present in human cortical post-mortem AD brain section.

Funding: Sachdev Foundation, Yulgibar-Dementia Foundation, Australian Research Council Discovery Early Career Research Fellowship to Dr Nady Braidy

The additive and interactive effects of cerebrovascular and Alzheimer-type pathology in the aetiology of neurocognitive disorders

CHeBA staff: Perminder Sachdev, Nady Braidy, Anne Poljak (conjoint), Yue Liu (MSc candidate).

Other investigators: Professor Daniel Chan (Department of Aged Care and Rehabilitation, Bankstown-Lidcombe Hospital).

Aims:

- Develop a greater understanding of vascular factors that contribute to the aetiology and heterogeneity of Alzheimer's and related dementias, by examining both the additive and interactive effects of cerebrovascular and Alzheimer-type pathologies in humans and animal models, using a cross-disciplinary and integrative approach.
- Establish animal models for both AD (transgenic) and cerebral vessel disease (hypoperfusion, small vessel disease, transgenic) to examine the interaction of the two pathologies, and the role of inflammation, oxidative stress, mitochondrial dysfunction, permeability of the blood-brain barrier, and stress response in the genesis of either pathology.
- Discover peripheral markers of vascular risk and/or cerebral vessel disease which alone, or in combination with markers of AD, can predict the onset of clinical symptoms and disease progression.

Findings: At present, the molecular basis of vascular dementia (VaD) remains elusive. Plasma samples were collected from Bankstown-Lidcombe hospital with VaD patients (n=50) and normal controls (n=50). Lipids were extracted and liquid chromatography coupled to mass spectrometry was used to comprehensively analyze the plasma lipidome in VaD and normal controls. The abundance of glycerides were significantly higher in VaD than in normal controls. Ceramides(Cer), cholesterol(CHE), phopholipids and lysophospholipids for VaD were significantly lower in VaD than for normal controls. Sphingomyelin was not significantly different between the 2 groups. Lipidomics can help to predict development of VaD.

Funding: Australian Research Council Discovery Early Career Research Fellowship to Dr Nady Braidy

The effects of intravenous NAD+ on Ageing and Metabolic Syndrome

CHeBA staff: Nady Braidy.

Other investigators: James Clement (Better Humans Inc.).

Aims:

- Investigate the safety and tolerability of intravenous NAD+ as well as its efficacy in elevating NAD+ levels in healthy elderly people between the ages of 70 and 80.
- Determine whether intravenous NAD+ will significantly increase cellular concentrations of NAD+, improve the NAD+/NADH ratio, favourably change metabolic biomarkers, and upregulate expression of anti-ageing genes in elderly individuals.

Findings: We evaluated infusions of IV NAD+, 1000 mg/day for 6 days, in a population of 10 healthy adults between the ages of 70 and 80 years. Our data is the first to show that IV NAD+ increases the blood NAD+ metabolome ("NADome") in elderly humans. These findings were accompanied by increased concentrations of glutathione peroxidase -3 (GPX-3) and paraoxonase-1 (PON1), and decreased concentrations of 8-iso-prostaglandin F2α (8-iso-PGF2α), advanced oxidative protein products (AOPPs), protein carbonyl (PCO), C-reactive protein and interleukin 6. IV NAD+ infusions also altered the plasma lipid profile in a favourable manner. We also report a significant increase in the mRNA expression and activity of SIRT1 (a nuclear sirtuin), and Forkhead box O1 (FOXO1), and reduced acetylated p53 in peripheral blood mononuclear cells isolated from these subjects. No major adverse effects were reported in this study. The study shows that repeated

IV infusions of NAD+ are a safe and efficient way to slow down age-related decline in NAD+ levels and upregulate certain pro-longevity genes.

Recently, transdermal NAD+ patches have been used as a holistic approach to maintain energy levels and improve well-being. We evaluated the effect of a transdermal NAD+ patch (400 mg) for 24 h in a population of 8 healthy adults between the ages of 70 and 80 years. Our data is the first to show that transdermal NAD+ increases the plasma NAD+ metabolome (NADome) in elderly humans after 24 h. These findings were accompanied by decreased superoxide and NF-κB levels, increased nitric oxide (NO) levels, and increased platelet cGMP content, and SIRT1 activity. No major adverse effects were reported in this study. This study is the first to show that transdermal NAD+ patches are a safe way to increase blood NAD+ and improve vascular function in the elderly.

Five papers were published for this project.

Funding: Better Humans Inc., Australian Research Council Discovery Early Career Research Fellowship to Dr Nady Braidy

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

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

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

Aims:

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

Findings: A reliable and sensitive mass spectrometry based MRM method has been established in our laboratory (Jayasena et al *Scientific Reports* 2016 Oct 20; 6:35391) making quantification of all seven sirtuins in the human brain, with SIRT2 being the most abundant. Our post-doctoral fellow Tharusha Jayasena has plans to explore binding partners of the sirtuins, to gain greater insight into their functional roles. Furthermore she has been involved in developing an assay for NAD and metabolites (cofactor of sirtuins), publishing this work in 2018 (Bustamante, Jayasena et al *Metabolomics*, January 2018, 14:15, http://dx.doi.org/10.1007/s11306-017-1310-z). Two additional papers were published by our group in 2018 utilising this assay (Clement et al Rejuvenation Research. http://doi.org/10.1089/rej.2018.2077, and Braidy et al Antioxidants & Redox Signaling 2018 May 11. doi: 10.1089/ars.2017.7269), and two additional manuscripts are currently being drafted.

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

The neural correlates of memory improvement following transcranial direct current stimulation combined with cognitive training (tDCS + CT) in patients with amnestic mild cognitive impairment

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

Other investigators: Professor Colleen Loo (Black Dog Institute), Dr Donel Martin (Black Dog Institute), Associate Professor Marcus Meinzer (University of Queensland), Professor Caroline Rae (NeuRA).

Aim: Investigate the neural correlates for improved memory in people diagnosed with amnestic mild cognitive impairment (aMCI) receiving cognitive training (CT) combined with mild non-invasive brain stimulation (transcranial direct current stimulation (tDCS)) using functional magnetic resonance imaging (fMRI). Participants are a subset of a larger cohort drawn from a randomised control trial investigating tDCS combined with CT in aMCI.

Findings: We have now completed recruitment for this study and conducted initial analyses on pre- and post-treatment fMRI data for the 20 participants. These results showed no statistical differences between the 2 groups using conservative correction for multiple comparisons for regions of interest (ROIs) for the task related and resting state data. In early 2019 we plan complete a more sophisticated network based analysis (i.e., network based statistics) which would be more sensitive to changes.

Funding: Alzheimer's Australia Dementia Research Foundation

The transcriptomic profile of normal ageing in the human brain: An RNA sequencing (RNAseq) study using non-pathological, human post mortem brain tissue from two brain regions

CHeBA staff: Adith Mohan, Perminder Sachdev, Karen Mather, Anbupalam Thalamuthu, Dr Vibeke S Catts, Dr Mari Kondo.

Other investigators: Professor Marc Wilkins (Ramaciottti centre for genomics, UNSW), Dr Susan Corley (Ramaciottti centre for genomics, UNSW), Dr Madhav Thambisetty (National Institute on Aging, USA).

Aims:

- Undertake a discovery driven RNA sequencing (RNAseq) study to examine age-associated changes in the gene expression profiles of two distinct human brain regions, the dorsolateral prefrontal cortex (DLPFC), and the posterior cingulate cortex (PCC).
- Identify changes in cortical gene expression that may drive changes in neocortical plasticity, as well the excitation-inhibition imbalance known to occur in the ageing human brain.

Findings: Post mortem tissue cohort assembled, RNA sequencing to commence in February 2019.

Funding: NHMRC

The Older Australian Twins Study (OATS)

CHeBA staff:

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

Study Coordinator: Vibeke S. Catts

NSW Administrative Assistant: Suzy Forrester

Data Manager: Kristan Kang

Other Researchers: Anne Poljak (conjoint), Jiyang Jiang, Jessica Lazarus (PhD student), Ruby Tsang (PhD student), Helen Wu (PhD student), Annette Spooner (PhD student), Rebecca Koncz (PhD student), Liliana Ciobanu (PhD student), Andrea Lammel (PhD Student), Matthew Wong (PhD student), Russell Chander (PhD Student), Abdullah Alqarni (PhD Student), Heidi Foo (PhD Student), Maboobeh Hosseini (Masters student), Emily Hartman (Honours student), Wey-Lynn Liew (ILP student), Sri Chandana Kanchibhotla, Mari Kondo.

Other investigators and staff:

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

Other Researchers: Dr Michelle Lupton (QIMR Berghofer Medical Research Institute), Nicola Armstrong (Murdoch University).

Aims:

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

Findings:

- We analysed data for the amyloid imaging project which investigates the deposition of amyloid plaques in the brain using positron emission tomography (PET) scans in 207 individuals. The majority of participants also provided a blood sample for genetics analysis and had a structural MRI scan of their brain. Preliminary analysis of data from this study was presented at VasCog, the annual conference for the International Society of Vascular Behavioural and Cognitive Disorders in Hong Kong in September 2018.

- The OATS online project aims to give OATS access to more participants, particularly those in non-metropolitan areas. The online questionnaires have been conducted for most of our amyloid imaging project participants and we are modifying delivery to make it the best possible experience for our research volunteers. We have agreement to use computerised cognitive tests from Cogstate and Cambridge Brain Sciences, which will be incorporated into the online delivery of our assessments. We anticipate starting recruitment for the next wave of OATS in early 2019.
- OATS participants are assessed for their language ability using three neuropsychological tests, naming (BNT), letter fluency (FAS), semantic fluency (ANIMALS). Analysis of these data demonstrate that heritability for each of these measures varies, and is strongly influenced by level of education and a measure of global cognition. The heritability of ability differed between sexes, and was higher in women than men across the three tests. The study suggests that a common set of genes contribute to the correlations in ability across the three tests.
- Genetic data and measure of cognitive function from OATS participants contributed to a large study (total sample 300,486 individuals), which identified 148 genetic loci associated with general cognitive function. Many of these genetic loci are known to influence the risk of neurodevelopmental and neurodegenerative disorders, and well as physical and psychiatric illnesses and brain structure.
- Genetic data and MRI scans of brain structures from OATS participants contributed to a large study (total sample 23,533 individuals) of genetic contributions to brain ventricular volume. The brain ventricles are filled with cerebrospinal fluid which helps rid the brain of waste and cushions it and the spinal cord, and enlargement of ventricles have been associate with numerous psychiatric and neurological disorders. Seven independent genetic loci were associated with ventricular volume, including two regions associated with tau pathology and Alzheimer's disease risk, and two other regions associated with angiogenesis and small vessel disease.
- Using MRI images, white matter hyperintensities (WMH) can commonly be observed in middle-aged individuals and increasingly so with advancing age. These WMHs are a biomarker of cerebral ischemia and closely related to the pathological processes of stroke and dementia. The WMH burden is commonly evaluated visually, a time-consuming process prone to high inter-rater variability. Our team developed a reliable, efficient and fully automated process for detection of WMH in MRI images for use by the research community.
- DNA methylation is an epigenetic modification of the genome, which is influenced by an individual's genetic code and by exposure to various environmental factors. Recently, data obtained from blood samples collected from OATS participants and in other twin studies (total of 2299 individuals aged 0 to 90 years) suggested that the environment in utero is a major determinant of DNA methylation at birth, and importantly that the effects of this persist throughout life. Environmental factors shared by co-habiting family members (siblings and spouses) throughout the lifespan also contribute to higher correlations in DNA methylation in these individuals.
- To date, OATS have contributed data to 23 student projects, including 10 PhD projects using OATS samples and data in 2018. As part of her PhD, Helen Wu, is focusing on a small sub-sample of monozygotic twins, where PET scans revealed one twin has a high burden of amyloid and the other does not. The presence of plaques predicts memory decline and are one of the hallmark features of Alzheimer's Disease (AD). Helen is investigating gene expression in blood samples, with a specific focus on microRNA. MicroRNAs are an example of epigenetics, and is one way in which the environment influences gene expression. In monozygotic twins, who are genetically identical, changes in microRNA levels may be related to the differences in amyloid burden in the brain and it is hoped Helen's study will provide insight into the pathobiology of AD.
- A total of 44 OATS participants have consented to donate their brain upon death to the OATS brain donor program.

Funding: NHMRC

The organisation of the elderly connectome

CHeBA staff: Jiyang Jiang, Heidi Foo, Wei Wen, Anbupalam Thalamuthu, Perminder Sachdev.

Aims:

- Examine the core features of both structural and functional networks in the brain of the oldest of the old (centenarian) and how this compares to the brain of the young-old (e.g. 70 - 75) and previously published data.
- Examine whether changes in both structural and functional connectivity is predictive of cognitive performance in the elderly, especially the centenarians.

- Examine whether age-related changes in cognition can be predicted by changes in structural and functional connectivity.
- Our focus is now in the longitudinal changes of the elderly brain network using multiple time-points scans.
- Another new focus is the centenarian brain.

Findings: We examined functional default mode network of 57 centenarian brains using independent component analysis implemented in FSL. Comparisons of centenarian default mode networks with young-old (mean age: 78.3) default mode networks have revealed some interesting and significant differences. This work will be the focus of current project. We have also processed 60 DTI scans of the centenarians. Analysis is underway.

Funding: NHMRC

The prevalence of subjective cognitive decline in and across different geographical and ethno-cultural regions

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

Other investigators:

- Workgroup from the University of Leipzig, Germany: Susanne Roehr, Dr Alexander Pabst, Professor Steffi Riedel-Heller.
- Contributing COSMIC study leaders and associates: Representing cohorts from around 15 countries.

Aim: Establish the prevalence of subjective cognitive decline (SCD) in and across different geographical and ethno-cultural regions.

Findings: Data were analysed for 44,228 dementia-free individuals at least 60 years of age (mean = 73.3) and with a female proportion of 58.1 %. While the heterogeneity of SCD assessments was high, qualitative and quantitative measures showed comparable estimates, robustly suggesting an age- and sex-standardized SCD prevalence of one third in the population above 60 years of age. Regional income and education may be associated with differences in SCD prevalence.

Funding: Direct donations to The Dementia Momentum Fund, NIH grant, NHMRC grant

The relationship between diabetes mellitus, prediabetes and post-stroke cognitive impairment in diverse ethno-regional cohorts from the STROKOG consortium

CHeBA staff: Perminder Sachdev, Jessica Lo, John Crawford.

Other investigators: STROKOG collaborators.

Aims: To explore the relationship between diabetes and pre-diabetes with cognitive function in 5 cognitive domains at 3-6 months post-stroke in diverse ethno-racial groups.

Findings: Key analyses completed in 2018 with paper to be drafted in 2019.

Funding: Vincent Fairfax Family Foundation

The role of polyphenolic compounds in modulating AD pathology

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

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

Aims:

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

Findings: We are exploring the efficacy of polyphenols to prevent the neurotoxicity, using astrocytes as a brain cell model for oxidative stress and amyloid toxicity. The polyphenols, EGCG, resveratrol and curcumin, displayed neuroprotective properties by preventing loss of cell viability caused by amyloid and transition metals. This work will be extended with a new UPA funded PhD candidate, Fatemeh Khorshidi, who will explore the mechanisms by which polyphenolic compounds may be neuroprotective.

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

The Sydney Centenarian Study (SCS)

CHeBA staff: Perminder Sachdev, Henry Brodaty, John Crawford, Wei Wen, Nicole Kochan, Karen Mather, Adam Theobald, Kristan Kang, Fleur Harrison, Yvonne Leung, Anbu Thalamuthu, Jiyang Jiang, Catherine Browning, Mary Revelas (PhD student), Adrian Cheng (ILP student).

Aims:

- Determine the prevalence of major medical and neuropsychiatric disorders in individuals aged ≥95 years.
- Establish tools for the valid assessment of cognitive function in centenarians.
- Examine brain structure and function in centenarians and relate it to neuropathology.
- Determine the major genetic and environmental factors that influence longevity and normal cognitive function.
- Explore the determinants of 'successful ageing'.

Findings:

- We performed analyses with the baseline data collected from 343 participants recruited from seven local government areas in Sydney. Results indicated that dementia prevalence was 25.53% among men and 40.95% among women. Centenarians had the highest prevalence of 47.22%, while participants aged 95-96.99 and 97-99.99 showed a prevalence of 28.42% and 46.73% respectively.
- Risk of dementia increased with age and decreased with more years of education. However, we did not find any significant sex differences after other sociodemographic and clinical statuses were considered.
- Participants with hypertension but never had medication also had a significantly higher risk of having dementia than those without or on medication.
- Men showed significantly better performance and women in language and visual-spatial related cognitive tests and less cognitive decline. However, they performed worse than women in tests on psychomotor speed. Similar to the results on dementia risk, more years of education was associated with better performance in a number of cognitive tests and less cognitive decline.
- A meta-analysis including data from SCS showed five out of nine genetic variants were significantly associated with exceptional longevity. For example, the APOE ε4 variant that is a major risk factor for Alzheimer's disease, was also associated with a decreased chance of living to an exceptional age. This work suggests that cardiovascular pathways may play a crucial role in longevity.

Funding: NHMRC

The Sydney Memory and Ageing Study (Sydney MAS)

CHeBA staff: Henry Brodaty, Perminder Sachdev, Julian Trollor (conjoint), Brian Draper (conjoint), Nicole Kochan, Kristan Kang, John Crawford, Karen Mather, Wei Wen, Adam Bentvelzen, Katya Numbers (Study Coordinator).

Other staff: Liesbeth Aerts (UNSW).

Aims:

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

Findings:

- Mild cognitive impairment (MCI), defined as subjective impairment in cognition confirmed by objective cognitive assessment in absence of significant functional decline is considered an intermediate stage between normal aging and dementia. We found that objective assessment of cognitive impairment alone is a better predictor of progression to dementia than a formal MCI diagnosis, no matter how it was operationalised, in a community sample. Clinical assessment procedures need to be refined to improve the identification of pre-dementia individuals (Brodaty et al., *The American Journal of Geriatric Psychiatry)*. Subjective cognitive decline (SCD) is the subjective experience of cognitive decline in the absence of objective impairment on cognitive assessments. We found that SCD preceded Alzheimer's and other dementias. Additional risk factors included age, performance on a brief cognitive screen (MMSE), apolipoprotein ε4 status and recruitment setting (Rosalinde, et al., *Alzheimer's & Dementia*).
- Obesity is linked to general quality of life in general adult population. This study was one of the first to examine the cross-sectional and longitudinal

relationships between obesity and aspects of quality of life in elderly adults. Obesity was associated with and predicted lower quality of life in community dwelling elderly Australians aged 70–90 years. The areas most affected by obesity in older adults were independent living, social relationships and the experience of pain *(Wang, et al., Quality of Life Research).*

- Cerebral microbleeds (CMB) are common in patients with cerebrovascular disease and in those with cognitive impairment. This study examined the relationship between CMB, cognitive decline and incident dementia in non-demented community-dwelling older Australians. The presence of CMB were not associated with increased progression to dementia. However, CMB were associated with impairments in specific cognitive domains: executive function and visuospatial ability, independent of other markers of cerebrovascular disease. This suggests a direct contribution CMB to cognitive impairment regardless of an underlying association with incident dementia (Paradise, et al., *Brain Imaging and Behavior*).
- Blood levels of growth differentiation factor-15 (GDF-15) have been associated with various pathological processes and diseases, including cardiovascular disease and cancer. Prior studies suggest genetic factors play a role in regulating blood GDF-15 concentration. The current study is the largest genome-wide association study to date to explore the genetic variants associated with GDF-15 blood concentration. Gene-based analysis confirmed the locus on chromosome 19 was associated with GDF-15 blood concentration with evidence for a potential new locus on chromosome 1 (Jiang, et al., *Frontiers in Genetics*)

Funding: NHMRC

The VASCOG criteria for vascular cognitive disorders: a validation study

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

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

Findings: The VASCOG criteria have greater sensitivity, modest concurrent validity and better predictive validity than older criteria for vascular dementia, but comparable to the DSM-5 and VICCCS criteria. Their operationalisation and inclusion of a mild VCD category make them attractive for clinical and research applications.

Funding: Direct donations to The Dementia Momentum Fund

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

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

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

Aim: Identify differentially expressed genes associated with ageing-related phenotypes.

Findings: This work is ongoing with analyses using data from both the Sydney Memory and Ageing Study and the Older Australian Twins Study, examining a variety of phenotypes. Replication cohorts are currently being sought for this work, including cohorts from the CHARGE Consortium.

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

Upregulation of NAD+ Anabolism to Promote Lifespan

CHeBA staff: Nady Braidy.

Other investigators: Dr Kristine McGrath (UTS), Dr Mojtaba Golzan (UTS).

Aims:

- Determine the effect of SIRT2 transgene on lifespan and underlying age-related degeneration in chow and high fat diet fed aged Wistar rats.
- Examine whether SIRT2 over-expression alters NAD+ levels and improves cognition in chow and high fat diet fed aged Wistar rats.
- Measure the changes in intracellular NAD+ levels and SIRT2 expression in physiologically aged Wistar rats treated with the natural polyphenols: resveratrol (increases NAD+ synthesis) and apigenin (an inhibitor of the NAD+ degrading enzyme CD38).
- Assess whether treatment with the apigenin and resveratrol, can extend lifespan, delay age-related degeneration, and delay/postpone cognitive decline in aged Wistar rats.

Findings: We tested whether restoration of NAD+ levels in the brain of obese mice can improve brain function. Increasing NAD+ levels enhanced insulin secretion in a SIRT1-dependent manner, and reduced brain oxidative stress and neuroinflammation. We also identified a novel compound oxaloacetate as a 'new' precursor for the promotion of NAD+ anabolism. Five studies were published for this project.

Funding: Better Humans Inc., Australian Research Council Discovery Early Career Research Fellowship to Dr Nady Braidy

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

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

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

Aim: Identify differentially methylated regions of the genome and/or environmental factors associated with various traits.

Findings: Analyses continue to be undertaken seeking to identify epigenetic and environmental factors that contribute to discordance of various age-related phenotypes. PhD student, Helen Wu, has examined miRNA expression differences in brain amyloid discordant identical twins from OATS and found several differentially expressed miRNAs. These results are currently being written up for publication.

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

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

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

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

Aims:

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

Findings: Dr Fei Song has evaluated an ELISA assay for VDBP, which will facilitate her work on MCI and AD plasma. Methods development is in progress to evaluate a VDBP ELISA method.

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

COMPLETED PROJECTS

Anatomical mapping of white matter hyperintensity - TOPMAL (Toolbox for probabilistic mapping of lesions)

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

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

Aim: Investigate whether associations between regional white matter hyperintensities (WMH) and cognition are independent of global grey matter (GM) and white matter (WM) volumes, which have also been linked to cognition.

Findings:

- We created a new module called TOPMAL (TOolbox for Probabilistic MApping of Lesions) to expend our pipeline's (UBO Detector, see https://cheba.unsw.edu.au/research-groups/neuroimaging/pipeline) functionalities. TOPMAL can be used for mapping white matter WMH burdens to strategic WM tracts. Together with UBO Detector, this new module is open-source and open to all for downloading.
- This new module has been tested with a a community-based cohort of 466 older individuals. We examined the associations of WMH loadings on strategic WM tracts with cognitive domains and diagnostic classifications (mild cognitive impairment vs. cognitively normal), and compared them with the relationships of total WMH, GM and WM volumes with cognition. We found that regional (fibre tract specific) WMH burdens were independently associated with poorer performance in processing speed (e.g. cingulum, inferior fronto-occipital fasciculus, and uncinate fasciculus), and executive function (inferior fronto-occipital fasciculus, uncinate fasciculus, anterior thalamic radiation, superior longitudinal fasciculus). The findings emphasize the association of regional WM deficit with cognitive decline, and the importance of studying the distribution of structural lesions in ageing and neuropathology.
- A journal paper was published in 2018: Jiang, J., Paradise, M., Liu, T., Armstrong, N. J., Zhu, W., Kochan, N. A., Brodaty, H., Sachdev, P. S., Wen, W. The association of regional white matter lesions with cognition in a community-based cohort of older individuals, NeuroImage: Clinical 19:14-21, doi. org/10.1016/j.nicl.2018.03.035 (2018).

Funding: NHMRC, John Holden Family Foundation

Genetic influences on cerebral blood perfusion using arterial spin labelling (ASL) data

CHeBA staff: Jiyang Jiang, Anbupalam Thalamuthu, Forrest Koch, Wei Wen, Perminder Sachdev.

Aim: Examine the heritability of cerebral blood flow (CBF) using a community-based cohort of twins.

Findings: Adequate CBF is necessary to maintain brain metabolism and function. ASL is an emerging MRI technique offering a non-invasive and reliable quantification of CBF. The genetic basis of CBF has not been well documented, and one approach to investigate this is to examine its heritability. Our project aimed to examine the heritability of CBF using ASL data from a cohort of community-dwelling older twins (including both monozygotic and dizygotic twin pairs; aged between 65-93 years). We have found:

- The cerebral cortex had higher CBF than subcortical grey matter (GM) regions, and CBF in the GM regions of the anterior cerebral artery (ACA) territory was lower than that of the middle (MCA) and posterior (PCA) cerebral arteries.
- After accounting for the effects of age, sex and scanner, moderate heritability was identified for global CBF, as well as for cortical and subcortical GM and the GM in the major arterial territories.
- Strong genetic correlations were found between CBF in subcortical and cortical GM regions, as well as among the three arterial territories (ACA, MCA, PCA), suggesting a largely convergent genetic control for the CBF in brain GM.
- The moderate heritability of CBF warrants future investigations to uncover the genetic variants and genes that regulate CBF.

A journal paper is currently under revision.

Funding: John Holden Family Foundation

Inflammatory markers and brain structure

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

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

Aims:

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

Findings: This project was completed last year with a meta-analysis as the latest publication of the project in 2018. The findings published in the last two years by our group, which explored the relationship between blood levels of macrophage inhibitory cytokine-1 (MIC-1) and brain grey matter and white matter, have been strengthened by this meta-analysis which found that MIC-1 was associated with various pathological processes and diseases. In this meta-analysis, we conducted the largest genome-wide association study (GWAS) to date using a sample of ~5,400 community-based Caucasian participants, to determine the genetic variants associated with MIC-1 blood concentration. Conditional and joint (COJO), gene-based association, and gene-set enrichment analyses were also carried out to identify novel loci, genes, and pathways. Consistent with prior results, a locus on chromosome 19, which includes nine single nucleotide polymorphisms (SNPs), was significantly associated with blood MIC-1 concentration. In conclusion, a locus on chromosome 19 was associated with MIC-1 blood concentration with genome-wide significance, with evidence for a new locus (chromosome 1). Future studies using independent cohorts are needed to confirm the observed associations especially for the chromosomes 1 locus, and to further investigate and identify the causal SNPs that contribute to MIC-1 levels.

There was one journal paper published in 2018: *Jiang J, Thalamuthu A, Ho JE, Mahajan A, Ek WE, Brown DA, Breit SN, Wang TJ, et al. (2018), A Meta-Analysis of Genome-Wide Association Studies of Growth Differentiation Factor-15 Concentration in Blood. Front Genet 9:97.*

Funding: NHMRC, John Holden Family Foundation.

Profile and risk factors of post-stroke cognitive impairment in diverse geographical and ethno-racial groups: An individual participant data meta-analysis from the STROKOG consortium (Formerly called: Profile of cognitive impairment at 3 to 6 months post-stroke or TIA in diverse geographical and ethno-cultural settings as represented by the STROKOG member cohorts)

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

Other investigators: STROKOG collaborators.

Aims:

- Harmonise shared data from STROKOG studies.
- Perform joint analyses using combined, harmonised data to estimate prevalence of post-stroke cognitive impairment.
- Compare prevalence estimates and profile of post-stroke cognitive impairment across geographical regions and ethnic groups.
- Perform individual participant data (IPD) meta-analysis on harmonised data to investigate the relationship between putative risk factors and cognitive function with greater statistical power.

Findings:

- From our combined sample of 11 hospital-based studies from Africa, Asia, Australia, Europe and USA, overall 45% of post-stroke or TIA participants were impaired in global cognition, and 30 to 35% in different cognitive domains, at 2-6 months after stroke or TIA.
- The degree of impairment was similar in the five cognitive domains (attention & processing speed, memory, language, perceptual motor and frontal executive function).
- The prevalence of impairment in global cognition was similar amongst Whites, Koreans, and Black Americans, and slightly lower in Singaporean Chinese and Black Nigerians; however, the

difference was not statistically significant. Additional studies in non-White groups are required to further explore ethno-racial differences in cognitive impairment.

- Diabetes and a history of past-stroke had strong negative effects on cognitive function in all domains; these effects were independent of stroke, age and gender. Hypertension, atrial fibrillation, and smoking had less strong or domain specific negative associations.
- A manuscript has been submitted to a journal and is currently under review.

Funding: Vincent Fairfax Family Foundation

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

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

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

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

Findings: Sixty-eight participants (45 females) completed the trial with thirty three participants receiving the active tDCS and cognitive training intervention. Although at the 3 month follow-up, both groups showed large sized memory improvements compared to pre-treatment, CT + Active tDCS did not produce greater memory improvement compared to CT + Sham tDCS. Our study findings raise the possibility that both active and sham tDCS may have enhanced the effects of CT. Based on the observed treatment effects, further study of this combined intervention for improving memory in aMCI is warranted. This manuscript has been submitted for publication.

Funding: Thomas Foundation, DCRC-ABC

White matter hyperintensity extraction pipeline development

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

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

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

Findings: A fully automated WMH detection and quantification pipeline has been created and it is now online for general neuroimaging research community to download at: https://cheba.unsw.edu.au/research-groups/neuroimaging/pipeline. A journal paper about the pipeline was published in 2018. A journal paper describing the methodology was published in *NeuroImage: Jiang, J., Liu, T., Zhu, W., Koncz, R., Liu, H., Lee, T., Sachdev, P.S., Wen, W. UBO Detector – A cluster-based, fully automated pipeline for extracting white matter hyperintensities. NeuroImage, doi. org/10.1016/j.neuroimage.2018.03.050 (2018)*.

Funding: NHMRC, John Holden Family Foundation

APPENDICES

APPENDIX A: STAFF LIST

Leadership

Henry Brodaty
Scientia Professor, *Co-Director CHeBA, Co-Leader Epidemiology Group, Montefiore Chair of Healthy Brain Ageing*

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

Angela (Angie) Russell
Centre Manager

Academic Staff

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

Anne-Nicole Casey
Postdoctoral Fellow

Vibeke Catts
Postdoctoral Fellow, *Older Australian Twins Study (OATS) Co-ordinator*

Lynn Chenoweth
Professor of Nursing

Debjani Das
Postdoctoral Fellow, *Social Cognitive Change in Late Adulthood (SocCog) Study*

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

Tharusha Jayasena
Postdoctoral Fellow, *Molecular Biology & Stem Cell Group*

Jiyang Jiang
Postdoctoral Fellow, *Neuroimaging Group*

Nicole (Nicky) Kochan
Research Fellow, *Co-Leader Neuropsychology Group; Leader – CogSCAN Study*

Mari Kondo
Vice Chancellor's Postdoctoral Fellow, *Genetics & Epigenomics Group*

Yvonne Leung
Postdoctoral Fellow, *ICC-Dementia Consortium Co-ordinator*

Darren Lipnicki
Postdoctoral Fellow, *COSMIC Consortium Co-ordinator*

Steve Makkar
Postdoctoral Fellow, *Consortia*

Karen Mather
Senior Research Fellow, *Leader Genetics & Epigenomics Group*

Adith Mohan
Research Fellow

Katya Numbers
Postdoctoral Fellow, *Memory & Ageing Study (MAS) Co-ordinator*

Anbupalam Thalamuthu
Postdoctoral Research Fellow

Wei Wen
Associate Professor, *Leader Neuroimaging Group, Director Neuroimaging Laboratory*

Professional & Technical Staff – Research

Karen Allison
Research Officer, *CogSCAN Study Co-ordinator*

Adam Bentvelzen
Research Assistant, *Memory & Ageing Study (MAS)*

Josephine (Josie) Bigland
Student Assistant (Casual), *Older Australian Twins Study (OATS) (until 30 August 2018)*

Research Assistant (Casual), *Maintain Your Brain Project (until 31 December 2018)*

Research Assistant (Casual), *CHeBA longitudinal studies*

Kim Burns
Research Assistant (Casual), *Maintain Your Brain Project (until 31 December 2018)*

Catherine Browning
Research Assistant, *Sydney Centenarian Study (SCS)*

Russell Chander
Research Assistant (Casual), *Maintain Your Brain Project (until 31 December 2018); CHeBA Longitudinal Studies*

Tiffany Chau
Research Assistant, *Maintain Your Brain Project*

John Crawford
Senior Statistician

Karen Croot
Research Officer, *CogSCAN Study*

Sumangali (Sumi) Gobhidharan
Research Officer, *Genetics & Epigenomics Group*

(Naga) Rekha Gorantla
Research Assistant (Casual) *(until 17 October 2018)*

Fleur Harrison
Research Assistant, *Sydney Centenarian Study (SCS)*

Michael Homer
Research Assistant (Casual), *Maintain Your Brain Project (until 15 November 2018)*

Mahboobeh (Mabi) Hosseini
Research Assistant, *CHeBA Biobank*

Sri Chandana Kanchibotla
Research Assistant, *Genetics & Epigenomics Group*

Kristan Kang
Research Manager (from November 2018)

Forrest Koch
Research Assistant (Casual), *Neuroimaging Group*

Rebecca Koncz
Research Assistant (Casual), *NSW Memory Clinic Network Project*

Man Chin Yo Yo Kun
Research Assistant (Casual), *Maintain Your Brain Project (until 31 December 2018)*

Yue Liu
Student Assistant (Casual), *Neuroimaging Group*

Jessica (Jess) Lo
Research Associate, *STROKOG Consortium Co-ordinator*

Naga Sowjanya Mutyala
Research Officer, *Genetics & Genomics Group*

Min Yee Ong
Research Assistant, *CogSCAN Study*

Matilda Rossie
Research Assistant, *CogSCAN Study*

Juan Carlo San Jose
Research Officer, *Maintain Your Brain Project*

Fei Song
Research Assistant (Casual), *Molecular Biology & Stem Cell Group (until 20 April 2018)*

Paul Strutt
Research Assistant, *Sydney Memory & Ageing Study (MAS) (until 3 April 2018)*

Adam Theobald
Research Officer, *Older Australian Twins Study (OATS) Coordinator*

Matthew Wallace
Research Assistant (Casual), *Maintain Your Brain Project (until 31 December 2018)*

Ashleigh Wesseling
Research Assistant, *Memory & Ageing Study (MAS) (until 19 Dec 2018)*

Professional & Technical Staff – Support

Alexandra (Alex) Bentley
Administrative Assistant *(from July 2018)*

Melissa Chungue
Administrative Assistant *(until April 2018)*

Kate Crosbie
Administrative Assistant (Casual)

Sophia Dean
Administrative Officer

Heidi Douglass
Communications & Projects Officer

Suzanne (Suzy) Forrester
Administrative Assistant, *Older Australian Twins Study (OATS)*

Michelle Savignano
Digital Communications Officer

Ashton Trollor
Student Assistant (Casual), *Older Australian Twins Study (OATS); Memory & Ageing Study (MAS) (until 31 December 2018)*

Conjoint & Adjunct Staff

Gavin Andrews
Emeritus Professor, Chief Investigator, *NHMRC Program Grant ID1093083*

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

Nicola Gates
Senior Lecturer *(2014-2018)*

Rebecca Koncz
Associate Lecturer *(2015-2018)*

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

Charlene Levitan
Adjunct Associate Lecturer *(2015-2019)*

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

Melissa Slavin
Senior Lecturer *(2014-2018)*

Julian Trollor
Professor, *Leader Neuroinflammation Group*

Visiting Academics

Bernhard Baune
Visiting Professorial Fellow *(January 2013 - present)*

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

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

CHeBA Honorary Research Fellows

Nicola Armstrong

Simone Reppermund

Haobo Zhang

APPENDIX B: EXTERNAL APPOINTMENTS

Dr Nady Braidy

- Honorary Fellow, Australian School of Advanced Medicine, Macquarie University
- Adjunct Lecturer, School of Biotechnology and Biomolecular Sciences, UNSW Sydney
- Health Services Advisor, Department of Aged Care and Rehabilitation, Bankstown-Lidcombe Hospital, Sydney, Australia
- Scientific Advisor, Better Humans Inc.
- Editor: *Current Alzheimer Research; CNS and Neurological Disorders; Analytical Cellular Pathology, oxidative metabolism and cellular longevity*
- Reviewer for ARC, NHMRC, European Research Council, German-Israeli Foundation for Scientific Research and Development

Professor Henry Brodaty

- Scientia Professor, Ageing and Mental Health, (previously Professor of Psychogeriatrics, 1990-2010), School of Psychiatry, UNSW Sydney (2011-present)
- Montefiore Chair of Healthy Brain Ageing (2012-present)
- Director, Dementia Centre for Research Collaboration, UNSW Sydney (2006-present)
- Acting Head of School of Psychiatry, UNSW Sydney (July 2017-present)
- Head (and Founder), Memory Disorders Clinic, Prince of Wales Hospital (1985 -present)
- Senior Clinician, Aged Care Psychiatry, Prince of Wales Hospital (1990-present)
- President International Psychogeriatric Association (2013-2015); Immediate Past-President (2015-2017)
- Member, International Advisory Committee of the National Institute of Dementia, South Korea (2013-present)
- Honorary Professor, Kiang Wu Nursing College, Macau (2014-present)
- Honorary Lifetime Vice-President, Alzheimer's Disease International (ADI) (2005-present)
- Honorary Medical Advisor, Dementia Australia NSW (1992-present)
- Chairman, Dementia Research Foundation Ltd, Dementia Australia (2002-2016) and member (2018-present)
- Member, Australian Advisory Board for Nutricia, (2012-present)
- Member, WHO Consultation Group on the Classification of Behavioural and Psychological Symptoms in Neurocognitive disorders for ICD-11 (2012-2016)
- WHO Advisory Group of Global Dementia Observatory (2015-2017)
- Ambassador, Montefiore Homes (2006-present)
- Chair, Clinical Advisory Committee, Montefiore Homes (2012-present)
- Expert Advisory Panel, NHMRC National Institute for Dementia Research (2016-present)
- Member, Commonwealth Department of Health, Consultative Group for Special Care Dementia Units (2017-present)
- Member, International Research Network for Dementia Prevention Advisory Group (2017-present)
- Editorial board member for *Aging and Mental Health* (1996-present), *Alzheimer Disease and Associated Disorders : an International Journal* (1995-present), *Alzheimers and Dementia: Journal of the Alzheimers Association* (2005-present), *Australian and New Zealand Journal of Psychiatry* (1981-present), *CNS Drugs* (1999-present), *Dementia and Geriatric Cognitive Disorders* (2010-present), *International Psychogeriatrics* (1996-2017), *Neurodegenerative Disease Management* (2010-present), *The Australian Journal of Dementia Care* (2012-present)
- Deputy Editor, *International Psychogeriatrics* (2017-present)

Professor Lynn Chenoweth

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

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

Dr Mari Kondo

- Visiting Fellow, John Curtin School of Medical Research, Australian National University

Dr Rebecca Koncz

- Senior Lecturer, Sydney Medical School, University of Sydney
- Staff Specialist, Sydney Local Health District
- Fellow, Royal Australian and New Zealand College of Psychiatrists (RANZCP)
- Member, Section of Neuropsychiatry, RANZCP
- Member, Section of Psychiatry of Intellectual and Developmental Disabilities, RANZCP
- Member, "Motivation" taskforce, The Human Affectome Project

Dr Teresa Lee

- Senior Clinical Neuropsychologist and Clinical Psychologist, Neuropsychiatric Institute, Prince of Wales Hospital
- Honorary Associate, Department of Psychology, Macquarie University
- Fellow, College of Clinical Neuropsychologists, Australian Psychological Society
- Fellow, College of Clinical Psychologists, Australian Psychological Society
- Member, Australasian Society for the Study of Brain Impairment
- Member, Behavior Genetics Association
- Approved Supervisor, College of Clinical Neuropsychologists, Australian Psychological Society

Dr Karen Mather

- Senior Research Scientist, Team Leader, Neuroscience Research Australia (NeuRA)

Dr Adith Mohan

- Consultant Neuropsychiatrist, Neuropsychiatric Institute, Prince of Wales Hospital
- Senior Lecturer, School of Psychiatry, UNSW Sydney
- Fellow, Royal Australian and New Zealand College of Psychiatrists (RANZCP)
- Committee member, Section of Neuropsychiatry, RANZCP

Dr Anne-Nicole Casey

- Research Coordinator, Susan Wakil School of Nursing and Midwifery, Faculty of Medicine and Health, University of Sydney, Evaluation study of the Meeting Centres Support Program (MCSP) Australian pilot

Dr Anne Poljak

- Senior Research Scientist, Bioanalytical Mass Spectrometry Facility, Mark Wainwright Analytical Centre, UNSW Sydney
- Conjoint Lecturer, School of Medical Sciences, UNSW Sydney
- Member, Scientific Review Committee, NSW Brain Bank Network (NSWBBN)
- Member, Scientific Advisory Committee, Rebecca L. Cooper Medical Research Foundation
- Member, Cochrane Community
- Reviewer, Alzheimer's Association International Conference (biomarkers, non-neuroimaging)

Professor Perminder Sachdev

- Scientia Professor, Neuropsychiatry (previously Professor of Neuropsychiatry, 1999-2009), School of Psychiatry, UNSW (2009- present)
- Clinical Director, Neuropsychiatric Institute, Prince of Wales Hospital, Sydney (1987-present)
- Visiting Fellow, Australian National University (2009-present)
- Visiting Professor, National University of Korea, Seoul (2014-2018)
- Visiting Professor, Jiao Tong University, Shanghai (2018- present)

- Committee Member of the WHO's Expert Advisory Committee for the Global Dementia Observatory (GDO)
- Executive Member of the International Society of Vascular Behavioural and Cognitive Disorders (VASCOG) (2012-present)
- Member, Scientific Program Committee, Alzheimer's Association International Conference
- Member, Expert Advisory Panel, NHMRC National Institute for Dementia Research
- Founding Executive Committee Member of the Tourette Syndrome Association of Australia (1989-present)
- Chair, Medical Advisory Committee of the Tourette Syndrome Association of Australia (1996-present)
- Fellow of the Australian Academy of Health & Medical Sciences (2015-present)
- Fellow of the NHMRC Academy 2011 (2011-present)
- Member of the NHMRC Assigner's Academy (2012-present)
- Invited Member, Task Force of the International League Against Epilepsy (ILAE) Neuropsychobiology Commission (2011-present)
- Editorial board for *Neuropsychiatric Disorders and Treatment*, *Acta Neuropsychiatrica, Current Opinion in Psychiatry*, *Middle Eastern Journal of Ageing*, *Middle Eastern Journal of Psychiatry & Alzheimer's*, *Brain and Mind Matters*, *The Open Neuroimaging Journal*, *American Journal of Geriatric Psychiatry*, *International Psychogeriatrics*
- Deputy Director, Alzheimer's Disease Network (ADNeT)
- Committee Member, Ageing Futures Institute, UNSW Sydney

APPENDIX C: POSTGRADUATE STUDENTS

CURRENT

Andrew Affleck

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

Abdullah Alqarni

- The association of cerebellar network with age-related cognitive decline
- PhD student
- School of Psychiatry, Faculty of Medicine, UNSW Sydney
- Supervisors: Associate Professor Wei Wen, Dr Jiyang Jiang, Professor Perminder Sachdev

Russell Chander

- Risk factors and biomarkers of alzheimer's disease and vascular dementia
- Scientia PhD student
- School of Psychiatry, Faculty of Medicine, UNSW Sydney
- Supervisors: Professor Perminder Sachdev, Associate Professor Wei Wen

Xi (Sophie) Chen

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

Lucia (Premilla) Chinnapa-Quinn

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

Heidi Foo

- Risk factors and biomarkers of alzheimer's disease and vascular dementia
- Scientia PhD student
- School of Psychiatry, Faculty of Medicine, UNSW Sydney
- Supervisors: Professor Perminder Sachdev, Associate Professor Wei Wen

Fleur Harrison

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

Fatemeh Khorshidi

- Pharmacological promotion of NAD+ anabolism to reduce ad pathology and delay cognitive decline
- PhD student
- School of Psychiatry, Faculty of Medicine, UNSW Sydney
- Supervisors: Dr Nady Braidy, Professor Perminder Sachdev, Dr Anne Poljak

Rebecca Koncz

- The relative genetic and environmental contributions to amyloid deposition in the brains of older adults: amyloid imaging using the twin design
- PhD student
- School of Psychiatry, Faculty of Medicine, UNSW Sydney
- Supervisors: Professor Perminder Sachdev

Jessica Lazarus

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

Matthew Lennon

- The relationship between hypertension and cognition

- Masters by Research student
- St Vincents Clinical School, Faculty of Medicine, UNSW Sydney
- Supervisors: Professor Perminder Sachdev, Dr John Crawford, Dr Steve Makkar

Yue Liu

- Dementia and neuroimaging
- PhD student
- School of Psychiatry, Faculty of Medicine, UNSW Sydney
- Supervisors: Professor Perminder Sachdev, Dr Nady Braidy, Dr Anne Poljak, Associate Professor Wei Wen

Janet Mitchell

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

Adith Mohan

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

Matthew Paradise

- Neuroimaging of cerebrovascular disease
- PhD student
- School of Psychiatry, Faculty of Medicine, UNSW Sydney
- Supervisors: Professor Perminder Sachdev

Mary Revelas

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

Upul Senanayake

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

Annette Spooner

- Machine learning techniques for identifying individuals at risk of developing Alzheimer's disease
- PhD student
- School of Computer Science and Engineering, Faculty of Engineering, UNSW Sydney
- Supervisors: Professor Arcot Sowmya, Professor Perminder Sachdev

Marina Ulanova

- Superparamagnetic iron oxide nanoparticles as contrast agents for mr imaging of amyloid beta plaques in alzheimer's disease
- PhD student
- School of Medical Sciences, Faculty of Medicine, UNSW Sydney
- Supervisors: Dr Nady Braidy, Dr Anne Poljak

Gurjeet Kaur Virk

- Development of blood biomakers for early onset Alzheimer's disease using discovery proteomics
- Scientia PhD student
- School of Psychiatry, Faculty of Medicine, UNSW Sydney
- Supervisors: Professor Perminder Sachdev, Dr Anne Poljak, Dr Nady Braidy

Jacqueline Wesson

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

Matthew Wong

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

Helen Wu

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

Mark Yates

- Does the dementia care in hospitals program reduce the incidence of hospital acquired adverse events in patients with cognitive impairment?
- PhD student
- School of Psychiatry, Faculty of Medicine, UNSW Sydney
- Supervisors: Professor Henry Brodaty

COMPLETED

Ruby Tsang

- Nature and nurture: Insights from genetic, environmental and epigenomic studies 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
- PhD conferred July 2018

APPENDIX D: AWARDS & PROMOTIONS

Dr Anne-Nicole Casey

- Kwan Fung and Yuet Ying Fung Healthy Brain Ageing Research Award
- Alzheimer's Association International Conference (AAIC) Travel Award
- Alzheimer's Disease International (ADI) Conference Travel Award

Dr Kristan Kang

- Promotion to Research Manager

Dr Nicole Kochan

- Promotion to Senior Lecturer in the School of Psychiatry

Dr Mari Kondo

- 2018 UNSW Sydney Career Advancement Award

Dr Yvonne Leung

- Kwan Fung and Yuet Ying Fung Healthy Brain Ageing Research Award
- Alzheimer's Association International Conference (AAIC) Travel Award

Dr Darren Lipnicki

- Promoted to Research Fellow

Dr Matthew Paradise

- Josh Woolfson Memorial Scholarship
- Yulgibar Alzheimer's Research Program Travel Award

APPENDIX E: RESEARCH GRANTS & FUNDING

GRANTS

Innovative approaches to the application of nanotechnology for specific diagnosis and treatment of the dementias

Funding Source: Dementia Australia Research Foundation (DARF) – Yulgilbar Innovation Grant
Project ID: RG181392
Investigator/s: Prof Perminder Sachdev, Prof Richard Tilley, Scientia Prof Justin J Gooding, Dr Andre Bongers, Prof Ashley Bush, Laureate Prof Frank Caruso, Dr Nady Braidy, Dr Lucy Gloag, Dr Karen Mather, Dr Anne Poljak, A/Prof Wei Wen
Duration: 3 years: 1 March 2019-1 March 2022
Total Funds: $1,000,000

Understanding cognitive disorders in relation to cerebrovascular disease in an international collaborative effort: The Stroke and Cognition (STROKOG) Consortium

Funding Source: NHMRC
Project ID: RG180366
Investigator/s: Prof Perminder Sachdev, A/Prof Wei Wen, Dr John Crawford
Duration: 3 years: 2019-2021
Total Funds: $649,205

Co-designing dementia diagnosis and post-diagnostic care (COGNISANCE)

Funding Source: National Health & Medical Research Council (NHMRC)
Project ID: RG181644
Investigator/s: Prof Henry Brodaty, A/Prof Lee-Fay Low, Prof Perminder Sachdev, Prof Yun-Hee Jeon, Dr Lyn Phillipson
Duration: 3 years: 2019-2021
Total Funds: $742,041

Social Health And Reserve in the Dementia patient (SHARED)

Funding Source: NHMRC
Project ID: RG181672
Investigator/s: Prof Henry Brodaty, Prof Perminder Sachdev
Duration: 3 years: 2019-2021
Total Funds: $724,254

Lipids in brain ageing and cognitive disorders

Funding Source: Rebecca Cooper Foundation
Project ID: RG182333
Investigator/s: Dr Anne Poljak, Prof Perminder Sachdev
Duration: 2 years: 2019-2020
Total Funds: $100,000

The Brain Ageing Research Laboratory (BARL) for collaborative research

Funding Source: UNSW / Research Infrastructure Scheme (RIS)
Project ID: RG182773
Investigator/s: Prof Perminder Sachdev, Prof Henry Brodaty, Dr Nady Braidy, Dr Anne Poljak, Dr Karen Mather, ..., Prof Julian Trollor, A/Prof Wei Wen, ..., Dr Adith Mohan, Dr Lucy Gloag, Dr Tharusha Jayasena, et al
Duration: 1 year: 2019
Total Funds: $179,167

A novel cellular approach for early detection of Alzheimer's disease, modelling and developing diagnostics

Funding Source: UNSW Medicine Neuroscience, Mental Health and Addiction Theme and SPHERE Clinical Academic Group Funding (Mindgardens Seed Funding Grant)
Project ID: PS50645
Investigator/s: Dr Nady Braidy, A/Prof Kuldip Sidhu, Prof Perminder Sachdev
Duration: 1 year: 2019
Total Funds: $20,000

The Australian Dementia Network (ADNet): Bringing together Australia's dementia stakeholders

Funding Source: NHMRC
Project ID: RG181548
Investigator/s: Prof Christopher Rowe, Prof Perminder Sachdev, Prof Sharon Naismith, Prof Michael Breakspear, Prof Henry Brodaty, Prof Kaarin Anstey, Prof Ralph Martins, Dr Stephanie Ward, Prof James Vickers, Prof Colin Masters
Duration: 5 years: 1 July 2018-30 June 2023
Total Funds: $18,000,000

Clarify risk and protective factors for dementia with the Interplay of Genes and Environment in Multiple Studies (IGEMS) Consortium

Funding Source: National Institute on Aging
Project ID: RG182556
Investigator/s: Prof Nancy Pedersen, ..., Dr Margaret Gatz, Dr Vibeke Catts, ..., Prof Perminder Sachdev, et al.
Duration: 5 years: 1 July 2018-30 June 2021
Total Funds: USD40,534.34

BRAIN-MEND: biological resource analysis to identify new mechanism and phenotypes in neurodegenerative diseases

Funding Source: National Health & Medical Research Council (NHMRC)
Project ID: RG173345
Investigator/s: Prof Naomi Wray, Dr Nicola Armstrong, A/Prof Ian Blair, A/Prof John Kwok, A/Prof Simon Laws, Dr Karen Mather, Dr Allan McRae, Prof George Mellick, Prof Perminder Sachdev
Duration: 3 years: 1 January 2018-31 December 2020
Total Funds: $42,154

COSMIC: An international consortium to identify risk and protective factors and biomarkers of cognitive ageing and dementia in diverse entho-racial groups and geographical settings

Funding Source: National Institute on Aging (NIA) | National Institutes of Health (NIH)
Project ID: RG172507
Investigator/s: Prof Perminder Sachdev, Prof M Ganguli, Prof Karen Ritchie, Prof Ki Woong Kim, Prof Richard Lipton, Prof Ron Petersen
Duration: 5 years: 15 September 2017-30 June 2020
Total Funds: USD2,573,572

Cross-comparison, validation and performance of computerised neuropsychological assessment devices in the evaluation of mild cognitive impairment and dementia (CogSCAN)

Funding Source: NHMRC
Project ID: RG163145
Investigator/s: Dr Nicole Kochan
Duration: 3 years: 2017-2020
Total Funds: $700,482

Social cognitive change in late adulthood (SocCog)

Funding Source: Australian Research Council (ARC)
Project ID: RG170732
Investigator/s: Prof Julie Henry, Prof Perminder Sachdev, Dr Karen Mather
Duration: 4 years: 2017-2020
Total Funds: $323,250

Infrastructure Support for the Centre for Healthy Brain Ageing (CHeBA)

Funding Source: Black Dog Institute/NSW Health Medical Research Support Program
Project ID: RG170787
Investigator/s: Prof Perminder Sachdev, Prof Henry Brodaty
Duration: 2 years: 2017-2020
Total Funds: $377,086

Modulation of SIRT2 through upregulation of NAD+ anabolism to promote lifespan

Funding Source: ARC - DECRA
Project ID: RG161166A | RG161166
Investigator/s: Dr Nady Braidy
Duration: 3 years: 2017-2019
Total Funds: $372,000

Involvement of SIRT3 and related energy metabolite changes in the Alzheimer brain

Funding Source: Alzheimer's Australia Dementia Research Foundation Dementia (AADRF)/Dementia Grants Program
Project ID: RG170876
Investigator/s: Dr Tharusha Jayasena, Prof Perminder Sachdev, Dr Anne Poljak, Dr Naidy Braidy
Duration: 2 years: 2017-2018
Total funds: $50,000

Centre of Research Excellence in Cognitive Health: Evidence, intervention and population modelling

Funding Source: National Health & Medical Research Council (NHMRC)
Project ID: RG173231-A (ex-RG161515)
Investigator/s: Prof Perminder Sachdev
Duration: 2 years: 2017-2018
Total Funds: $147,322

Slowing progression of Alzheimer's disease by modulating the kynurenine pathway

Funding Source: National Health & Medical Research Council (NHMRC)
Project ID: RG171146-A
Investigator/s: Dr Nady Braidy
Duration: 2 years: 2017-2018
Total Funds: $10,000

The role of peripheral blood microRNAs as biomarkers of Alzheimzer's disease

Funding Source: National Health & Medical Research Council (NHMRC)
Project ID: RG161785
Investigator's: Dr Karen Mather (Supervisor), NHMRC Postgraduate Scholarship for Dr Helen Wu
Duration: 2 years: 2017-2018
Total Funds: $83,867

Ageing and Cognition Clinics: A state-wide harmonised approach

Funding Source: UNSW Medicine Neuroscience, Mental Health and Addiction Theme and SPHERE Clinical Academic Group Funding (Mindgardens Seed Funding Grant)
Project ID: PS45977
Investigator/s: Prof Perminder Sachdev, Prof Henry Brodaty, Prof Sharon Naismith, A/Prof Peter Gonski, Dr Danielle Lasschuit, Dr Rowena Mobbs
Duration: 1 year: 2018

SJTU-UNSW Collaboration on Research in Cognitive Ageing and Dementia

Funding Source: UNSW / SJTU-UNSW Collaborative Research Fund – Seed Grant
Project ID: RG173379
Investigator/s: Prof Perminder Sachdev, A/Prof Wei Wen, Dr Jiyang Jiang, Dr Rebecca Koncz
Duration: 1 year: 2018

Risk factors, early diagnosis and effective interventions for neurocognitive disorders

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

BRIDGET: Brain imaging, cognition, dementia and next generation genomics: a transdisciplinary approach to search for risk and protective factors of neurodegenerative disease

Funding Source: NHMRC NIDR-EU JPND Co-funded Project Grant
Project ID: RG152067
Investigators: Prof Perminder Sachdev, Dr Karen Mather, Dr Anbupalam Thalamuthu, A/Prof Wei Wen, Dr Nicola Armstrong
Duration: 3 years: 2016-2018*
Total Funds: $1,081,489
***Extended to 31 December 2019**

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

Funding Source: NHMRC NIDR-EU JPND Co-funded Project Grant
Project ID: RG152100
Investigators: Prof Perminder Sachdev, Dr Karen Mather, Dr Anbupalam Thalamuthu, Dr Nicola Armstrong, Prof Henry Brodaty
Duration: 3 years: 2016-2018
Total Funds: $1,556,995*
***Extended to 31 December 2019**

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

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

Maintain Your Brain

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

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

Funding Source: Australian Society of Anaesthetists / PhD Grant Support
Project ID: RG123624
Investigator/s: Premilla Chinnappa-Quinn
Duration: 3 years: 2013-2015*
Total Funds: $9,091
***Extended to March 2017**

PHILANTHROPIC

The CHeBA Cerebral Small Vessel Disease (SVD) Fund

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

The Dementia Momentum Grants (excluding miscellaneous donations & Wipeout Dementia Campaign)

Funding Source: Henroth Investments Pty Ltd
Project ID: PS38235_PS38252
Awardees: Prof Perminder Sachdev
Prof Henry Brodaty
Duration: 5 years: 2016-2020
Total Funds: $90,000

Funding Source: Sachdev Foundation
Project ID: PS38235_PS38252
Awardees: Prof Perminder Sachdev
Prof Henry Brodaty
Duration: 2 years: 2016-2017*
Total Funds: $80,000
***Extended to 31 December 2018**

Funding Source: Vincent Fairfax Family Foundation
Project ID: PS42069_PS42704
Awardees: Prof Perminder Sachdev
Prof Henry Brodaty
Duration: 5 years: 2015-2019
Total Funds: $500,000

Funding Source: The Yulgilbar Foundation
Project ID: PS38235_PS38252
Awardees: Prof Perminder Sachdev
Prof Henry Brodaty
Duration: 5 years: 2015-2019
Total Funds: $250,000

New therapeutic strategies for the treatment of Alzheimer's disease

Funding Source: Biospecialties Australia Pty Ltd
Project ID: PS44710_PS44672
Awardee/s: Dr Naidy Braidy
Duration: 2 years: 2017-2018
Total Funds: $25,000

The Thomas Foundation Grant & Thomas Foundation Matching Funds

Funding Source: The Thomas Foundation
Project ID: PS34586_PS34589
Awardee/s: Prof Henry Brodaty
Prof Perminder Sachdev
Duration: 5 years: 2011-2015*
Total Funds: $1,000,000
***Extended to 31 December 2019**

SPONSORSHIP & OTHER

The Montefiore Chair of Healthy Brain Ageing at UNSW

Funding Source: Montefiore Home
Project ID: PS34587_PS34590
Awardee/s: Prof Henry Brodaty
Prof Perminder Sachdev
Duration: 5 years: 2017-2021
Total Funds: $529,183

The Healthy Brain Ageing Fund

Funding Source: Miscellaneous Donor Contributions
Project ID: PS22384_PS4163
Awardees: Prof Henry Brodaty
Prof Perminder Sachdev
Duration: Ongoing
Total Funds: $416,477*
***As at 31 December 2018**

Centre for Healthy Brain Ageing Event & Sponsorship Fund

Funding Source: Miscellaneous
Project ID: PS33379_PS33397
Awardees: Prof Henry Brodaty
Prof Perminder Sachdev
Duration: Ongoing
Total Funds: $18,827*
***As at 31 December 2018**

APPENDIX F: STATEMENT OF IN-KIND CONTRIBUTIONS

- Anthony Glick Photography
- ARIA Restaurant Sydney
- Bates Smart
- Blanca
- Bounce Australia
- Brain Snacks
- Charter Hall
- Colliers International Residential
- DHD Performance Surfboards
- Dripping Wet
- FDC Construction and Fitout
- Fine Fettle Foods
- Harvest Box
- Honkas Bar and Eats
- Hurley
- HWL Ebsworth Lawyers
- KPMG Sydney
- Loving Earth
- Monster Health Foods
- Pacific Mag – Men's Health
- Queenscliff Surf Life Saving Club
- Scentre Group
- Slim Secrets
- Stomp Surf Wax
- Surf Yogis
- The Bucket List
- The Happy Snack Company
- Think Products

APPENDIX G: STATEMENT OF FINANCIAL PERFORMANCE

STATEMENT OF FINANCIAL PERFORMANCE FOR THE YEAR ENDED 31 DECEMBER 2018

	Notes	2018 $	2017 $
Funds			
Research Revenue		3,592,567	3,011,949
Donations		922,881	866,627
Fees		-	-
Faculty Funds	3	-	-
UNSW Contribution - Competitive	1	40,164	29,636
UNSW Contribution - Strategic	2	-	39,507
Sundry Other Revenue		59,980	50,160
Total Funds		**4,615,591**	**3,997,879**
Costs			
People Costs		3,318,824	3,104,235
Scholarship Stipends		92,921	110,372
Contract & Consulting Services		1,124,527	378,725
Repairs and Maintenance		9	163
Consumables		116,534	132,717
Travel		83,889	81,039
Equipment		50,064	54,820
Other Expenses		54,418	139,007
Internal Expense		141,669	(41,322)
Total Costs	=	**4,982,854**	**3,959,755**
Operating result		(367,263)	38,125
Opening Balance		3,385,716	3,347,592
Closing Balance		**3,018,453**	**3,385,716**

Notes to the Statement of Financial Performance

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

APPENDIX H: PUBLICATIONS

Book Chapters

Sachdev P, Mohan A. Neuropsychiatry and key clinical competencies (Chapter 12). In: Faruqui RA, Agrawal N, Bodani M (Eds) *Oxford Textbook of Neuropsychiatry*. Oxford University Press: Oxford, UK. 2018; in press.

Journal articles

Brodaty H, Aerts L, Harrison F, Jessop T, Cations M, Chenoweth L, Shell A, Popovic GC, Heffernan M, Hilmer S, Sachdev PS, Draper B. Antipsychotic Deprescription for Older Adults in Long-term Care: The HALT Study. J Am Med Dir Assoc. 2018 Jul; 19(7):592-600.e7. DOI: 10.1016/j.jamda.2018.05.002. PMID: 29941156 [Epub 2018 June 27].

Bustamante S, Jayasena T, Richani D, Gilchrist RB, Wu LE, Sinclair DA, Sachdev PS, Braidy N. Quantifying the cellular NAD+ metabolome using a tandem liquid chromatography mass spectrometry approach. Metabolomics. 2018; 14(1):15. DOI: 10.1007/s11306-017-1310-z [Epub 2017 Dec 23].

Cations M, Draper B, Low L-F, Radford K, Trollor J, Brodaty H, Sachdev P, Gonski P, Broe GA, Withall A. Non-Genetic Risk Factors for Degenerative and Vascular Young Onset Dementia: Results from the INSPIRED and KGOW Studies. J Alzheimers Dis. 2018; 62(4):1747-1758. DOI: 10.3233/jad-171027. PMID: 29614682 [Epub 2018 Mar 27].

Chenoweth L, Jessop T, Harrison F, Cations M, Cook J, Brodaty H. Critical contextual elements in facilitating and achieving success with a person-centred care intervention to support antipsychotic deprescribing for older people in long-term care. Biomed Res Int. 2018; 2018:7148515. DOI: 10.1155/2018/7148515. PMID: 30069476 [Epub 2018 Aug 3].

Chopra S, Shaw M, Shaw T, Sachdev PS, Anstey KJ, Cherbuin N. More highly myelinated white matter tracts are associated with faster processing speed in healthy adults. NeuroImage. 2018 May 1; 171: 332-340. DOI: 10.1016/j.neuroimage.2017.12.069. PMID: 29274747 [Epub 2017 Dec 22].

Ciobanu LG, Sachdev PS, Trollor JN, Reppermund S, Thalamuthu A, Mather KA, Cohen-Woods S, Stacey D, Toben C, Schubert KO, Baune BT. Co-expression network analysis of peripheral blood transcriptome identifies dysregulated protein processing in endoplasmic reticulum and immune response in recurrent MDD in older adults. J Psychiatr Res. 2018 Oct 1; 107:19-27. DOI: 10.1016/j.jpsychires.2018.09.017. PMID: 30312913. [Epub 2018 Oct 13].

Clement J, Wong M, Poljak A, Sachdev P, Braidy N. The Plasma NAD+ Metabolome is Dysregulated in 'normal' Ageing. Rejuvenation Res. 2018; Aug 19. DOI: 10.1089/rej.2018.2077. PMID: 30124109. [Epub 2018 Aug 21].

Connors MH, Ames D, Woodward M, Brodaty H. Psychosis and clinical outcomes in alzheimer disease: a longitudinal study. Am J Geriatr Psychiatry. 2018 Mar; 26(3):304-313. DOI: 10.1016/j.jagp.2017.10.011. PMID: 29174998 [Epub 2017 Nov 28].

Connors MH, Ames D, Woodward M, Brodaty H. Predictors of driving cessation in dementia: baseline characteristics and trajectories of disease progression. Alzheimer Dis Assoc Disord. 2018 Jan-Mar; 32(1):57-61. DOI: 10.1097/wad.0000000000000212. PMID: 28984640 [Epub 2017 Oct 7].

Connors MH, Quinto L, McKeith I, Brodaty H, Allan L, Bamford C, Thomas A, Taylor JP, O'Brien JT. Non-pharmacological interventions for Lewy body dementia: a systematic review. Psychol Med. 2018 Aug; 48(11):1749-1758. DOI: 10.1017/s0033291717003257. PMID: 29143692 [Epub 2017 Nov 17].

Connors MH, Seeher KM, Crawford J, Ames D, Woodward M, Brodaty H. The stability of neuropsychiatric subsyndromes in Alzheimer's disease. Alzheimers Dement. 2018 Jul; 14(7):880-888. DOI: 10.1016/j.jalz.2018.02.006. PMID: 29548721 [Epub 2018 Mar 20].

Cordato NJ, Kearns M, Smerdely P, Seeher KM, Gardiner MD, Brodaty H. Management of Nursing Home Residents Following Acute Hospitalization: Efficacy of the "Regular Early Assessment Post-Discharge (REAP)" Intervention. J Am Med Dir Assoc. 2018 Mar; 19(3):276.e211-276.e219. DOI: 10.1016/j.jamda.2017.12.008. PMID: 29396192 [Epub 2018 Feb 6].

Davies G, Lam M, Harris SE, Trampush JW, Luciano M, Hill WD, …, Thalamuthu A, …, Armstrong NJ, Assareh AA, …, Brodaty H, …, Kochan NA, …, Reppermund S, …, Sachdev PS, …, Trollor JN, et al. Study of 300,486 individuals identifies 148 independent genetic loci influencing general cognitive function. Nat Comms. 2018 May 29; 9(1):2098. DOI: 10.1038/s41467-018-04362-x. PMID: 29844566 / PMCID: PMC5974083 [Epub 2018 May 29].

Dong C, Liu T, Wen W, Kochan NA, Jiang J, Li Q, Liu H, Niu H, Zhang W, Wang Y, Brodaty H, Sachdev PS. Altered functional connectivity strength in informant-reported subjective cognitive decline: A resting-state functional magnetic resonance imaging study. Alzheimers Dement (Amst). 2018; 10: 688-97. DOI: 10.1016/j.dadm.2018.08.011. PMID: 30426065 / PMCID: PMC6222034. [Epub 2018 Nov 15].

Engel M, Balez R, Munoz SS, Cabral-da-Silva MC, Stevens CH, Bax M, Do-Ha D, Sidhu K, Sachdev P, Ooi L. Viral-free generation and characterization of a human induced pluripotent stem cell line from dermal fibroblasts. Stem Cell Res. 2018 Oct; 32:135-8. DOI: 10.1016/j.scr.2018.09.014. PMID: 30278375. [Epub 2018 Oct 3].

Evered L, Silbert B, Knopman DS, Scott DA, DeKosky ST, Rasmussen LS, Oh ES, Crosby G, Berger M, Eckenhoff RG, The Nomenclature Consensus Working Group. Recommendations for the nomenclature of cognitive change associated with anaesthesia and surgery - 2018. Acta Anaesthesiol Scand. 2018 Nov; 62(10): 1473-80. DOI: 10.1111/aas.13250. PMID: 30325016. [Epub 2018 Oct 17]. ***Sachdev PS is part of The Nomenclature Consensus Working Group***

Evered L, Silbert B, Knopman DS, Scott DA, DeKosky ST, Rasmussen LS, Oh ES, Crosby G, Berger M, Eckenhoff RG, The Nomenclature Consensus Working Group. Recommendations for the nomenclature of cognitive change associated with anaesthesia and surgery - 2018. Br J Anaesth. 2018 Nov; 121(5):1005-12. DOI: 10.1016/j.bja.2017.11.087. PMID: 30336844. [Epub 2018 Oct 20]. ***Sachdev PS is part of The Nomenclature Consensus Working Group***

GBD 2016 Healthcare Access and Quality Collaborators. Measuring performance on the Healthcare Access and Quality Index for 195 countries and territories and selected subnational locations: a systematic analysis from the Global Burden of Disease Study 2016. Lancet. 2018 Jun 2; 391(10136):2236-71. DOI: 10.1016/s0140-6736(18)30994-2. PMID: 29893224 [Epub 2018 June 13]. ***Sachdev PS is a collaborator***

GBD 2017 DALYs and HALE Collaborators. Global, regional, and national disability-adjusted life-years (DALYs) for 359 diseases and injuries and healthy life expectancy (HALE) for 195 countries and territories, 1990-2017: a systematic analysis for the Global Burden of Disease Study 2017. Lancet. 2018; Nov 10; 392(10159):1859-922. DOI: 10.1016/s0140-6736(18)32335-3. PMID: 30415748 / PMCID: PMC6252083. [Epub 2018 Nov 13]. ***Sachdev PS is a collaborator***

GBD 2017 Disease and Injury Incidence and Prevalence Collaborators. Global, regional, and national incidence, prevalence, and years lived with disability for 354 diseases and injuries for 195 countries and territories, 1990-2017: a systematic analysis for the Global Burden

of Disease Study 2017. Lancet. 2018; Nov 10; 392(10159):1789-858. DOI: 10.1016/s0140-6736(18)32279-7. PMID: 30496104 / PMCID: PMC6227754. [Epub 2018 Nov 30]. ***Sachdev PS is a collaborator***

GBD 2017 Mortality Collaborators. Global, regional, and national age-sex-specific mortality and life expectancy, 1950-2017: a systematic analysis for the Global Burden of Disease Study 2017. Lancet. 2018; Nov 10; 392(10159):1684-735. DOI: 10.1016/s0140-6736(18)31891-9. PMID: 30496102. [Epub 2018 Nov 30]. ***Sachdev PS is a collaborator***

GBD 2017 Population and Fertility Collaborators. Population and fertility by age and sex for 195 countries and territories, 1950-2017: a systematic analysis for the Global Burden of Disease Study 2017. Lancet. 2018; Nov 10; 392(10159):1995-2051. DOI: 10.1016/s0140-6736(18)32278-5. PMID: 30496106 / PMCID: PMC6227915. [Epub 2018 Nov 30]. ***Sachdev PS is a collaborator***

GBD 2017 Risk Factor Collaborators. Global, regional, and national comparative risk assessment of 84 behavioural, environmental and occupational, and metabolic risks or clusters of risks for 195 countries and territories, 1990-2017: a systematic analysis for the Global Burden of Disease Study 2017. Lancet. 2018; Nov 10; 392(10159):1923-94. DOI: 10.1016/s0140-6736(18)32225-6. PMID: 30496105 / PMCID: PMC6227755. [Epub 2018 Nov 30]. ***Sachdev PS is a collaborator***

GBD 2017 SDG Collaborators. Measuring progress from 1990 to 2017 and projecting attainment to 2030 of the health-related Sustainable Development Goals for 195 countries and territories: a systematic analysis for the Global Burden of Disease Study 2017. Lancet. 2018; Nov 10; 392(10159):2091-138. DOI: 10.1016/s0140-6736(18)32281-5. PMID: 30496107 / PMCID: PMC6227911. [Epub 2018 Nov 30]. ***Sachdev PS is a collaborator***

Ghanavati T, Smitt MS, Lord SR, Sachdev P, Wen W, Kochan NA, Brodaty H, Delbaere K. Deep white matter hyperintensities, microstructural integrity and dual task walking in older people. Brain Imaging Behav. 2018 Oct; 12(5):1488-1496. DOI: 10.1007/s11682-017-9787-7. PMID: 29297156 [Epub 2018 Jan 4].

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APPENDIX I: CONFERENCE/PUBLISHED ABSTRACTS

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Lipnicki DM, Makkar SR, Crawford JD, Thalamuthu A, Kochan KA, Brodaty H, Sachdev PS. Cohort Studies of Memory in an International Consortium (COSMIC). Risk and protective factors for cognitive performance and decline in diverse ethno-regional groups: the COSMIC collaboration [Abstract]. *Australian Dementia Forum*. 3-5 June 2018; Sydney, Australia. *NHMRC National Institute for Dementia Research (NNIDR) Australian Dementia Forum Abstracts*. 2018; p.77.

Lipnicki DM, Makkar SR, Crawford JD, Thalamuthu A, Kochan NA, Brodaty H, Sachdev PS. Determinants of cognitive performance and decline in diverse ethno-regional groups: the cosmic collaboration [Poster Abstract P2-603]. *Alzheimer's Association International Conference (AAIC) 2018*. 22-26 July 2018; Chicago, USA. *Alzheimers Dement*. 2018 July; 14(7 Suppl): P968-P70. DOI: 10.1016/j.jalz.2018.06.1299.

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Lo JW, Crawford JD, Kochan N, Sachdev PS, et al. Profile and risk factors of post-stroke cognitive impairment in diverse ethno-regional groups: an individual participant data meta-analysis from the STROKOG consortium [Abstract P-36]. *The 9th International Conference of the International Society of Vascular Behavioural and Cognitive Disorders (VASCOG 2018)*. 14-17 November 2018; Hong Kong.

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Makkar SR, Lipnicki DM, Crawford JD, Thalamuthu A, Kochan NA, Brodaty H, Sachdev PS. Age-dependent association between body mass index (BMI) and cognitive decline in diverse ethno-regional groups: the cosmic collaboration [Abstract O3-11-03]. *Alzheimer's Association International Conference (AAIC) 2018*. 22-26 July 2018; Chicago, USA. *Alzheimers Dement*. 2018 July; 14(7 Suppl): P1047-P8. DOI: 10.1016/j.jalz.2018.06.2833.

Makkar SR, Lipnicki DM, Crawford JD, Thalamuthu A, Kochan NA, Brodaty H, Sachdev PS. Relationship between apolipoprotein-ε4 and cognitive decline and the moderating effects of age, sex, and ethnicity: the cosmic collaboration [Poster Abstract P3-594]. *Alzheimer's Association International Conference (AAIC) 2018*. 22-26 July 2018; Chicago, USA. *Alzheimers Dement*. 2018 July; 14(7 Suppl): P1354-P5. DOI: 10.1016/j.jalz.2018.06.1960.

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APPENDIX J: WORKSHOPS, CONFERENCES & SPEAKING ENGAGEMENTS

Braidy N. Invited Speaker. Oxidative Stress in Alzheimer's Disease and Ageing: Revisiting the Ancient Phenomenon". *The 3th International Congress on Biological and Medical Sciences*. 31 Oct-3 Nov 2018; Nigde, Turkey.

Braidy N. Invited Speaker. "Oxidative Stress in Alzheimer's Disease and Ageing: Revisiting the Ancient Phenomenon". *The 3rd Brain Research School*. Isparta, Turkey.

Braidy N. "Intravenous NAD+ effectively increased the NAD metabolome, reduced oxidative stress and inflammation, and increased expression of longevity genes safely in elderly humans". *3rd ISANH Middle East Antioxidants World Congres*. 2-3 May 2018; Amman, Jordan.

Brodaty H. "Living well to 100". *2nd International 'Living to 100' Conference*. 7-8 Sept 2018; Sydney, Australia.

Brodaty H. Invited plenary speaker. "Psychosocial Research in Dementia: Past, Present, and Future". *Alzheimer's Association International Conference*. 24 July 2018; Chicago, USA.

Brodaty H. Invited speaker. "Depression, Dementia, Pseudodementia, Pseudodepression". *Psychogeriatrics in Perspective*. 27 Apr 2018; Parliament House, Sydney.

Brodaty H. Keynote speaker. "Healthy cognitive ageing". *2018 NSW Seniors Festival 'Your Brain Matters'*. 11 Apr 2018; Hunters Hill.

Casey A-N. Invited speaker. "Friendships and social relationships of people living in residential aged care. *Gerontological Society of America (GSA) Annual Scientific Meeting*. 15 Nov 2018; Boston, USA.

Casey A-N. Invited speaker. "A systematic review and meta-analysis of the association between social engagement, loneliness, and risk of dementia". *33rd International Conference of Alzheimer's Disease International (ADI)*. 28 July 2018; Chicago, USA.

Kochan NA. "Memory Fitness: Training your brain and maximizing your memory". *Presentation to Hospital patient group – Pink Panthers*. Aug 2018; Prince of Wales Hospital, Sydney.

Kochan NA. "How does memory work and how you can improve your memory". *Community event for Seniors, Centre on Ageing Sydney*. Mar 2018; Bondi Junction.

Kochan NA. Invited Speaker. "Approaches to harmonise neuropsychological data across studies". *Alzheimer's Association International Conference*. 22-26 July 2018; Chicago, USA.

Kochan NA. Invited Speaker. "Cognitive assessment in CALD individuals: Issues related to dementia research (invited speaker)". *NNIDR/NARI CALD Dementia Research Consultation Workshop*. 20 Nov 201; Melbourne, Australia.

Kochan NA & Crawford JD. Invited Speaker. "Overview of neuropsychological data harmonization and its challenges". *International Centenarian Consortium*

(ICC) Dementia Meeting. 5-6 Sept 2018; Blue Mountains, NSW, Australia.

Koncz R. "Australian Symposium: Vascular risk in Alzheimer's disease: what is the evidence?" *11th International Congress of the International Neuropsychiatric Association*. 15-17 Feb 2018; Bangalore, India.

Koncz R. "Psychiatry Training in Intellectual Disability Mental Health". *The 2nd National Mental Health Round Table*. 2-3 May 2018; Sydney, Australia.

Heffernan M. "Maintain Your Brain - an internet-based RCT to prevent cognitive decline". *33rd International Conference of Alzheimer's Disease International*. 26-29 July 2018; Chicago, USA.

Leung Y. Poster Presentation. "Dementia and exceptional longevity: A study of cognitive and functional impairment in centenarians and near-centenarians from 17 population-based studies". *Australia Dementia Forum*. June 2018; Sydney, Australia.

Leung Y. Group oral presentation with Lo J and Lipnicki D. "Three international consortia of cognitive ageing and dementia studies". *Alzheimer's Association International Conference,* 22-26 July 2018; Chicago, USA.

Leung Y. Invited speaker for AAIC press release. "100 years and beyond: Investigating the prevalence of dementia in centenarians and near-centenarians from 17 studies".

Leung Y. Invited speaker. "Investigating the prevalence of dementia in centenarians and near-centenarians from 17 studies". *International Centenarian Consortium (ICC) Dementia Meeting*. 5-6 Sept 2018; Blue Mountains, NSW, Australia.

Leung Y. Poster presentation. "Living beyond 95: Dementia prevalence in centenarians and near-centenarians from the Sydney Centenarian Study". *2nd International 'Living to 100' Conference*. 7-8 Sept 2018; Sydney, Australia.

Lipnicki D, Lo J, Leung Y. "Three international consortia of cognitive ageing and dementia studies". *NNIDR Australia Dementia Forum*. June 2018; Sydney, Australia.

Lo J. "STROKOG symposium". *9th International Conference of The International Society of Vascular Behavioural and Cognitive Disorders (VasCog)*.14-17 Nov 2018; Hong Kong.

Lo J. "Profile of and risk factors for post-stroke cognitive impairment in diverse ethno-regional groups: an IPD meta-analysis from the STROKOG consortium". *9th International Conference of The International Society of Vascular Behavioural and Cognitive Disorders (VasCog)*.14-17 Nov 2018; Hong Kong.

Lo J. "STROKOG, Stroke and Cognition Consortium." *ISTAART (The Alzheimer's Association International Society to Advance Alzheimer's Research and Treatment) Webinar*. 6 Feb 2018; online.

Makkar S. Poster presentation. "Relationship between apolipoprotein-ε4 and cognitive decline and the moderating effects of age, sex, and ethnicity: the COSMIC Collaboration". *Alzheimer Association International Conference*. 22-26 July 2018; Chicago, USA.

Makkar S. "Age-dependent association between body mass index (BMI) and cognitive decline in diverse ethno-regional groups: the COSMIC collaboration". *Alzheimer Association International Conference*. 22-26 July 2018; Chicago, USA.

Makkar S. "Age-dependent association between body mass index (BMI) and cognitive decline in diverse ethno-regional groups: the COSMIC collaboration". *RANZCP Faculty of Psychiatry of Old Age (FPOA) and the Asian Society Against Dementia (ASAD) Conference*. 8 Nov 2018; Melbourne, Australia.

Mather KA. "Identifying the genetic and epigenetic factors linked to successful ageing by studying exceptional longevity". *Neuroscience Research Australia Forum*. Sept 2018; Sydney, Australia.

Mather KA. "Can epigenetics reveal the secrets to exceptional longevity". *2nd International 'Living to 100' Conference*. 7-8 Sept 2018; Sydney, Australia.

Mather KA. "Genetics & epigenetic studies of exceptional longevity". *International Centenarian Consortium (ICC) Dementia Meeting*. 5-6 Sept 2018; Blue Mountains, NSW, Australia.

Mather KA. "Genetics of ageing and age-related disease". Nanchang University. July 2018; Nanchang, China.

Mather KA. "The Centre for Healthy Brain Ageing: An overview with a focus on genetics & epigenomics". Chinese Academy of Sciences Workshop. July 2018; Institute of Neurosciences, Shanghai, China.

Mather KA. "Successful aging: Successful ageing research – what do genetic studies of centenarians tell us?". *School of Psychiatry Forum*. June 2018; UNSW Medicine, Australia.

Mohan A. "Differential expression of synaptic and interneuron genes in the aging human prefrontal cortex". *Alzheimer's Association International Conference (AAIC) 2018*. 22-26 July 2018; Chicago, USA.

Sachdev P. "The COSMIC consortium". *All India Institute of Speech & Hearing Meeting*.12 Feb 2018; Bengaluru, India.

Sachdev P. "Imaging small vessel diease". *National Institute of Mental Health and Neurosciences (NIMHANS) Meeting*. 14 Feb 2018; Bengaluru, India.

Sachdev P. Invited Speaker. ¿Cómo funciona el cerebro? Lecciones desde la clínica neuropsiquiátrica. *El Aleph Festival de Arte y Cienca*. 30 May – 3 June 2018; Mexico City, Mexico. [Presentation translated in Spanish].

Sachdev P. Invited Session Chair. *Alzheimer's Association International Conference (AAIC) 2018*. 22-26 July 2018; Chicago, USA.

Sachdev P. Invited Speaker. *International Centenarian Consortium (ICC) Dementia Meeting*. 5-6 Sept 2018; Blue Mountains, NSW, Australia.

Sachdev P. Invited Speaker. "Imaging the brains of centenarians". *2nd International 'Living to 100' Conference*. 7-8 Sept 2018; Sydney, Australia.

Sachdev P. Invited Speaker. "Why do we age?" *2nd International 'Living to 100' Conference*. 7-8 Sept 2018; Sydney, Australia.

Sachdev P. Invited Speaker. Debate: "Vessels or Tangles? Do we really need diagnostic criteria for vascular and Alzheimer dementias?" *VAS-COG 2018*. 14-17 Nov 2018; Hong Kong.

Theobald A. "The Sydney Centenarian Study". *2nd International 'Living to 100' Conference*. 7-8 Sept 2018; Sydney, Australia.

Theobald A. "The Sydney Centenarian Study". *International Centenarian Consortium (ICC) Dementia Meeting*. 5-6 Sept 2018; Blue Mountains, NSW, Australia.