UNSW SYDNEY

Centre for Healthy Brain Ageing (CHeBA)

Annual Report 2020

prevention

big data

positive ageing

research

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Centre for Healthy Brain Ageing (CHeBA)
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Design: Laurie Mock

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Co-Directors' Report

2020 proved to be a difficult year, with the COVID-19 pandemic impacting each one of us. Never before have we, as a global collective, stared down the face of such an immediate health and economic crisis.

We are exceptionally proud of our staff and students who responded to the crisis with a positive spirit and managed to continue to expand their research activities, generate online engagement and support each other in such unknown territory. As a research group, we were acutely aware that although we are living in a complex time with a worldwide pandemic, we could not forget that dementia remains one of our biggest global public health challenges. We are grateful to you, our CHeBA family of community, donors, collaborators, and fellow staff members at UNSW who remained connected and understanding of the challenges we faced. Although some face-to-face research had to be suspended, much of our research was able to be modified to virtual contacts and we acknowledge the generosity of study participants who were able to adapt with us.

2020 marked the eighth anniversary of CHeBA and despite the challenges, CHeBA further expanded its research activities and continued to strive for ways to both prevent dementia as well as improve treatment and care for those already impacted. This report summarises our achievements across the Centre, with several highlights including:

- a $3.289 million National Health & Medical Research Council (NHMRC) Investigator Grant awarded to Professor Perminder Sachdev to develop robust biomarkers for vascular cognitive impairment and dementia;
- significant success for Professor Henry Brodaty in collaborative grants to improve family carers' abilities to support people with dementia in Vietnam, China and Indonesia;
- world-first research from our Neuroimaging Group looking at the connectivity of brains in study participants 95 years and older from CHeBA's Sydney Centenarian Study;
- significant success in research across two major CHeBA-led consortia – STROKOG and COSMIC.

Several CHeBA researchers, including Dr Karen Mather and Dr Louise Mewton, were successful with competitive grant funding. These successes along with continued support from Montefiore, the Vincent Fairfax Family Foundation, the John Holden Family Foundation, the Yulgilbar Foundation and the Mostyn Family Foundation, enable CHeBA to augment its record of innovative research in the fields of Alzheimer's disease and other dementias as well as healthy ageing.

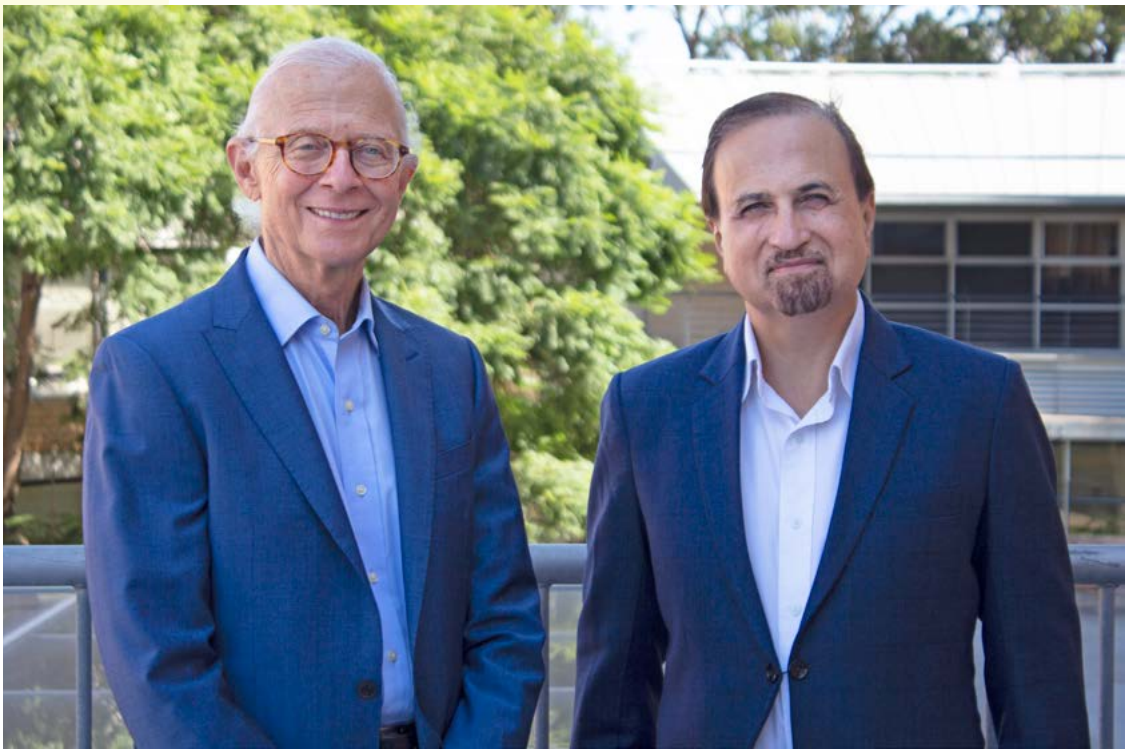
Another substantial funding outcome was a $2.2 million national collaboration to create a secure platform for data sharing, governance, control and management services for researchers. We are delighted to see this partnership with Monash University become a reality. Dementias Platform Australia plans to host data on scores of longitudinal studies of brain ageing and dementia which could transform the epidemiology of ageing and dementia. It is a partnership with Dementias Platform UK, which will generously provide the software and their expertise, and COSMIC collaboration, which brings several Australian and international studies to this platform to make them accessible to researchers around the globe.

> **"We are grateful to you, our CHeBA family of community, donors, collaborators, and fellow staff members at UNSW who remained connected and understanding of the challenges we faced."**
>
> Professor Henry Brodaty AO &
> Professor Perminder Sachdev AM

Although our annual events were unable to be held in 2020, we remain fortunate to have the generous support of Richard Grellman AM, Spokesman for The Dementia Momentum and Ambassador for our Wipeout Dementia, who led the Wipeout Dementia Appeal in June 2020 and remains committed to his role leading into 2021. We extend our sympathies to his family who, like many others across Australia, spent considerable time unable to see their mother and grandmother Suellen in aged care.

In 2020, CHeBA published several noteworthy research papers, including a major paper led by Jess Lo in *Stroke* from the STROKOG consortium and one from our Genetics & Epigenomics Group also published in *Stroke*, as well as many more highlighted throughout this Report.

It takes a team to undertake research. Our team comprises group leaders, study co-ordinators, research assistants, PhD scholars and post-doctoral research associates, our long-standing Centre Manager Angie Russell who ensures CHeBA's operations run flawlessly and Dr Sophia Dean who continues to provide research and administrative support that is instrumental.



We thank Heidi Douglass and Laurie Mock for their communications and media outreach and for creating innovative means to continue to connect with and engage our community during a pandemic. This team forms the hub of CHeBA's research activities from which we connect with fellow researchers across the university, Australia and globally, as well as with service providers and policy makers nationally.

Our global links enable us to extend our research to understand racial and ethnic factors in the causes and care of dementia. As always, we gratefully acknowledge the contributions of our collaborators, supporters, fundraisers, volunteers and most of all our research participants. We look forward to continuing to deliver on CHeBA's vision and mission in 2021.

As we look forward to the year ahead, we continue to take every precaution in the wake of the COVID-19 pandemic and remain extremely thankful to our CHeBA colleagues and community for the sense of unity that has been retained through 2020.

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, Professor Henry Brodaty AO and Professor Perminder Sachdev AM.

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 conduct innovative research and provide the empirical basis to prevent and treat dementia and achieve healthy brain ageing for all Australians.

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.

Research Highlights

"Our goal is to make a major impact on the societal burden due to dementia and related disorders."

Professor Perminder Sachdev AM &
Professor Henry Brodaty AO

Research Grant to Fund Major Advance in Fight Against Dementia

Co-Director of CHeBA, **Professor Perminder Sachdev AM**, has been awarded a $3.289 million National Health & Medical Research Council (NHMRC) Investigator Grant to develop robust biomarkers for vascular cognitive impairment and dementia.

The prestigious award, which provides funding over five years, will allow researchers at CHeBA to identify, validate and demonstrate the research and clinical utility of biomarkers, especially small vessel disease, contributing to cognitive decline and dementia.

By the year 2030, Australians over the age of 65 years will comprise 22% of the population with a current estimate of 447,116 Australians living with dementia and over a million people involved in their care.

About 250 new diagnoses of dementia are made each day and by 2050 the prediction is that there will be nearly 900,000 Australians living with dementia. Professor Sachdev's research in cognitive ageing and dementia spans two decades with the over-arching objective of reducing the burden of late-life cognitive disorders.

Dementia is estimated to cost greater than $15 billion per year and is the second leading cause of death in Australia - first in women – and there is no cure.

The two leading causes of dementia are Alzheimer's disease and vascular dementia and it is generally claimed that vascular dementia accounts for 15-30% of all dementia. Further, cerebrovascular disease is a common co-occurrence with other brain pathologies and the total contribution of vascular pathology to dementia may be as high as 50-70%.

While research in Alzheimer's disease has advanced rapidly in the last three decades and we may be at the threshold of disease-modifying drugs, the research effort in vascular dementia has been much more modest, even though vascular dementia has been referred to as 'preventable' dementia', said Professor Sachdev.

"While research in Alzheimer's disease has advanced rapidly in the last three decades and we may be at the threshold of disease-modifying drugs, the research effort in vascular dementia has been much more modest, even though vascular dementia has been referred to as 'preventable' dementia."

Professor Perminder Sachdev AM

The Investigator Grant will allow Professor Sachdev and his team to explore several biomarkers to determine the most robust single or combined set of biomarkers.

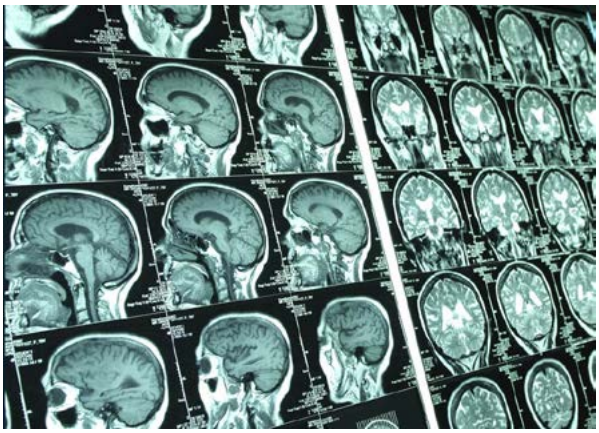
"A research program will then follow to translate the biomarkers into both research and clinical practice, and the application of surrogate markers of vascular cognitive impairment and dementia to clinical trials," he said.

"The expectation is that in five years, these biomarkers will have routine application in research and in the clinic, which will be a major advance in our fight against dementia," said Professor Sachdev.

Professor Perminder Sachdev AM

People Aged 95+ Show Greater Brain Connectivity

World-first research led by **Dr Jiyang Jiang** has found that those aged 95 and over demonstrated more activation between the left and ride side of their brain than their younger counterparts.



Given the prevalence of dementia increases with age, near-centenarians and centenarians without dementia are generally considered as models of successful ageing and resistance against age-related cognitive decline.

We wanted to see if there was something particularly special about the brain's functional connectivity of those aged 95 and older that helps them preserve brain function into the 11th decade of their life, says Dr Jiang.

The research, published in *Neuroimage*, investigated brain functional characteristics in the extreme age range using resting-state functional MRI to depict characteristics of neural activity in near-centenarians and centenarians.
It expands upon previous research from this group that identified the brain structural profile of near-centenarians and centenarians using data from CHeBA's Sydney Centenarian Study.

According to Associate Professor Wei Wen, resting-state functional MRI offers an unprecedented opportunity to study human brain function and neural activity in this special group of elders.

"Findings suggested that, compared to young-old controls, centenarians showed more synchronised activation of left and right fronto-parietal control networks," said Dr Jiang.

In near-centenarians and centenarians, this coupled activation of bilateral fronto-parietal control networks contributed to better performance on visuospatial cognitive tasks.

Professor Perminder Sachdev, Co-Leader of CHeBA's Sydney Centenarian Study, says this paper is a fine example of how the study of centenarians can reveal the secrets of healthy ageing, and how the brain adapts to age-related changes and continues to perform so well in these exceptional individuals.

DOI: 10.1016/j.neuroimage.2020.116855

This research was supported by the J Holden Family Foundation.

Dr Jiyang Jiang

Certain Memory Complaints Predict Future Dementia

Research led by Sydney Memory and Ageing Study Coordinator **Dr Katya Numbers** has shown that certain presentations of memory concerns by older adults are predictive of future dementia.

The findings published in *PLOS ONE* highlight the importance of general practitioners in listening to their older adult patient population in relation to memory.

"We found that when older adults go to their general practitioner with memory-specific subjective cognitive complaints it would be wise to take it seriously as they may predict future dementia," said Dr Numbers.

Subjective cognitive complaints refer to an individual's self-experience of cognitive decline and can refer to specific changes in memory ability or changes in other cognitive domains like language or processing speed.

Research increasingly suggests that these subjective complaints may be the earliest detectible stage of preclinical dementia.

Participant and informant memory-specific cognitive complaints were associated with the rate of global cognitive decline.

Dr Katya Numbers

If an informant noted that the person had poorer memory, six years later we found a decline in memory and executive function (planning, understanding, abstract thinking). The risk of dementia at follow-up was also greater if participants complained about poorer memory or if their informant noted changes in memory and non-memory types of cognition.

The findings emphasised the importance of an older adult's subjective presentations and the relevance of the perceptions of informants in relation to predicting cognitive decline.

"While many people with memory complaints will not develop dementia, where possible, informants should be asked to report any changes on the individual's memory and non-memory abilities, as such symptoms increases the risk of further decline," said Dr Numbers.

DOI: 10.1371/journal.pone.0232961

Metformin Treatment Linked to Slowed Cognitive Decline

A study conducted over six years using participants from CHeBA's Sydney Memory and Ageing Study has revealed that individuals with type 2 diabetes who used metformin experienced slower cognitive decline with lower dementia rates than those who did not use the medication.

Metformin is the first-line treatment for most cases of type 2 diabetes and one of the most commonly prescribed medications worldwide, with millions of individuals using it to optimise their blood glucose levels.

The findings, published in *Diabetes Care*, provide new hope for a means of reducing the risk of dementia in individuals with type 2 diabetes, and potentially those without diabetes who number nearly 47 million people worldwide.

In the data analysed, 123 study participants had type 2 diabetes, and 67 received metformin to lower blood sugar levels. The researchers tested cognitive function every two years, using detailed assessments that measured cognition over a number of capabilities, including memory, executive function, attention and speed, and language.

The findings revealed individuals with type 2 diabetes taking metformin had significantly slower cognitive decline and lower dementia risk compared to those not taking metformin. Remarkably, in those with type 2 diabetes taking metformin, there was no difference in the rate of decline in cognitive function over 6 years compared to those without diabetes.

Professor Perminder Sachdev, senior author of the study and Co-Director of CHeBA, says: "While an observational study does not provide conclusive 'proof' that metformin is protective against dementia, it does encourage us to study this and other anti-diabetic treatments for dementia prevention. Metformin has even been suggested to be anti-ageing. The intriguing question is whether metformin is helpful in people in those with normal glucose metabolism. More work is clearly needed."

DOI: 10.2337/dc20-0892

Effects of Alcohol Greatest in Three Key Periods

Writing for *The BMJ*, **Dr Louise Mewton** says evidence suggests three periods of dynamic brain changes that may be particularly sensitive to the harmful effects of alcohol: gestation (from conception to birth), later adolescence (15-19 years), and older adulthood (over 65 years).

The editorial highlights alcohol use as being the strongest modifiable risk factor for dementia when compared with other established risk factors, and the need to develop an integrated approach to harm reduction from alcohol across the lifespan.

Globally, around 10% of pregnant women consume alcohol, with the rates considerably higher in European countries than the global average.

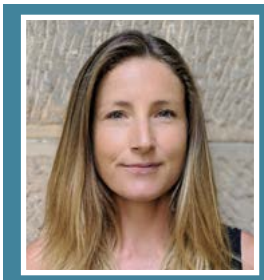
Heavy alcohol use during pregnancy can cause foetal alcohol spectrum disorder, associated with widespread reductions in brain volume and cognitive impairment.

In terms of adolescents, studies indicate that the transition to binge drinking in this age group is associated with reduced brain volume, poorer white matter development (critical for efficient brain functioning), and small to moderate deficits in a range of cognitive functions.

And in older people, alcohol use disorders were recently shown to be one of the strongest modifiable risk factors for all types of dementia (particularly early onset) compared with other established risk factors such as high blood pressure and smoking. Population based interventions such as guidelines on low-risk drinking, alcohol pricing policies, and lower drink driving limits need to be accompanied by the development of training and care pathways that consider the human brain at risk throughout life.

“The formulation of such health interventions has promise for increasing longevity and quality of life including preventing foetal alcohol spectrum disorders, neurocognitive disorders in teenagers, and dementia in later life,” says Dr Mewton.

DOI: 10.1136/bmj.m4691



"The maintenance of brain health is central to health and wellbeing across the lifespan."

Dr Louise Mewton

Our Groups

"The goal is to identify factors that can be modified so that we can slow the process of brain ageing and therefore prevent or delay dementia."

Professor Perminder Sachdev AM

Epidemiology

The Epidemiology Group is interested in studying the patterns, causes, risks, protective factors and effects of neurocognitive disorders, in particular dementia, in older 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 Vibeke Catts, Dr Ben Lam, Dr Louise Mewton, Dr Katya Numbers, Dr Catherine Browning, Jess Lo, Suzi Artiss

Professor Henry Brodaty, Dr Ben Lam, Dr Vibeke Catts, Dr Nicole Kochan, Dr Katya Numbers, Dr Karen Mather, Jess Lo, Dr Louise Mewton, Dr Anbu Thalamuthu, Professor Perminder Sachdev

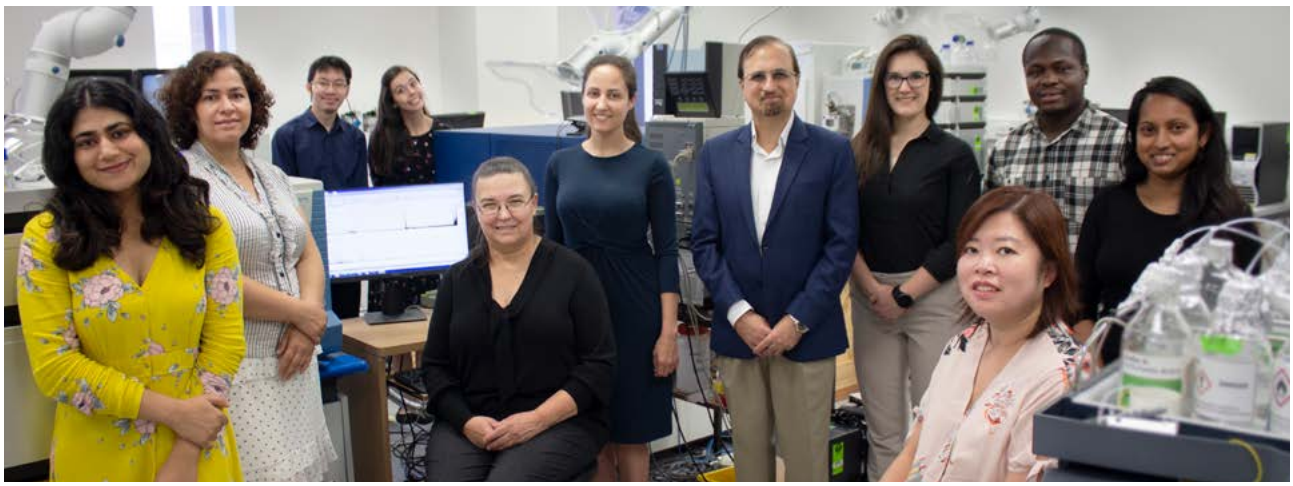
Proteomics

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

Staff: Dr Tharusha Jayasena, Scientia Professor Perminder Sachdev, Maboobeh Hossieni, Dr Fei Song

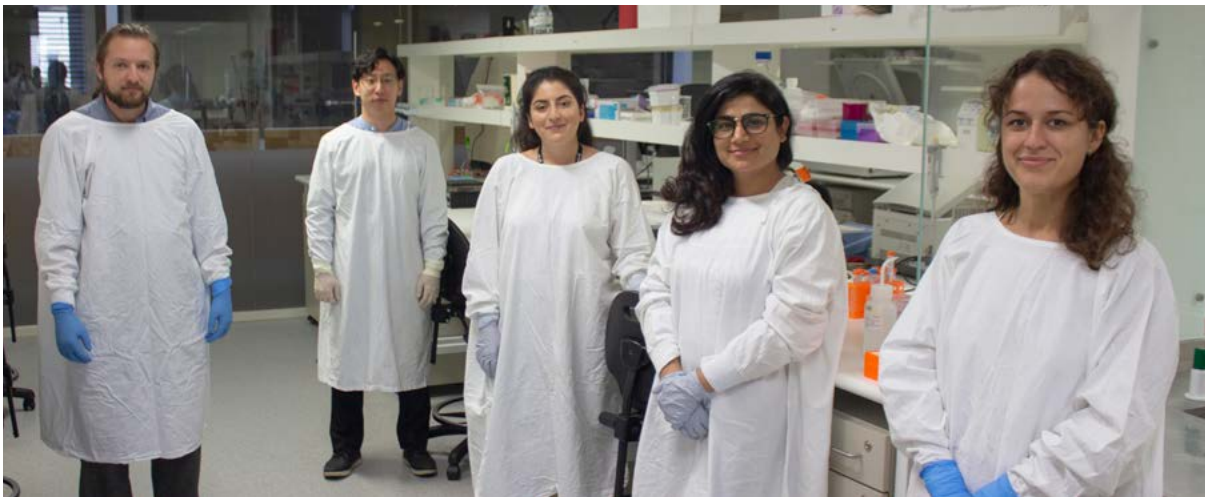
PhD Students: Gurjeet Virk (Scientia PhD candidate), Fatemeh Khorshidi (UPA PhD candidate), Rene Jezewski (Scientia PhD candidate), Toyin Abdulsalam (Scientia PhD candidate), Dr Matthew Wong (BSc Hons, PhD)



Gurjeet Virk, Maboobeh Hossieni, Matthew Wong, Rene Jezewski, Dr Anne Poljak, Fatemeh Khorshidi, Professor Perminder Sachdev, Rhiagh Cleary, Dr Fei Song, Toyin Abdulsalam, Dr Tharusha Jayasena

Brain Ageing Research Laboratory

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 team consists of neuroscientists, protein and analytical chemists, psychiatrists and bioinformaticians working in Australia and abroad. CHeBA's Brain Ageing Research Laboratory was the sole recipient of a $1 million research grant from The Yulgilbar 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.



Dr Nady Braidy, Chul-Kyu Kim, Maria Villalva, Gurjeet Virk and Marina Ulanova

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. The group also has 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 Leader: Dr Nady Braidy

Staff: Professor Perminder Sachdev, Maria Villalva

PhD Students: Chul-Kyu Kim, Dr Yue Liu, Marina Ulanova, Gurjeet Virk, Dr Matthew Wong

New Mechanisms to Reduce Impact of Debilitating Neuroinflammatory Diseases

A research collaboration between CHeBA, Macquarie University and St Vincent's Hospital identified a new process for the update of neurotoxin quinolinic acid (QUIN) that has the potential to reduce the impact of major neuroinflammatory diseases such as Alzheimer's disease, multiple sclerosis and motor neuron disease, with findings published in *Molecular Neurobiology Journal*.

The study is a world first in characterising a mechanism for QUIN uptake into primary human neurons via a transporter called EAAT3.

"Our research is significant as it opens new potential targets for reducing neuroinflammatory disorders that have been induced by toxins from the build-up of QUIN in the brain," said Dr Nady Braidy.

DOI: 10.1007/s12035-020-02046-6

Dr Nady Braidy

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 Sumangali Gobhidharan, Dr Naga Mutyala, Sri Chandana Kanchibhotla
Students: Mary Revelas, Adith Mohan, Jessica Lazarus, Irina Freitag, Toyin Abdulsalam, Annabel Matison, Russell Chander

Annabel Matison, Dr Karen Mather, Sri Chandana Kanchibhotla, Russell Chander, Dr Adith Mohan, Dr Anbupalam Thalamuthu, Toyin Abdulsalam, Dr Sumangali Gobhidharan, Mary Revelas

Funding Success to Unravel Human Brain Ageing

In 2020 **Dr Karen Mather** was awarded a $100,000 Rebecca Cooper Grant to research the molecular processes underlying brain ageing. The grant, entitled 'Unravelling human brain ageing – a multi-omics approach', will be used to investigate epigenomic age-related changes in brains from deceased adults aged up to 103 years of age.

Genetic Variants linked to White Matter Abnormalities

A world-first international genetics study co-led by **Dr Karen Mather** has identified genetic variants for two neuroimaging abnormalities – periventricular and deep white matter hyperintensities. The findings were published in *Stroke*.

White matter hyperintensities are an age-related brain abnormality, commonly observed on neuroimaging scans of older adults, and begin to appear in approximately 50% of all adults in their mid-late 40s and progress with age.

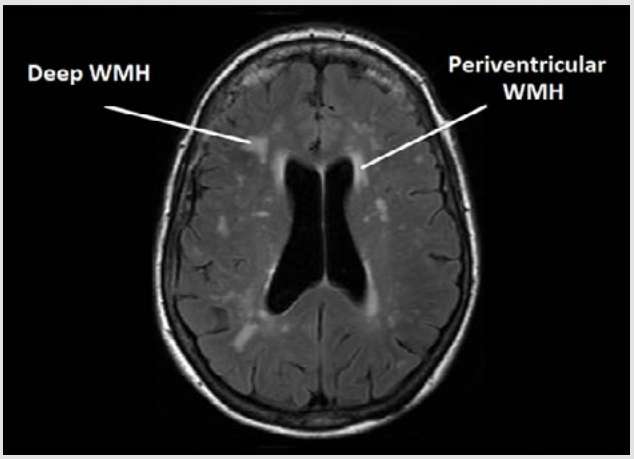
A high burden of white matter hyperintensities has been associated with negative health outcomes, such as stroke. They are thought to be related to brain small vessel disease but the causal factors are still largely unknown.

Traditionally, total white matter hyperintensity volume has been examined but it is also possible to distinguish between deep and periventricular white matter hyperintensities based on their location in the brain. These two categories are thought to reflect different pathological, physiological and functional differences. Genetics plays a significant role in the development of deep and periventricular white matter hyperintensities as shown in our own twin study, OATS, and by other family studies.

In the first genome-wide association studies of these two categories, Dr Mather used data from over 26,000 participants from CHeBA's Sydney Memory and Ageing Study and the Older Australian Twins Study, as well as international studies from the CHARGE and ENIGMA consortia and the UK Biobank.

The research assessed participants aged 45 years and older who were free of stroke and dementia. Genetic variants that were associated with both periventricular and deep white matter hyperintensities on chromosome 17 were found.

Importantly, a number of other genetic variants were identified for periventricular white matter hyperintensities only, suggesting that these two neuroimaging measures have shared but also different genetic underpinnings.



Dr Mather said that a large genetics study such as this one provides further evidence that these subclassifications of white matter hyperintensity are two separate entities that may have different implications for brain health – and are therefore important neuroimaging measures to study.

DOI: 10.1161/STROKEAHA.119.027544

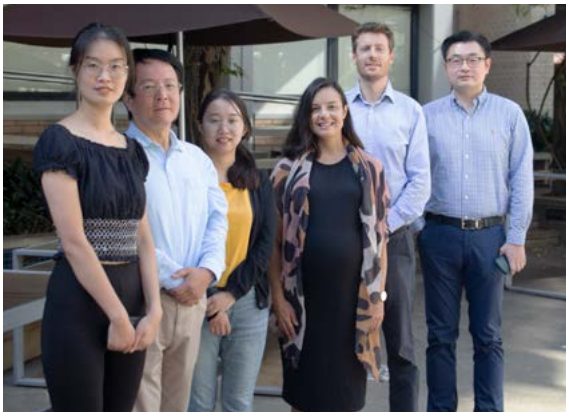
CHeBA Promotion

Congratulations to **Dr Anbu Thalamuthu** who in July 2020 was promoted to Senior Research Fellow.

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, Kelvin Lau, Yue Liu
Students: Heidi Foo, Abdullah Alqarni, Dr Jing Du, Chao Dong



Chao Dong, Professor Wei Wen, Dr Jing Du, Dr Rebecca Koncz, Dr Matt Paradise, Dr Jiyang Jiang

New Rating Scale Developed to Quantify Cerebrovascular Damage

Research led by **Dr Matt Paradise** has developed a rating scale to better understand the effects of certain aspects of cerebrovascular disease and its association with dementia, with findings published in the *Journal of the Neurological Sciences*.

The research, which assessed 414 community dwelling older adults aged between 70 and 90 found that perivascular spaces are a common MRI finding in the elderly. Perivascular spaces surround small blood vessels as they penetrate into the brain tissue. They have a normal physiological role in homeostasis of the cerebral environment, including draining of tissue fluid and removal of toxins. With improved imaging technology and better resolution of MRI, they are increasingly seen in routine scans, particularly when dilated.

Dilation of perivascular spaces may be due to a number of pathological processes including hypertension, obstruction, inflammation and atrophy. They are also a feature of small vessel disease – cerebrovascular disease affecting small blood vessels.

Dr Matt Paradise

Currently, there is no widely used rating scale for perivascular spaces and the researchers found poor inter-rater reliability when using existing scales. As such, they developed a visually rated perivascular space scale, based on the number of perivascular spaces in two representative slices, where they are likely to occur.

The new rating scale is easy to use, quick, has good psychometric properties and performs better than existing scales in community dwelling older individuals. Perivascular spaces may turn out to be a useful biomarker of cerebrovascular disease and help inform dementia diagnosis and treatment in the future.

DOI: 10.1016/j.jns.2019.116621

We extend our thanks to the Josh Woolfson Memorial Scholarship for part-funding this project.

Measuring Complexity of the Brain

An international collaboration between CHeBA's Neuroimaging Group and Beihang University in China, published in *Neurobiology of Aging*, researched differential longitudinal changes in structural complexity and volumetric measures in community-dwelling older individuals.

The research analysed the brain scans of community-dwelling older individuals aged 70-90 without dementia, using data from CHeBA's Sydney Memory and Ageing Study.

Researchers discovered that a measure of 'complexity' of the brain is more sensitive to brain changes over time than more conventional measures such as cortical thickness or cortical volumes. Findings could provide a useful measure for future brain morphological and cognitive studies.

DOI: 10.1016/j.neurobiolaging.2020.02.023

We extend our thanks to the J Holden Family Foundation for part-funding this project.

Neuropsychiatry

The Neuropsychiatry Group 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

Professor Perminder Sachdev, Dr Rebecca Koncz, Dr Adith Mohan, Dr Matt Paradise

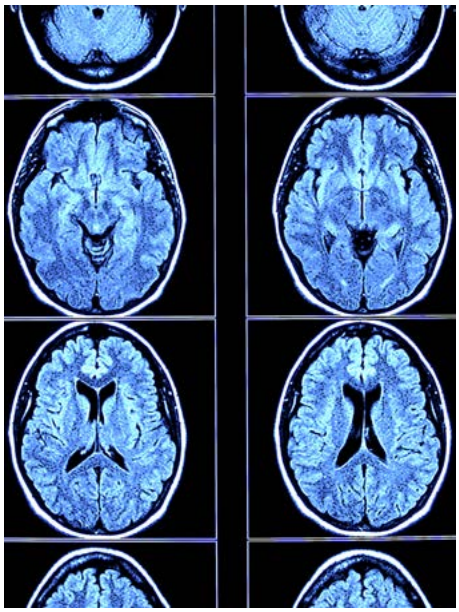
2018 Honours student Adrian Cheng

was awarded a scholarship by The Royal Australian and New Zealand College of Psychiatrists to present at their Congress based on his research supervised by CHeBA Co-Director Professor Henry Brodaty and drawing evidence from CHeBA's ***Sydney Centenarian Study***.

Australian Mental Health Prize

CHeBA Co-Directors Professor Henry Brodaty and Professor Perminder Sachdev, both members of the Australian Mental Health Prize Committee, extend congratulations to the 2020 winners of this prestigious prize - Professor Gordon Parker and Professor Helen Milroy.

Professor Henry Brodaty (5th from right) at the ceremony



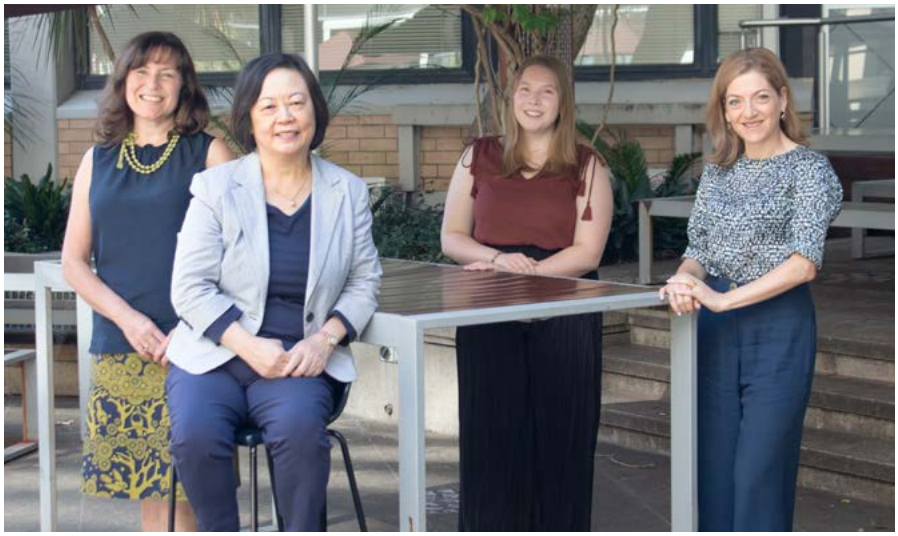
Neuropsychology

The Neuropsychology Group is interested in investigating the cognitive changes associated with normal ageing, mild neurocognitive syndromes and dementia, and developing the most efficient and accurate methods for measuring cognitive decline. The group is developing normative data for several cognitive tests and identifying appropriate cognitive instruments for individuals coming from culturally and linguistically diverse backgrounds. We are also conducting the CogSCANproject which is evaluating the use of computerised neuropsychological assessment to improve accessibility and diagnostic accuracy of mild neurocognitive disorders and dementia. We have established strong collaborative links with researchers in CHeBA and with international consortia such as IGEMS and ENIGMA, 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.

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, Jessica Turner

Students: PhD candidates: Dr Rebecca Koncz, Annette Spooner, Zara Page, Premilla Chinnappa-Quinn; Fourth year medical students (Independent Learning Projects 2020): Sophia Xi



Dr Karen Croot, Dr Teresa Lee, Zara Page, Dr Nicole Kochan

Additional focus on remote computerised cognitive assessments with CogSCAN At Home

The COVID pandemic and the associated physical distancing requirements presented an enormous challenge to clinical work and research alike. Given that face-to-face assessments were not possible, and older adults, a vulnerable group for COVID, were unable to attend UNSW, the CogSCAN team pivoted to remotely-delivered cognitive assessments in the person's home. iPads and study materials were provided through contactless delivery. Study participants self-administered the cognitive tests with support from research assistants by phone. The feedback from a pilot group was very positive.

They told us in debriefing interviews that they enjoyed the convenience of being at home while participating in the study and felt well-supported by the study staff in managing any technical difficulties or questions. The remote testing approach will be further investigated as a means of providing more accessible and flexible cognitive assessments for older Australians with the potential to facilitate a timely diagnosis of cognitive impairment and dementia. This is particularly important for Australians who live in regional areas who have limited access to dementia assessment services.

CHeBA-led Consortia

"By pooling data we can create 'big data sets' that produce more robust statistical models and more precise estimates than individual cohort studies."

Professor Perminder Sachdev AM

Cognisance

COGNISANCE is an international consortium led by CHeBA that is focused on improving clinicians' communication of a diagnosis of dementia and provision of effective support to patients and families in the first year following diagnosis.

International data collected from surveys, interviews and focus groups during 2020 supported previous findings that communicating a diagnosis of dementia is not universally done well. In Australia, interviews and focus groups with 9 people living with dementia, 17 care partners and 19 health care practitioners found the support following diagnosis was, at best 'hit or miss'.

While there are services, these usually focus on supporting people with functional decline which are often not key needs immediately following diagnosis. Existing services do not routinely promote reablement which could maintain or even improve engagement with life and prevent issues arising from dementia before they occur. Counselling and support from peak bodies was appreciated by people living with dementia and their care partners but long waiting lists indicate that there is simply not enough to go around. People living with dementia and their care partners expressed the need for tools to enable them to planahead. Lack of support was more keenly felt by people living in rural Australia.

COGNISANCE research teams in Australia, Canada, Netherlands, Poland and United Kingdom are working towards changing this situation.

Over 2020 we brought together a diverse range of stakeholders in co-design groups to develop a marketing campaign for social change. The campaign champions change of practice to make diagnosis a starting point for an effective plan of support, and to empower people living with dementia and their care partners to take action and to seek and receive support. The overall goal is to tangibly improve their lives in the 12-months following diagnosis.

Work in 2020 has resulted in the development of a global campaign "Forward with Dementia". The campaign is spearheaded with an international website containing practical, action oriented, evidence informed content that speaks directly to people living with dementia, their care partners and health and social care professionals. Local campaigning including webinars and capacity building activities are being planned in each of our participating countries. The website and campaigns will be launched mid-2021.

Ashley Stevens, Dr Meredith Gresham, Nora Wong

Dementia Divide Between Rural and Metropolitan Areas

In 2020 CHeBA partnered with Dementia Australia on this opinion piece.

The proportion of people with dementia in rural and regional Australia is consistent with that of metropolitan areas. Access to diagnosis and support however is not. This inequality across the country poses enormous challenges to people with dementia and carers.

Dementia is one of the leading causes of chronic disability in Australia and the second leading cause of death overall. It is the leading cause of death amongst women. By the middle of the century, it is predicted that the number of people living with a diagnosis of dementia will increase from 459,000 to over one million people.

According to Professor Henry Brodaty, this increase largely reflects an ageing population in Australia, with age being the most significant risk factor for developing dementia, and the population in regional Australia being older than that in city areas.

However, capacity to access timely diagnosis and quality support services is, unequivocally, not equitable across Australia.

Nearly 30% of the Australian population live outside metropolitan areas, with a two and a half times higher rate of potentially preventable hospitalisation – likely related to distance and more limited access to health care compared to metropolitan dwellers.

CEO of Dementia Australia, Maree McCabe says that considerably fewer health care professionals, including general practitioners, practise in rural areas. Yet, the proportion of people with dementia in rural areas is consistent with that in metropolitan areas (Australia Dementia Report 2013) and is projected to increase equally over coming decades.

By 2050, it is projected that 2.9% of the population living in capital cities will have dementia compared with 3.8% in the rest of Australia.

The challenges for people living with dementia and their supporters are compounded in regional areas by geographic isolation, travel distances and limited services and resources.

Yet, as noted by Dementia Australia, decisions around the policy, planning and design of services tend to be city-centric.

People living in regional, rural and remote areas deserve to have equitable access to services and be supported to remain living in those areas throughout their experience with dementia.

The key concerns and challenges for people with dementia, carers and service providers in regional, rural and remote Australia are significant. Beyond assessment, diagnosis and management of dementia they include opportunities for social engagement and community participation for people with dementia and carers, workforce issues for community, as well as respite and residential aged care services.

Many people currently living with dementia never receive a formal diagnosis. Although exact figures for Australia are unknown, it is estimated that between 44 and 70% of people with dementia in the UK and Canada – countries with similar health care systems to ours – remain undiagnosed.

Factors such as stigma and fear of dementia, particularly in rural areas, can discourage people from seeking a diagnosis. Some doctors believe that as there is no cure for dementia a diagnosis will only cause the individual and the family distress. Even for those receiving a diagnosis, post-diagnostic support is sorely lacking.

According to Dr Meredith Gresham, Study Coordinator of the COGNISANCE project, these circumstances need to be overcome. Diagnosis and post-diagnostic support are fundamentally important; rural areas need to be as well supported as their metropolitan counterparts.

To address this, Professor Brodaty, Dr Gresham and their team at the Centre for Healthy Brain Ageing are leading COGNISANCE, an international project designed to improve the experience of dementia diagnosis and post diagnostic support, through the development of critical toolkits for people with dementia, their care partners and health care professionals.

Clearly, we need to find ways to address gaps in service provision for carers and people with dementia and the evident divide between dementia diagnosis and post-diagnostic support in rural and regional centres.

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.

Dr Darren Lipnicki, COSMIC Study Coordinator

By the end of 2020 there were 42 international studies participating in COSMIC. For a full list of studies involved, see: ***https://cheba.unsw.edu.au/consortia/cosmic/studies***

The major highlights for COSMIC in 2020 include:

1. Signing an MOU with a new study: the Atahualpa Project - Ecuador;
2. Six new projects were started, led by either CHeBA researchers or international workgroups:
   a. Sex differences in risk factors for dementia and cognitive decline;
   b. The prevalence of poor mobility in older adults;
   c. Social health and reserve in the dementia patient journey project;
   d. Differential effect of family history on the risk for dementia by sex;
   e. The global burden of dementia;
   f. White matter lesions and their neuropsychological correspondence.
3. Eight papers were published:
   a. Maasakkers et al. The association of sedentary behaviour and cognitive function in people without dementia: A coordinated analysis across five cohort studies. Sports Med. 2020 Feb;50(2):403-413;
   b. Turana et al. Factors associated with odour identification in older Indonesian and white Australian adults. Aging Clin Exp Res. 2020 Feb;32(2):215-221;
   c. Makkar et al. APOE ε4 and the Influence of Sex, Age, Vascular Risk Factors, and Ethnicity on Cognitive Decline. J Gerontol A Biol Sci Med Sci. 2020 May 12;glaa116;
   d. Makkar et al. Education and the moderating roles of age, sex, ethnicity and apolipoprotein epsilon 4 on the risk of cognitive impairment. Arch Gerontol Geriatr. 2020 Jul 13;91:104112;
   e. Bae et al. Does parity matter in women's risk of dementia?: a COSMIC collaboration cohort study. BMC Med. 2020 Aug 5;18(1):210. doi: 10.1186/s12916-020-01671-1;
   f. Carles et al. A Cross-National Study of Depression in Pre-clinical Alzheimer's Disease: a COSMIC Collaboration Study. Alzheimers Dement. 2020 Sep 3. doi: 10.1002/alz.12149;
   g. Bae et al. Parity and the risk of incident dementia: a COSMIC collaboration cohort study. Epidemiol Psychiatr Sci. 2020 Oct 20;29:e176;
   h. Roehr et al. Estimating prevalence of subjective cognitive decline across international cohort studies of ageing: A COSMIC study. Alzheimers Res Ther. 2020;12(1):167.
4. Holding virtual COSMIC collaborators meetings for Europe/Asia and USA/South America, including presentations from project leaders;
5. Listing on the SYNCHROS site: ***https://repository.synchros.eu/network/cosmic***
6. Receiving supplementary NIH funding to develop Dementia Platform Australia (DPAU), an online resource for researchers to access COSMIC metadata, and to streamline project proposals and data access.

More Years of Education Reduces Risk of Dementia

An international research study led by CHeBA has provided further support to the finding that more years of education are associated with a decreased risk of dementia.

The research, which compared people who had only completed elementary school with those who had completed middle or high school, used data from 30,785 older individuals aged 55-103 across 14 different countries.

Lead author Dr Steve Makkar said those who had completed middle or high school had lower chances of developing cognitive impairment, whereas those who had not completed elementary school were at greater risk of dementia. The research, published in *Archives of Gerontology and Geriatrics*, examined associations between education and late-life cognitive impairment, which was determined by scores on the Mini-Mental State Examination (MMSE); a screening test for dementia.

Data were provided by 18 international studies of ageing represented by Australia, Brazil, Cuba, France, Germany, Greece, Hong Kong, Italy, Japan, Singapore, Spain, South Korea, the United Kingdom and the United States; all of which are members of COSMIC.

Compared to men, women showed a stronger association between middle school completion and reduced risk of cognitive impairment. Asian people showed stronger associations between having completed high school and a lower risk of cognitive impairment when compared to White people.

Among people with a variant of the APOE gene known to be a risk factor for Alzheimer's disease, only high school completion was associated with a reduced risk of cognitive impairment. However, the effects of the APOE gene variant differed among Asian, Black and White people.

DOI: 10.1016/j.archger.2020.104112

Depression Unlikely to be a Risk Factor for Dementia

Research using data provided by 8 studies of ageing across 7 countries involved in COSMIC suggests that depression is more likely to be attributable to dementia-related brain changes than a risk factor or reaction to the disease.

Findings were published in *Alzheimer's & Dementia – The Journal of the Alzheimer's Association*.
This study looked at the associations between depression and dementia was conducted using data for 646 older individuals who developed dementia.

The association between years to dementia diagnosis and successive depressive states was assessed using a mixed effect logistic regression model. The researchers found that, in general, the chances of having depression increased with increasing proximity to the diagnosis of dementia, despite inter-cultural variability in depression rates.

The findings indicate that depression is less likely to be a risk factor or contributing cause of Alzheimer's disease and other dementias - and more likely a direct result of the brain changes that accompany dementia.

DOI: 10.1002/alz.12149

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

In 2019, the following new studies joined STROKOG:

- Bulgarian Poststroke Study, Bulgaria;
- The HKU Stroke Cohort, Hong Kong;
- STRATEGIC, Australia.

In 2019, the prestigious *Neurology* journal published the first STROKOG research paper written by CHeBA researchers. The paper focuses on the profile of and risk factors for 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.

Three external researchers from the UK and from Finland collaborated with CHeBA and worked on three separate STROKOG projects in 2019. Dr Eugene Tang from Newcastle University, UK led a project on validating dementia risk score models. Dr Tang found that dementia risk prediction models developed for the general population do not perform well in individuals with stroke.

Jess Lo, STROKOG Study Coordinator

His paper is due to be published in 2020. Dr Clare Flach from King's College London, UK has been examining stroke recovery associated with cognitive impairment.
Dr Hanna Jokinen from the University of Helsinki in Finland is investigating domain-specific cognitive impairment and depression as determinants of post-stroke functional disability. The latter two projects are on-going.

In 2019 CHeBA researchers worked on a paper looking at diabetes, prediabetes on cognitive function after stroke. Based on data from 7 international studies, we found that diabetes is strongly associated with worse cognitive function after stroke, but not prediabetes. This paper is due to be published in the high-impact journal *Stroke* in 2020. CHeBA researchers also began working on the next major project looking at cognitive decline after stroke. Longitudinal data on cognitive assessment were requested from 9 international studies and harmonised. The CHeBA imaging team also proposed to form a Neuroimaging Work Group within STROKOG and a project harmonising MRI scans and analysing white matter hyperintensities and stroke. These projects are on-going in 2020.

CHeBA was invited to present at the Vascular Neurodegeneration Symposium at the Florey Institute of Neuroscience and Mental Health, the University of Melbourne in February.

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

Type 2 Diabetes, Stroke and Cognitive Performance

New research led by CHeBA found that people with Type 2 diabetes, but not those with prediabetes, had worse cognitive performance three to six months after a stroke than those with normal fasting blood sugar levels. The findings were published in *Stroke*, a journal of the American Stroke Association, a division of the American Heart Association.

Type 2 diabetes increases the risk of stroke and has been associated with cognitive impairment and may increase dementia risk – which is why Type 2 diabetes is another important target in the prevention of dementia, and the focus should be on early treatment for prediabetes to delay or prevent the progression to Type 2 diabetes.

Previous research by Professor Sachdev and colleagues found that stroke patients with a history of Type 2 diabetes have worse cognitive function compared to stroke patients without Type 2 diabetes.

"In this study, we wanted to know if stroke patients with prediabetes also have worse cognitive function compared to stroke patients without prediabetes or diabetes," Professor Sachdev said.

"This is important because prediabetes is very common, and individuals can have prediabetes for several years before progressing to Type 2 diabetes. Early and aggressive treatment of prediabetes can delay or prevent Type 2 diabetes.

Lead author and Study Coordinator of STROKOG, Jess Lo, said the research combined data from 1,601 stroke patients (average age 66; 63% male; 70% Asian; 26% white; 2.6% African American) who participated in one of seven international studies from six countries.

Almost all had clot-caused strokes, and a variety of cognitive functions were assessed between three to six months after the stroke. Patients' fasting blood sugar levels measured at hospital admission and medical history were used to define Type 2 diabetes and prediabetes.

> **"The deficits we found in all areas of cognitive function highlight the importance of assessing the capacity for self-care in patients with Type 2 diabetes following a stroke."**
>
> Jess Lo

"While our study is focused on cognition after a stroke, there is strong evidence that Type 2 diabetes is associated with cognitive impairment. This is an important message for the general public. Since our study shows no evidence that prediabetes is associated with worse cognitive performance, this emphasises the importance of the early diagnosis and treatment of prediabetes (which is often under-diagnosed) in order to delay or prevent the progression to Type 2 diabetes," Jess Lo said.

The seven studies included in the analysis were all part of STROKOG. The studies were conducted in Australia, France, Korea, the Netherlands, Singapore and the United States.

DOI: 10.1161/STROKEAHA.119.028428Stroke. 2020;51:1640–1646

The study was funded by the Vincent Fairfax Family Foundation and the National Health and Research Council of Australia.

SHARED

Fifty million people worldwide have dementia (WHO, 2019). The world's ageing population presents unprecedented challenges to us. As we age and our memory fades, we may lose confidence and become isolated from our friends and family. Lifestyle may hold the key to modifying dementia risk. The brain has a 'use it or lose it' rule and social interactions may help keep our brain healthy.

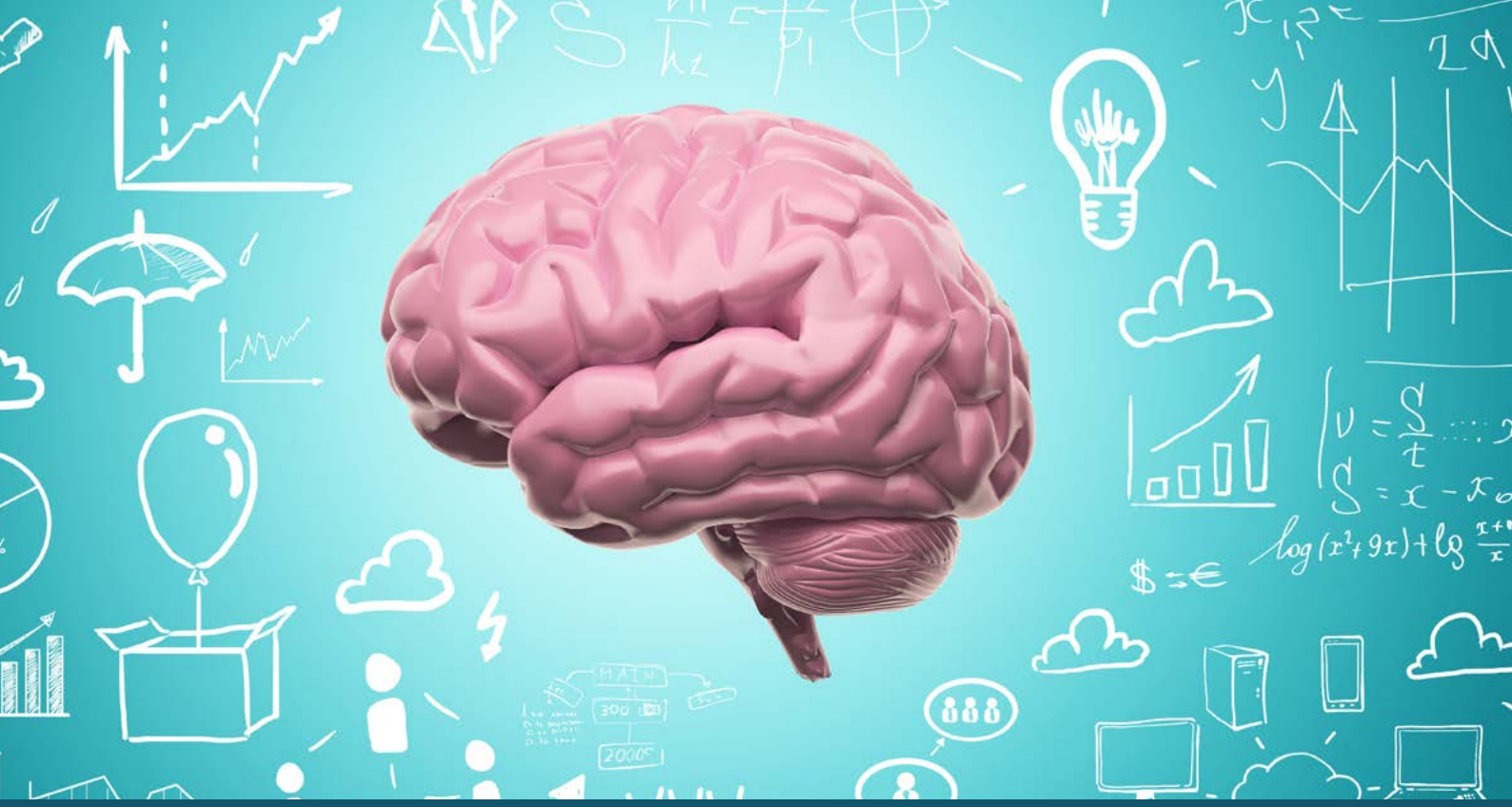
The NHMRC and European Union Joint Programme-Neurodegenerative Disease Research funded a project called SHARED, which stands for Social Health And Reserve in the Dementia patient journey to explore this question. Our team at CHeBA are working alongside our partners at Erasmus MC, Radboud UMC, Wroclaw Medical University, Karolinska Institute, Bremen University and University College London to understand how social factors (contacts, support, participation) impact cognitive decline in dementia and vice versa.

International data may unlock the secrets of social interactions and brain health. In 2020, the CHeBA team (Suraj Samtani, Ashley Stevens, Darren Lipnicki, Perminder Sachdev and Henry Brodaty) examined data from 12 longitudinal studies of ageing across 6 continents to explore this issue.

We received data from the United States, Puerto Rico, Brazil, the United Kingdom, Sweden, Germany, Greece, Central African Republic, the Republic of Congo, China, Singapore, South Korea and Australia. The global nature of this project is what sets it apart. We completed a meta-data inventory to catalogue the cognitive, physical and social variables which will enable us to test our hypotheses. We harmonised data from these 12 studies and ran models to test whether social factors distinguished between Mild Cognitive Impairment and people living with dementia. Our preliminary findings suggest that frequent social interactions and having someone to confide in may protect us against dementia risk.

In 2021, we plan to explore the trajectories of social factors over the course of dementia and examine the causal links between social and cognitive health.

Dr Suraj Samtani, Professor Henry Brodaty, Ashley Stevens, Professor Perminder Sachdev



Longitudinal Studies

"The best method to investigate the determinants of healthy ageing is to examine cohorts of individuals as they grow old. Longitudinal studies have provided many insights into ageing and dementia."

Professor Perminder Sachdev AM

Sydney Centenarian Study

The Sydney Centenarian Study (SCS) was launched in 2007 and to date has included 445 Sydney residents aged 95 and above.

Centenarians and near-centenarians are seen as exemplars of successful ageing. The overall aim of SCS is to identify factors that are important to longevity and maintenance of cognitive, physical and mental health. The project examines the cognition, physical health, psychological health, functional independence, brain structure and genetics of Australia's oldest individuals. The study now has had at least 197 participants who have reached 100 years or older; and some of our current participants have completed six research assessments over the course of three and a half years.

A wealth of data is gathered at each six-monthly in-person visit, including 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. 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.

In addition, optional components of the study provide invaluable information on the biology of centenarians. To date, 65% of participants have provided a blood sample for genetics and proteomics analysis; 11% of participants have undergone structural brain imaging (MRI).

There are currently 8 Honours and higher degree students and postdoctoral fellows who are using SCS data as part of their research projects.

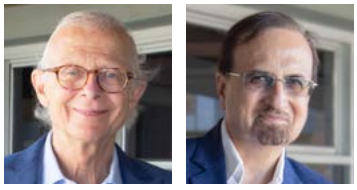
2020 was an eventful year for SCS, as indeed it was for Australian society and the world, with highlights as follows:

- SCS commenced its biggest recruitment effort to date in January 2020, inviting eligible individuals aged 95 and over to join the study from three local government areas in the eastern suburbs of Sydney. We were delighted with the response; more than 60 individuals expressed interest in joining the study.
- Eleven new participants were recruited into SCS in 2020, before the COVID-19 pandemic and ensuing lockdown in mid-March meant that we could no longer meet with our new participants face to face.

Dr Catherine Browning, departing SCS Coordinator & Fleur Harrison, Acting SCS Coordinator

- SCS continued to follow up our existing participants until December 2020. We could not visit participants, thus are extremely grateful to the participants who were able to speak with us over the phone, or completed written questionnaires where possible. We also talked to many close family or friends of our participants who gave us further perspectives about participants.
- All data collected by the study to date was entered and cleaned, and all consensus cases were reviewed by our panel of expert clinicians, by the end of 2020 in preparation for future scientific analysis.
- SCS joined a number of other studies led by CHeBA, along with those at Kings College London and Arizona State University, on a successful grant bid to examine impacts of the COVID-19 pandemic on older adults via the PLuS Alliance strategy. SCS distributed this questionnaire to current participants; to date, 67% of these have been returned.
- CHeBA's Genetics and Epigenomic Group whole genome sequenced 101 SCS participants who had reached 100 years of age, which provides us with detailed information about the genetic makeup of these long-lived SCS participants. 74% of the sample sequenced were women, which reflects the gender difference in reaching 100 years or over. This newly acquired data allows us to look at different types of genetic variants, including genomic repeats - sections of DNA that can vary in their copy number and even to estimate telomere length. Telomeres are the DNA caps found at the ends of our chromosomes that have a protective function, which shorten as we age. Our preliminary results, yet to be published, suggest that centenarians do have shorter telomeres compared to younger individuals aged in their 70s.

Project Leaders:



Professor Henry Brodaty, Professor Perminder Sachdev

Sydney Centenarian Study Project Members

Dr John Crawford, Dr Jiyang Jiang, Dr Kristan Kang, Dr Nicole Kochan, Dr Karen Mather Dr Anbu Thalamuthu, Associate Professor Wei Wen

Older Australian Twins Study

OATS commenced in 2007 as a collaboration between CHeBA, the National Ageing Research Institute (NARI) and the Queensland Institute of Medical Research (QIMR).

Dr Vibeke Catts, OATS Coordinator

Since then, we have assessed a total of 727 participants on up to four occasions - totalling over 1700 assessments. Since 2017, OATS staff have been located exclusively at CHeBA, UNSW Sydney.

The key objective of OATS is to identify genetic and environmental factors that contribute to healthy brain ageing, which is best done with a twin sample, where the genetic difference between identical (share same code) and non-identical twin (share 505 of code) pairs allows us to determine the relative contribution of genes and environment on specific outcomes.

Over its lifetime, OATS has contributed to 67 scientific publications. A minimum of 39 students have utilised OATS data for their research projects. About one-third of these students are/were medical doctor trainees, who perform small research projects as part of their medical degree, the remainder being higher degree students looking to obtain a PhD. Currently 10 Higher Degree students utilise OATS data in their studies.

OATS gratefully acknowledges the contribution of Twins Research Australia who mediated the initial contact to many of our participants, as well as funding received from the National Health and Medical Research Council, and the contribution of our participants, project staff and many collaborators in Australia and beyond.

Highlights from 2020:

- 17 scientific papers published.
- Surveyed our participants about their experiences in participating in OATS with the key motivation contributing to medical research, for the betterment of the participant's own health but also for society as a whole and for future generations. OATS participation has led to early discovery of health issues, in some cases allowing for preventative or early treatment of otherwise very serious conditions. welcomed Dr Amanda Selwood as Research Assistant, who is a psychologist and as an identical twin herself has enjoyed engaging with our study participants.
- Welcomed three new PhD students: Mr Toyin Abdulsalam will investigate the combined contribution of the genetic code and genetic modifications to gene and protein expression in ageing and longevity; Mr Chao Dong will work with our neuroimaging experts to investigate genetic and environmental influences on human brain changes in ageing and Ms Annabel Matison will be investigating the link between nutrition and the risk of depression using data from OATS and our collaborators in the IGEMS consortia.
- Continued our contribution to the IGEMS (Interplay of Genes and Environment across Multiple Studies) consortium, a collaboration between 18 international twin studies representing 76,000 twin participants. This large sample size allows us to look at differences in risk and protective factors between men and women in non-identical twin pairs consisting of one male and one female twin. It also allows us to look at the contributing factors to discordance (where one twin within a pair is exposed to a risk factor or has a disease and the other does not) in genetically identical twin. Much work that has gone into collating data across these studies and ensuring different measures of health and cognition used in different studies are comparable and able to be analysed together. This groundwork yielded 2 publications in 2020, with several more in the pipeline.

- Continued our strong contribution to the ENIGMA Network in 2020, with four papers that included OATS data published. The ENIGMA Network is an international effort to understand brain structure and function, based on MRI and genetic data from the six populated continents across the globe. One of these papers were led by Dr Karen Mather, Leader of CHeBA's Genetics & Epigenomics Group and Dr Nicola Armstrong, CHeBA collaborator from Murdoch University, WA. Their study brought together measures of blood pressure, genetic data and MRI scans from 26,654 research participants, including OATS participants, to identify genetic variations for neuroimaging markers that indicate high risk of stroke in an individual. The study team involved 96 authors, including 10 from OATS, representing 17 individual studies from across 11 different countries. As well as providing the above important research findings, this study illustrates how many smaller pieces of a puzzle can come together to increase our understanding of brain function and risk of life changing events, like strokes. While the contribution of one research participant, one researcher, or one study, may appear small, it demonstrates the power of many.
- Conducted an evaluation of the relative contributions of genetic and environmental factors to lipid levels in blood from OATS participants which showed that only about 13% of the lipids measured in the study have significant heritability, indicating that environmental and possibly epigenetic factors have a considerable influence on lipid profiles in healthy older age groups. This research was led by Dr Wong, a CHeBA PhD graduate, which he completed under the supervision of Dr Poljak and Professor Sachdev.
- In 2020 we farewelled Ms Suzy Forrester who has assisted with project administration and kept us organised since 2013.

Project Leaders


Professor Henry Brodaty, Professor Perminder Sachdev

Project Members







Dr John Crawford, Dr Teresa Lee, Dr Karen Mather, Dr Anne Poljak, Dr Anbu Thalamuthu, Professor Julian Trollor, Associate Professor Wei Wen

Sydney Memory & Ageing Study

After 15 years of assessments, the Sydney Memory and Ageing Study (MAS) officially concluded in December of 2020, making the largest continuous running study of cognitive ageing in Australia.

MAS began in 2005 with the aim of better understanding predementia syndromes such as Mild Cognitive Impairment (MCI). Over time, MAS evolved to focus on individual and lifestyle factors associated with both healthy brain ageing and cognitive decline.

MAS is renowned for its data nationally and internationally. This is largely because the study has followed the same cohort (e.g., study participants) for a decade and a half. In that time, researchers have gathered a wealth of data around sociodemographic, clinical, neuropsychological, neuroimaging, biochemical, genetics, and proteomics factors associated with brain ageing. These many data points from the same participants have allowed us to look at individual changes over time and better understand what factors predict healthy cognitive ageing versus neurodegenerative diseases like dementia.

Dr Katya Numbers, SMAS Coordinator

The MAS baseline cohort consisted of 1037 older adults (aged 70-90) recruited from Sydney's Eastern suburbs who did not have a diagnosis of dementia at the time. Participants underwent comprehensive biennial assessments (called "Waves") comprised of neuropsychological tests, medical exams, participant interviews, and questionnaires about sociodemographic, health, lifestyle, and other factors. A knowledgeable informant (close friend or family member) was also interviewed at each Wave.

In 2020, there were of course unique challenges to the MAS study in the wake of COVID-19. MAS, like all research studies, was impacted by the global pandemic and ensuing lockdowns, and as a result, 1/3 of the remaining 258 active MAS participants completed phone-only interview and questionnaires in Wave 7. Nevertheless, the study concluded on time and the MAS team was able to create and distribute a novel COVID-19 questionnaire to all active participants before the end of the year so that we can better understand the unique impacts of COVID-19 on our older participants.

To date, MAS data has contributed to 181 publications in in respected international scientific journals, with 20 of those being published in 2020 alone. Twenty-six independent groups of researchers reached out and requested MAS data in 2020, across 14 different national and international research institutions. There are currently 25 higher degree students and postdoctoral fellows who are using MAS data as part of their research projects.

Highlights from 2020 – Snapshots

- MAS wrapped up all participant and informant assessments after 15 years of continuous testing. All data has been entered and all consensus cases have been seen and diagnosed.
- MAS collected new data in 2020, including pure-tone audiometry data, and the Attitudes About Scale and Purpose in Life scale, for new analyses.
- MAS distributed a novel COVID-19 questionnaire to 250 active participants with a 90% return rate.
- MAS joined Kings College London and Arizona State University on a successful grant bid to examine impacts of the COVID-19 pandemic on older adults via the PLuS Alliance strategy.
- MAS contributed data 7 global consortia projects in 2020.

Funding: NHMRC Program Grants (ID350833; ID568969; APP1093083)
https://www.nhmrc.gov.au/funding

Project Leaders


Professor Henry Brodaty, Professor Perminder Sachdev

Project Members






Dr Adam Bentvelzen, Dr John Crawford, Professor Brian Draper, Dr Nicole Kochan, Dr Karen Mather, Professor Julian Trollor

Worldwide Study Using MAS and OATS Data Unlocks Genetic Secrets of the Grey Matter

A major international collaboration using data CHeBA's Sydney Memory & Ageing Study and the Older Australian Twins Study, has produced the first genetic map of the cerebral cortex, identifying more than 300 genetic variants that influence the structure of the key brain region.

The cerebral cortex, often referred to as the 'grey matter', plays a crucial role in thinking, information processing, memory and attention. It is the relatively thin, folded, outer layer of the brain. Its folds area way of packing in more neurons, or brain cells.

The extent of the folds – which are measured by surface area –and the thickness of the cortex have previously been linked to cognitive abilities and various psychiatric traits, including schizophrenia, bipolar disorder, depression, attention deficit hyperactivity disorder (ADHD), and autism. However, until now, not a lot was known about the genetic variants that influence the size of the surface area and thickness of the cortex.

More than 360 scientists from 184 different institutions - including CHeBA's Co-Directors Professor Perminder Sachdev and Professor Henry Brodaty and Leader of CHeBA's Genetics & Epigenomics Group Dr Karen Mather - contributed to the global effort, which was published in the prestigious journal *Science*.

"The longitudinal studies being conducted at CHeBA have generated rich datasets that have led to many novel discoveries, often in collaboration with several researchers overseas. This paper is another example of the rich dividends that the work of over the last 15 years is yielding," said Professor Perminder Sachdev.

Researchers identified 306 genetic variants that influenced the structure of the cerebral cortex. The study was conducted to identify genetic variants that influence brain structure to shed light on how genetics contribute to these differences among us.

Researchers found that the genetic variants that are linked to a smaller surface area of the cerebral cortex – or less folding – also contribute to a greater risk of ADHD, depression and insomnia.

The findings are now a resource that can be used by other scientists to help answer more questions about the genetic influences on the brain and how they relate to numerous behavioural or disease outcomes.

The researchers studied MRI scans and DNA from more than 50 thousand people.

It is only by sharing data through these major, international collaborations that researchers can continue to unpick the highly complex relationship between genes, brain structure and various disorders.

DOI: 10.1126/science.aay6690

Maintain Your Brain

Maintain Your Brain (MYB) is a randomised controlled trial of an online intervention designed to target modifiable risk factors for dementia in general and Alzheimer's disease in particular.

MYB aims to reduce cognitive decline across three years amongst 55-77 year olds. Risk factors are addressed through four intervention modules (physical activity, nutrition, brain training, and peace of mind) administered based on individual risk profiles.

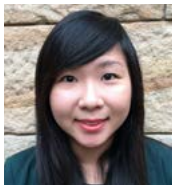
Work started on the MYB digital platform in 2016, the trial started in 2018 and 2020 saw participants complete their 24-month follow-up. MYB was designed to be fully online and we were able to continue study procedures with minimal impact from COVID-19. New materials and recommendations were shared with participants to maintain lifestyle changes despite restriction requirements. Participants were also encouraged to share their physical distancing stories with other participants during this period. Early indications are that the level of participation during this period was consistent with previous years. We appreciate the efforts of all participants during a time where usual routines were disrupted.

Study Coordinator: Dr Megan Heffernan

Project Leaders


Professor Henry Brodaty, Professor Perminder Sachdev

Project Members




Tiffany Chau, Juan Carlo San Jose

MAINTAIN YOUR BRAIN

Benefitting Future Generations

We are exceptionally grateful to all participants across our studies, including 77 year-old Paddy Goldsmith, who, along with 6,000 other Australians, is playing a vital role in changing the future of Alzheimer's disease and other dementias through her participation in Maintain Your Brain.

"My motivation to be involved in research came after losing two friends to dementia; one of whom was especially dear to me," says Paddy.

"We also know six other families who have a family member living with the disease and my simple hope is that our involvement will help others in the future. Witnessing our friends and their carers endure the downward path of dementia was undeniably a strong motivator to join a prevention trial."

Paddy was born in England and moved to Australia in 1969 with husband Geoff. They live in the beautiful countryside of Bowral not far from their two Sydney-dwelling sons, two grandchildren, a grand-dog and grand-cat.

For Paddy, the personal benefits of being involved in a research trial are enormous.

I firmly believe this program has benefited both Geoff and I greatly and we would love future generations to follow the same path, starting at a much younger age!

Paddy says she now concentrates better through the brain training, feels much better in herself through the dietary changes she has made as a result of the program and feels she has recovered more quickly from brain surgery than would have been the case without the benefit of the required exercise.

"The more I learn about dementia and the associated risk factors, the more I hope the work of Maintain Your Brain will bring about a change that is recognised by more people."

Paddy and Geoff Goldsmith

This is an excerpt from a blog in The Brain Dialogues. To read the full article: ***http://bit.ly/FutureGenerationsMYB***

SocCOG

With generous contribution from 134 Older Adult Volunteers and 251 under-60 volunteers, CHeBA's Social Cognition Project (SocCog) completed its cycle in 2020.

SocCog was a collaboration between UNSW Sydney and University of Queensland (UQ), funded by the Australian Research Council Discovery Project Grant. The project successfully achieved its main goal of uncovering links between social cognitive function and social difficulties at different life stages. With several papers underway, SocCog has already effectively contributed to the literature with a published paper in the Journal of Geriatric Psychiatry, with first authorship by UNSW PhD Candidate, Russell Chander. The hope is that findings from this research will assist in the development of programs and interventions aimed at enhancing social function and wellbeing in vulnerable groups. The CHeBA SocCog team - comprised of Professor Perminder Sachdev, Dr Karen Mather, Dr Nicole Kochan, Research Assistant Rhiagh Cleary and Russell Chander – together with key UQ members Professor Julie Henry and Dr Sarah Grainger, are grateful towards the many other UNSW Studies and staff at both the Prince of Wales Hospital and Neuroscience Research Australia, who each aided in the facilitation of this project. Most of all, the team is grateful for the wonderful volunteers who donated their time to the project. The effort truly was a social one!

PhD Completions

Dr Yue Liu: Contribution of cerebrovascular and Alzheimer-type pathology in the aetiology of neurocognitive disorders

Alzheimer's disease and cerebrovascular disease are the two most prevalent causes of dementia. However, the molecular basis of Alzheimer's disease and vascular dementia remains incompletely understood. Combined vascular and Alzheimer's disease pathology is the leading cause of dementia in the very old. My thesis explored the association and interaction between cerebrovascular disease and Alzheimer's disease pathology/dementia from the perspectives of plasma lipid profiles, imaging biomarkers, post-mortem pathology, and animal models.

Dr Yue Liu was supervised by Proessor Perminder Sachdev and Dr Nady Braidy

Associate Professor Anne Wand: Understanding self-harm in the very old: A qualitative study with implications for clinical care and wider society

My thesis presented novel insights into why the very old self-harm and the importance of relationships with family and clinicians, which influence the decision to self-harm and outcomes. A brief educational intervention based upon this qualitative work had immediate impact on the knowledge and confidence of multidisciplinary clinicians.

Anne Wand was awarded the Dean's Award for Outstanding PhD Theses 2020, UNSW Medicine.
She received a Seed Grant from the UNSW Ageing Futures Institute in 2019 to further her research into the prevention of suicide in older adults. She was appointed to the position of Conjoint Associate Professor at the University of Sydney in 2020.

Dr Anne Wand was supervised by Professor Carmelle Peisah, Professor Brian Draper and Professor Henry Brodaty

PhD Research Features

Making Mindreading Easier on the Mind

UNSW **Scientia PhD Candidate Russell Chander** has helped develop an enhanced version of a popular test for theory of mind, making it shorter and more effective for use with older adults. The research, published in the *v Journal of Geriatric Psychiatry*, was led by CHeBA's Social Cognition Ageing Study.

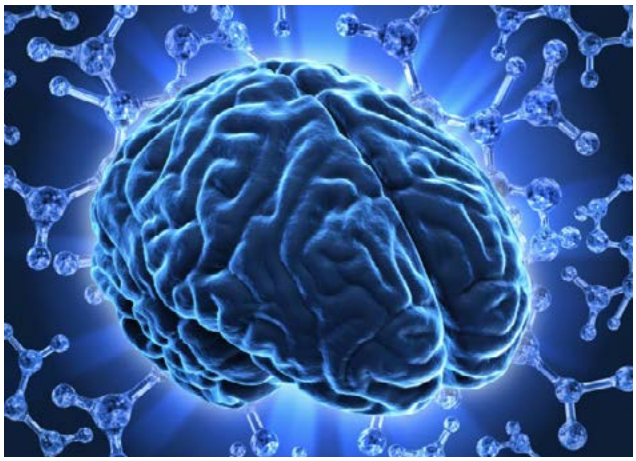
Theory of mind, sometimes known as "mindreading", is the social skill of being able to tell what someone is thinking or feeling without that person explicitly stating their thoughts. This is commonly done through reading social cues and people's expressions.

Currently, the most common assessment for theory of mind is the Reading the Mind in the Eyes Test; a 36-item assessment created by researchers from the Autism Research Centre at the University of Cambridge.

"The 36 items take some time to administer, and some older participants complained about its length," he said.

Under the supervision of CHeBA's Co-Director, Scientia Professor Perminder Sachdev, Mr Chander and the Social Cognition Ageing study team assessed data collected from 295 participants in the Sydney Memory and Ageing Study, with a mean age of 86 years, to shorten the Reading the Mind in the Eyes Test to a recommended 21 items. The data allowed them to identify the items in the original test most effective at measuring theory of mind performance, as well as determine which items could be removed without greatly affecting effectiveness of the test.

"This ensured we would not unconsciously let our biases affect which items we chose," explained Mr Chander.



The study team hopes that by making the test easier on older adults, it will help encourage more researchers and clinicians to use it with their patients and participants. They also hope to use this assessment in future CHeBA studies, to help improve participants' experiences with research.

Theory of mind, along with other social skills and abilities - collectively known as social cognition - appears to be affected in some older adults. Poor social cognition may affect one's ability to function well in social settings and may also be an early warning sign of dementia. More work is still needed to fully understand how social cognition functions in ageing and dementia, and the social cognition researchers at CHeBA are continuing to add to this knowledge.

DOI: doi.org/10.1002/gps.5369

This study is being performed in collaboration with Professor Julie Henry of the University of Queensland and is funded through an Australian Research Council grant.

Machine Learning Predicts Onset of Dementia

PhD Student Annette Spooner, with fellow researchers from CHeBA and the School of Computer Science and Engineering, has undertaken the largest comparison of survival analysis methods to date, to predict the onset of dementia using machine learning.

The comparison, published in *Nature Scientific Reports*, is the first work to apply these methods to CHeBA's Sydney Memory and Ageing Study and examines the most diverse variety of data in a study on dementia to date.

There is currently no cure for dementia and no treatment available that can successfully change the course of this disease.

"Machine learning models that can predict the time until a person develops dementia are critical tools in helping our understanding of dementia risks," said lead author and computer scientist."

Annette Spooner

"Using data from the Sydney Memory and Ageing Study we have found we are able to build models that predict the onset of Alzheimer's disease and other dementias with quite high accuracy."

"Machine learning can give more accurate results than traditional statistical methods when modelling high-dimensional, heterogeneous, clinical data," said Ms Spooner, whose research was supervised by Professor Arcot Sowmya and assisted by honours student Emily Chen.

The research compared the performance and stability of ten machine learning algorithms, combined with eight feature selection methods capable of performing predictions of this specific type of clinical data.

Co-author and Co-Director of CHeBA, Professor Perminder Sachdev, said the models they developed predicted survival to dementia using data from Alzheimer's Disease Neuroimaging Initiative as well as the Sydney Memory and Ageing Study.

"Using machine learning, we found that neuropsychology scores are the best predictors for onset of dementia."

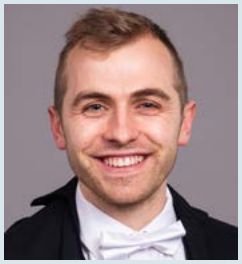
Future research through this collaboration will aim to improve the stability of which variables are selected by the models as being the most predictive of dementia.

DOI: 10.1038/s41598-020-77220-w

Blood Pressure Treatment Associated with Double Rate of Cognitive Decline in Older Individuals

A blood pressure reading that is greater than 140 mmHg and left untreated will significantly worsen cognitive decline in older persons. However, systolic blood pressure that is lower than 120 mmHg and is treated with antihypertensive medications may also increase cognitive decline.

The study, published in *The Journal of Gerontology: Medical Sciences*, is important given the 2017 changes to blood pressure management guidelines that recommended blood pressure should be maintained below 120/80mmHg.



PhD Student Dr Matt Lennon, a medical doctor and lead author on the study, said "Medical practitioners are being advised in people older than 70 that systolic blood pressure should be kept below 120 mmHg. Our study indicated that participants using antihypertensives with that blood pressure reading ended up with worsened cognitive decline.

"Over the course of our study they had approximately doubled the rate of cognitive decline compared to the average participant," said Dr Lennon.

"We also found that participants with blood pressure greater than 140 mmHg who did not use antihypertensives had similar worsened rates of cognitive decline, approximately double the average participant over the course of the study."

Co-Director of CHeBA and co-author, Professor Perminder Sachdev, said that ongoing treatment at new recommendations of lower systolic blood pressure targets should be considered carefully in older populations. Maintaining blood pressure at appropriate levels through all stages in life must be part of the prevention strategy if we are to mitigate the effects of dementia on our society in the future.

Dr Lennon said that it is important for patients and their families to know what their ideal blood pressure is for their age and to be aware of damaging cognitive effects of blood pressure that is too high or too low.

DOI: 10.1093/gerona/glaa232

Scholarship Success

The DCRC has awarded Zara Page a scholarship recognising and responding to the cultural and linguistic diversity of older Australians in our community through the dedicated study of assessment tools for cognitive decline. Zara is supervised by CHeBA's Co-Director Professor Henry Brodaty and Neuropsychology Group Leader Dr Nicole Kochan.

Sophia Xi Awarded

Congratulations to CHeBA ILP Student Sophia Xi who was awarded for her presentation Pencil vs Machine: Using Computerised Tests to Detect Subjective Cognitive Decline at the ILP 3 minute talks. Sophia is supervised by Dr Nicole Kochan and Dr Karen Croot.

Princess Neila Litkouhi Awarded

Princess Neila Litkouhi was also honoured at the ILP 3 minute talks. Neila, who is supervised by Professor Henry Brodaty and Dr Katya Numbers, presented Effects of lifestyle activities in early mid and late life on late-life cognition.

CHeBA Publication Awards

The highly competitive Inaugural CHeBA Publication Awards were open to all first authors who had papers published between 28th February 2019 and 31st October 2020. The awards aim to recognise excellent performance, quality research and outstanding papers published by CHeBA researchers. Winners were announced virtually.

Mary Revelas
Winner - Student Category

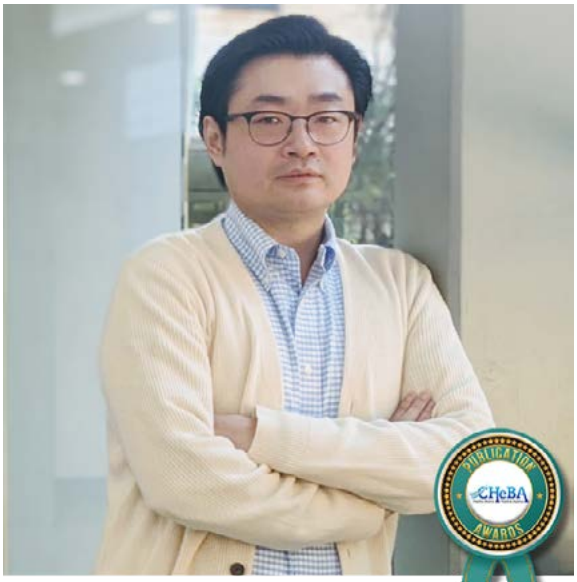
Revelas M, Thalamuthu A, et al. Exceptional Longevity and Polygenic Risk for Cardiovascular Health. *Genes* 2020, *10(3): 227*

DOI: 10.3390/genes10030227

Jess Lo
Winner - Professional Staff Category

Lo J, Crawford J, et al. Association of Prediabetes and Type 2 Diabetes With Cognitive Function After Stroke. *Stroke* 2020, *51: 1640-1646*

DOI: 10.1161/STROKEAHA.119.028428



Dr Jiyang Jiang
Winner - Early Career Category

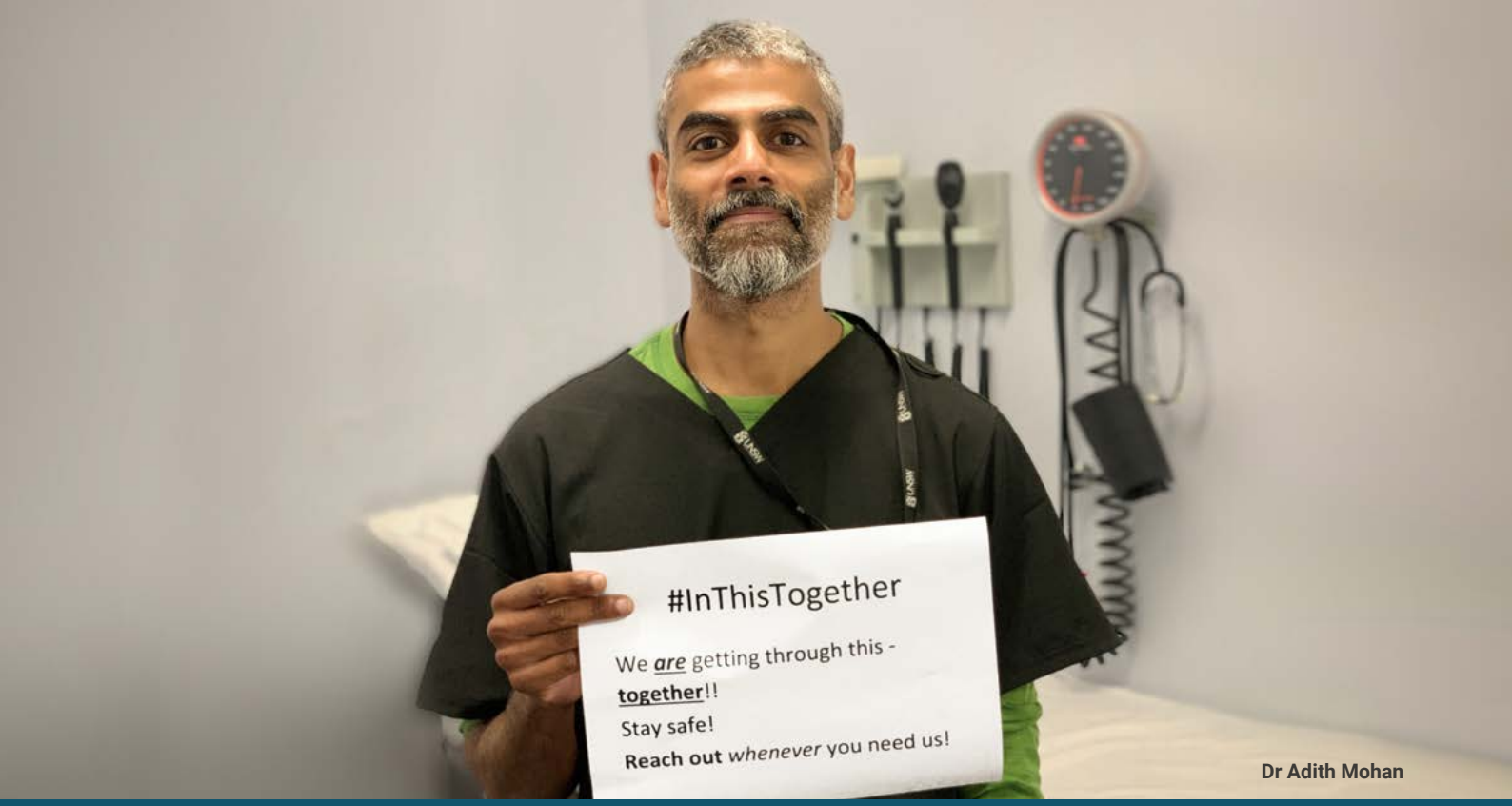
Jiang J, Liu T, et al. Stronger bilateral functional connectivity of the frontoparietal control network in near-centenarians and centenarians without dementia. *NeuroImage* 2020, *215: 116855*

DOI: 10.1016/j.neuroimage.2020.116855

Dr Karen Mather
Winner - Mid Career Category

Armstrong N, Mather A, et al. Common Genetic Variation Indicates Separate Causes for Periventricular and Deep White Matter Hyperintensities. *Stroke* 2020, *51: 2111-2121*

DOI: 10.1161/STROKEAHA.119.027544



Dr Adith Mohan

Our Community

"Despite the pandemic, the dementia curve remains unabated. Quality research remains the answer."

Richard Grellman AM
Spokesman, The Dementia Momentum

The Dementia Momentum – Spokesman's Report

There are very few industries that have not been significantly impacted by the global pandemic, with 2020 fundraising and engagement plans for The Dementia Momentum no exception to the rule.

All of us have had to adapt to life with COVID-19 - uncertainty, inability to plan with confidence, financial implications and of course loss of freedom to travel, domestically and internationally.

For those living with dementia, these losses are generally beyond their awareness. Many of the folk living with this disease are often described as 'living in the moment', and thus daily experiences that we live with such as emails, text messages, tax obligations, changing weather, news updates, politics and even mundane matters like shopping and what to prepare for dinner, quickly become matters of no import - if indeed any awareness of such things even exists.

COVID-19 has of course had a material impact on those in residential care and their loved ones. Either no visitation or visits on a restricted basis for the last 12 months have understandably become the norm. This has obvious implications for residents and their families alike, especially at special times like Christmas.

In our own case, our 3 adult children and 7 grandchildren were so looking forward to seeing my wife Suellen on Christmas Day, only to be denied by a last-minute lock-down. As with many others in the same situation as my family, so we endure....!

The reality is that despite the pandemic, the dementia curve remains unabated. It continues to affect 50 million people globally and is predicted to almost triple by 2050. Quality research remains the answer and following an enormously successful year with The Dementia Momentum in 2019, we had to divert our attention away from partnerships with KPMG Sydney and ARIA Restaurant Sydney who generously host our annual events and look to other means to support CHeBA's research and remain engaged with you, our community.

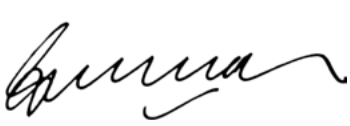
All events across Australia were suspended indefinitely, which also meant we had to shelve any plans to run Wipeout Dementia; a fundraiser which had built incredible momentum over the last five years and borne witness to the most successful event to date in November 2019, with the property industry raising over $210,000. Last year also saw us host the first ever intergenerational-event, with many senior corporates involving their children in their quest to support critical dementia research.

Richard Grellman AM is Chairman of IPH Limited, FBR Limited and Spokesman for The Dementia Momentum at the Centre for Healthy Brain Ageing (CHeBA).

I was humbled with the response to our 2020 Wipeout Dementia Appeal, with significant donations made despite the lack of face-to-face interaction. For this support, which certainly impacted the retention of researchers at CHeBA, I thank you.

I would also like to extend enormous thanks to the Vincent Fairfax Family Foundation, whose 5-year funding for The Dementia Momentum will come to its conclusion in 2021. This major grant has allowed for extraordinary inroads to be made across two major consortia at CHeBA which are identifying common risk factors for dementia and cognitive decline as well as facilitating a better understanding of the determinants of vascular contributions to cognitive disorders and striving to help improve the diagnosis and treatment of vascular cognitive disorders. A number of research papers were published in high impact journals this year with substantial media impact, largely as a result of this funding support from VFFF.

As we all look forward to 2021 and the possibility of reinstating our annual events, I sincerely thank you all for your continued support of The Dementia Momentum initiative but also specifically of the global dementia challenge, that we will continue to confront long after COVID-19 has passed.

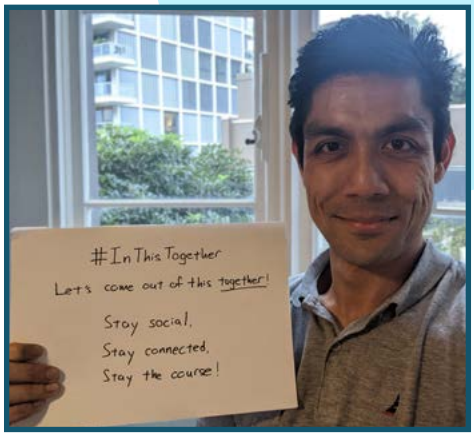


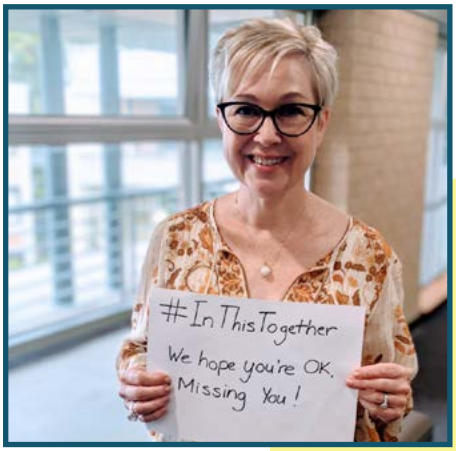
Richard Grellman AM

the dementia momentum

#InThisTogether

As a result of the COVID-19 pandemic, CHeBA staff and Ambassador PJ Lane joined the international **#InThisTogether** campaign to share messages of support with our community, study participants, colleagues and family.

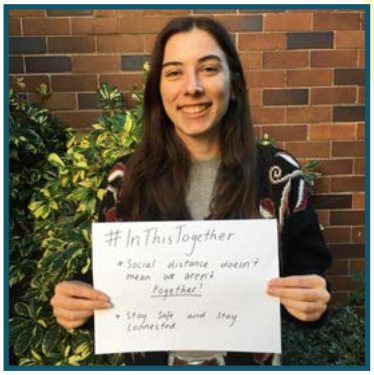





#InThisTogether
✓ DO PRACTICE SELF-COMPASSION & SELF-CARE
✓ DON'T BE AFRAID TO ASK FOR HELP (WE ARE HERE FOR YOU!)
#RainbowHunt

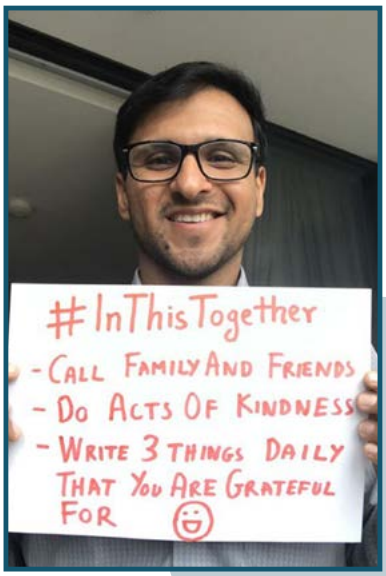

#InThisTogether
Lift one another up.
Put positive energy into this world.
Know how grateful we are for you.
x See You Soon!


#IN THIS TOGETHER
SOCIAL DISTANCING BUT
CREATING NEW KNOWLEDGE


#InThisTogether
* Social distance doesn't mean we aren't together!
* Stay Safe and stay connected


Take a moment to smile, laugh and be happy!
#InThisTogether


In This Together
Stay at home
and
... Read
... Do Puzzles
... Bake
... Paint/Art
... Learn a language
... STAY ENGAGED!


#InThisTogether
- CALL FAMILY AND FRIENDS
- DO ACTS OF KINDNESS
- WRITE 3 THINGS DAILY THAT YOU ARE GRATEFUL FOR


#InThisTogether
Social relationships sustain us. Sometimes...they can also drain us.
It is important to look after yourself while caring for others.
✓ It's ok to reach-out. Even the strongest person can feel overwhelmed now and then.
✓ Allow yourself proper rest and take a break from information overload by turning off phones and electronic devices.


#InThisTogether
TRY TO MAKE ONE PERSON HAPPY EACH DAY
START WITH YOURSELF!


#InThisTogether
Stay home and stay safe.
Be kind to yourself and others.
Keep your mind and body active.


Not all in the same boat, but...
#InThisTogether.
Accept differences, and Share experiences!


#InThisTogether
Physically separated but socially connected ♡
Thinking of you and hope you are well!


#IN THIS TOGETHER
SOCIAL DISTANCING, YES.
BUT LIKE A BRAIN
NETWORK WE ARE STILL
CONNECTED AND CREATIVE.


#InThisTogether
Reach out and connect with each other. You never know how much a simple hello can mean to someone!


#InthisTogether
Keep your MIND and BODY active

The Brain Dialogues

CHeBA's Blog, The Brain Dialogues, continued to have a strong readership in 2020. The blog covers a variety of aspects of brain health, research and donor impact articles.

This year we launched the CHeBA Meet Our Researcher Series. This fascinating series individually profiles CHeBA's innovative research team, covering their achievements, research projects and provides insight into why our dedicated academics enjoy working at CHeBA and what motivates them to make a difference through critical brain research.

Follow The Brain Dialogues at ***https://cheba.unsw.edu.au/content/blog***

We have included excerpts from two generous supporters of CHeBA. The full articles can be read in *The Brain Dialogues*.

Regular Giving – Former Staff Member Continues Support

Dr Karolina Krysinska obtained her PhD in Psychology in 2001 and has since had a rich career history in research. She is a Research Fellow at the Centre for Mental Health, Melbourne School of Population and Global Health at The University of Melbourne and an Adjunct Senior Lecturer at the Centre for Primary Health Care and Equity at the University of New South Wales.

She is also a CHeBA donor.

Professor Zdzislaw Krysinski, Dr Romana Krysinska and Dr Karolina Krysinska

Karolina, whose parents are both medical doctors, is originally from the city of Poznań which sits on the Warta River in West Poland. Many years in mental health eventually led Karolina to the Black Dog Institute where she remained focused on suicide prevention. It was during this time that she had the opportunity to meet CHeBA Co-Director Professor Henry Brodaty and not long after took a role with him in the Dementia Centre for Research Collaboration – eventually leading to what she describes as a privilege of observing his clinical work.

"It was experiencing Henry's interaction with his patients that encouraged me to work with people as a psychotherapist," says Karolina. "He was so exceptionally kind to every individual."

It was during the ensuing year and a half, while working on a scoping study for a national dementia registry in Australia to improve dementia clinical care at the Dementia Centre for Research Collaboration, that her father, Professor Zdzislaw Krysinski, declined significantly from Parkinson's disease.

Professor Krysinski's challenging journey with the disease had developed into dementia as well as tremors.

A poignant memory for Karolina that helped her retain her strength was advice from Henry, that it is "comforting to have knowledge." This advice proved to be Karolina's push into dementia research.

"Witnessing my father's suffering and seeing how my mother dealt with it with so much love and devotion keeps me motivated to create change for people diagnosed with dementia – and their families."

Peer to Peer Fundraising through Wipeout Dementia – A Tribute to Jean Nesbitt

In 1945 when Australians were celebrating the end of the Second World War, a baby girl was born west of Sydney, in Granville. Her parents named her Jean.

65 years later and with three loving sons, seven grandchildren and more than 50 years of a strong and happy marriage to husband Len Nesbitt, Jean was diagnosed with vascular dementia – the second most common form of dementia after Alzheimer's disease.

On Friday, 11 September, just over 10 years since she was first diagnosed, Jean's family said their loving goodbyes at a beautiful memorial held near their family home.

It was his Mother's diagnosis and his Father's ensuing dedication to her care that led Geoff Nesbitt to the Centre for Heathy Brain Ageing's ***Wipeout Dementia*** campaign.

He would go on to raise close to $10,000 for CHeBA's research in the corporate surfing fundraiser and be featured on the front cover of the local newspaper in tribute to his Mum. He even competed alongside 17-year-old son Lachlan in the first inter-generational Wipeout Dementia held in 2019.

In a sad twist of fate Jean witnessed and cared for many people with Alzheimer's disease and other dementias, so when her own diagnosis came at age 63 she was well aware of what was in store.

Although Geoff and his family miss their Mother and Grandmother, their gratitude to Len Nesbitt is immense. "He always maintained he would never place Mum in a Nursing Home and would instead care for her himself up until the very end, which he did."

To discuss contributing to CHeBA's research please contact ***h.douglass@unsw.edu.au***

Jean Nesbitt (front centre) and her family

CHeBA in the Media

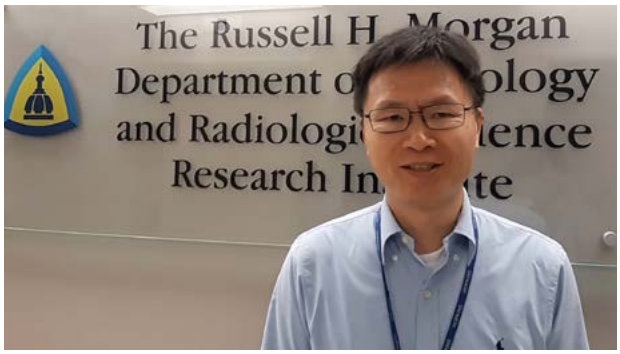
ABC Health Report – Dementia Prevention, Protection and Cures

Co-Director **Professor Henry Brodaty** was interviewed by Dr Norman Swan in a special ABC Radio National Report looking back at the last twenty years of dementia research toward a cure.

http://bit.ly/DementiaProtection

CHeBA Visiting Lecture Series

In 2020 we launched the CHeBA Visiting Lecture Series; hosting some of the world's leading brain and ageing researchers in a series of interactive webinars open to the public. We were privileged to host internationally acclaimed researchers Professor Hanzhang Lu and Professor Ron Petersen. Talks are available for streaming and will continue in 2021.



Professor Hanzhang Lu
Professor of Radiology and Radiological Science, Johns Hopkins University

Talk Title:
Brain Vascular Function in Ageing and Cognitive Impairment

Professor Ron Petersen
Professor of Neurology, Mayo Clinic

Talk Title:
Diagnosing Alzheimer's Disease in the Biomarker Era: Promises and Pitfalls

Success for Brain Bugs

In May 2020 Dr Katya Numbers, Dr Louise Mewton, Dr Claire Burley and Virginia Winter won the UNSW Medicine Movement Challenge. By logging their physical activity the CHeBA 'Brain Bugs' recorded over 1700 virtual kms to top a field of 57 teams and and win the race up Australia's West coast from Cerventes to Exmouth.

StepUp for Dementia Research

In 2020 CHeBA proudly became a Champion to StepUp For Dementia Research. The service connects individuals (both with and without dementia) with researchers conducting studies into dementia prevention, diagnosis, treatment, care and cure.

https://www.stepupfordementiaresearch.org.au/

StepUp for Dementia Research

Public Forums

Positive Mental Health, Positive Ageing

An engaged online audience of over 300 community seniors joined the Eastern Suburbs Older Persons Mental Health Service's annual healthy ageing forum, held for the first time by webinar due to the COVID-19 global pandemic.

Mr Mike Gatsi, Service Director for Eastern Suburbs Mental Health Service, officially opened the 2020 **Positive Mental Health, Positive Ageing** forum and acknowledged that it was a milestone year for the forum. "Thirty years ago, Professor Henry Brodaty founded the Older Persons Mental Health Service and has since maintained proactive promotion of good mental health as we age," said Mr Gatsi. He said that Professor Brodaty and his team had set a gold standard in mental health care while simultaneously working to ensure research findings were made available to all older people in the community.

The event, supported by CHeBA, sought to promote positive ageing with a highlight being a heart-warming feature interview with 88 year old award-winning performer and Australian icon Toni Lamond, who spoke candidly with Professor Brodaty on *Positive Ageing: My Story*.

Professor Henry Brodaty & Toni Lamond

The Hon Dr Kay Patterson AO, Age Discrimination Commissioner for the Australian Human Rights Commission, gave the keynote address from Melbourne and paid tribute to former Age Discrimination Commissioner, Susan Ryan AO. She outlined the vulnerabilities that exist for the senior community, including the risks for elder abuse.

Other speakers at the online forum were leading researchers in the area of purposeful and healthy ageing including Professor Maria Fiatarone Singh, University of Sydney Geriatrician, who explained that exercise supports prevention of age-related changes and said that many studies over decades have shown that exercise can make you age more slowly.

Old Age Psychiatrist, Professor Carmelle Peisah spoke passionately about *Positive Ageing: Being Positive About Your Rights*, challenging ageism and promoting human rights for seniors. *Positive Ageing: Mental Health of Older People* was presented by Professor Brodaty who noted the significant number of mental health issues in society, with a major study indicating that one in every two people had experienced a mental health concern over their lifetime.

He outlined that good emotional and psychological wellbeing were essential for positive mental health - and that reduction in all forms of stigma was necessary to ensure older people were confidently able to seek support for their own mental wellbeing. Professor Brodaty said that he and his colleagues will continue to strive to overcome ageism and to improve medical care and access to care, with an ultimate goal of positive mental health for all seniors.

TedX Talk

World leading authority on ageing and dementia, **Professor Henry Brodaty**, joined the TEDx community in February to highlight techniques you can employ to enhance brain health and help prevent or delay the onset of dementia.

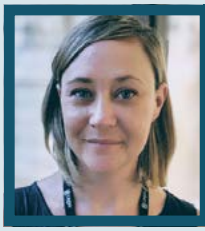
CHeBA Stitch Seminar Series

Throughout 2020 a number of CHeBA researchers shared the latest findings on healthy brain ageing with the Stitch community through a series of fun and informative presentations.

Rhiagh Cleary
The Companion Campaign

Russell Chander
Empathy and Genetics: Is there a link?

Dr Anne-Nicole Casey
Social Networks and Healthy Brain Ageing



Dr Katya Numbers
Challenging Negative Stereotypes of Ageing

Dr Ben Lam
Social Planning for Retirement

Major Supporters

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Australian Government
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NIH National Institutes of Health

DCRC Dementia Collaborative Research Centres

Black Dog Institute

NeuRA Discover. Conquer. Cure.

NHMRC

JPND research

Australian Dementia Network
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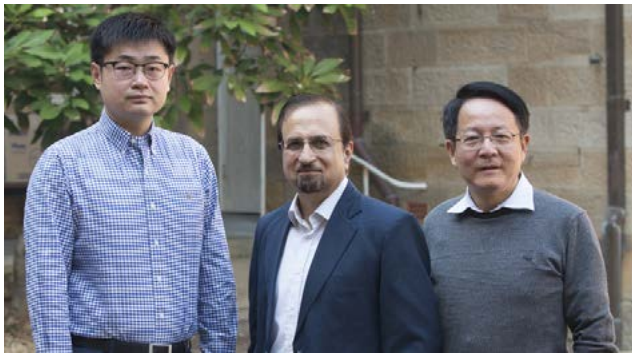
Major Gifts - J Holden Family Foundation Advances Neuroimaging Research

"Brain age" is an emerging hot research topic in brain ageing research.

Brain age refers to an estimate of "how old a person's brain is biologically", representing actual brain health status. For example, a person aged 80 years old may have a healthier brain and more intact brain structures relative to his/her age. In this case, a younger brain age of, for example, 70 will be assigned. By doing so, one can assess the brain's health relative to chronological age. Research can also be conducted by examining the protective factors in the individuals with younger brain age and risk factors in those with older relative brain age. CHeBA's Neuroimaging Group, led by Associate Professor Wei Wen, is taking this line of research to the next level.

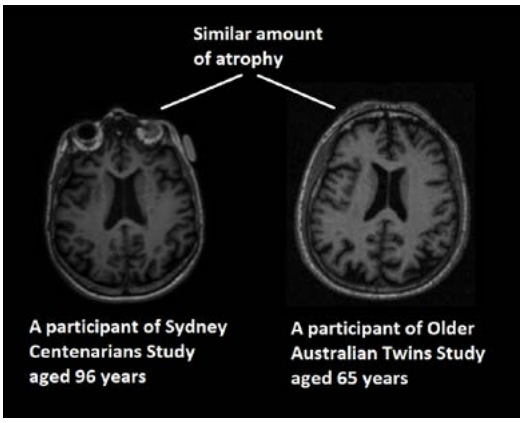


Dr Jiyang Jiang, Professor Perminder Sachdev and Associate Professor Wei Wen

"Most brain age studies to date focus on brain structural measures, including brain grey matter volumes and thickness," said Dr Jiyang Jiang, senior researcher within the Group.

"Our team at CHeBA believe vascular status should contribute significantly to the estimation of brain age," he said.

Thanks to continued and significant funding support from the J Holden Family Foundation, the Neuroimaging Group at CHeBA started collaborating with UNSW's School of Mathematics and Statistics in the Faculty of Science, to apply the latest deep learning algorithms to estimate vascular brain age from MRI scans. Specifically, the Neuroimaging Group has obtained access to a large cohort study, UK Biobank, with over 18,000 participants. UK Biobank has collected state-of-the-art diffusion-weighted imaging data which are demonstrated to be sensitive to vascular pathology. Using these data, the Neuroimaging Group has trained and validated a deep learning model. The model is now ready to be applied to any new datasets to predict vascular age.



Founded in 2010, the J Holden Family Foundation has since generously supported approximately 50 different organisations across research, education, student scholarships and community endeavours.

"We all just felt we should do something for society," said John Holden, Chairman of the Foundation.

The Foundation initially became CHeBA's first Diamond Member of The Dementia Momentum in 2016, which funded a project that brought together a large number of studies around the world to collectively examine the clinical implications and the genetic basis of white matter hyperintensities and lacunes (small silent strokes), and thereby cerebral small vessel disease.

"From the initial focus on genetics, the funding has allowed us to expand our research to examine several aspects of small vessel disease – which is recognised as a common contributor to dementia in older individuals," said Dr Jiang.

The funding specifically enabled the Neuroimaging Group to examine how closely white matter hyperintensities and lacunes are associated with dementia and cognitive decline.

Our hope is that through this support CHeBA can accelerate developments in knowledge and prevention of vascular dementia, said Mr Holden.

CHeBA's Co-Directors Professor Perminder Sachdev and Professor Henry Brodaty said the contribution had been integral to the expansion of this area of research.

"We have made significant progress in researching cerebral small vessel disease as a result of the generosity of the J Holden Family Foundation," said Professor Perminder Sachdev.

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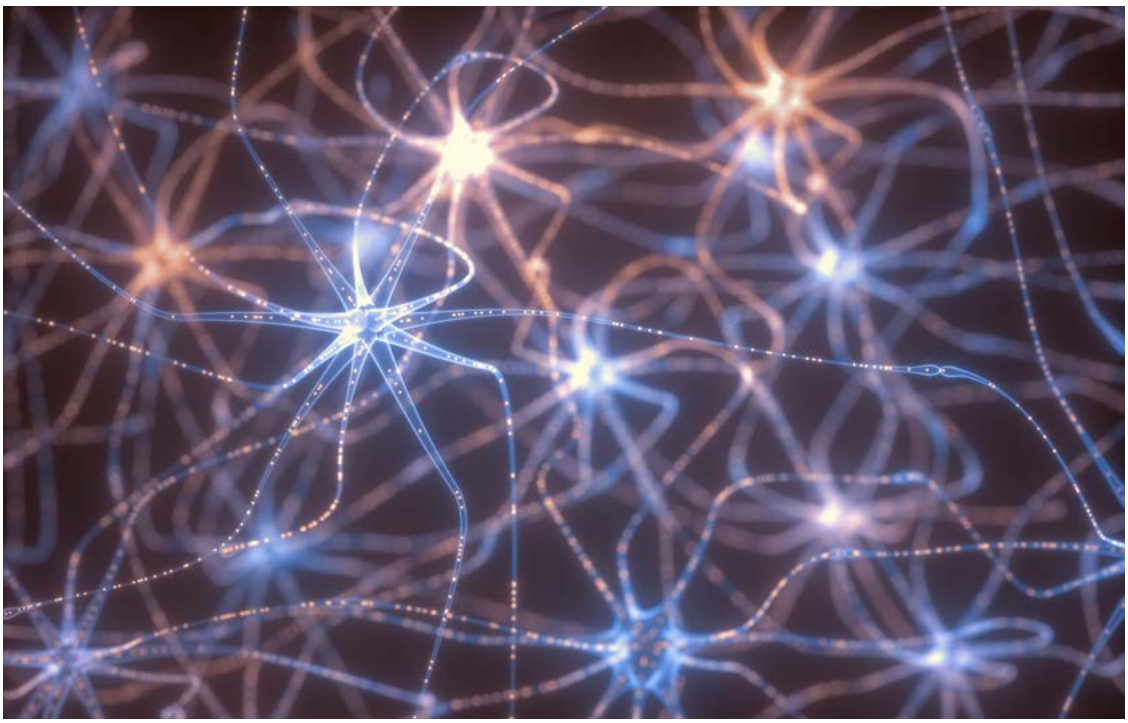

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University of Newcastle

University of Wollongong

Sydney

Academic Department for Old Age Psychiatry (ADFOAP), Prince of Wales Hospital

Aged Care and Rehabilitation, The Sutherland Hospital

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Australasian Research Institute, Sydney Adventist Hospital

Bankstown-Lidcombe Hospital

Bioanalytical Mass Spectrometry Facility, Mark Wainwright Analytical Centre, UNSW Sydney

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Clinical Research Unit for Anxiety and Depression (CRUfAD), UNSW Sydney

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University of Macau, Macau

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Universiti Putra Malaysia, Malaysia

Department of Neuropsychiatry, Gyeonggi Provincial Hospital for the Elderly, Republic of Korea

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Leiden University, The Netherlands

Maastricht University, The Netherlands

Radboud University Nijmegan (Radboud University Medical Center), The Netherlands

University of Groningen, The Netherlands

University of Utrecht, The Netherlands

VU University, The Netherlands

Faroese Hospital System (Department of Occupational Medicine & Public Health), Faroe Islands, Denmakr

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UK

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Cognitive Function & Ageing Studies, England

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CHeBA CONSORTIA COLLABORATIONS

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

- BRAIN-MEND (Biological Resource Analysis to Identify New Mechanisms and phenotypes in Neurodegenerative Diseases;
- 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);
- FORCE (Fatty Acids and Outcomes Research Consortium);
- IALSA (Integrative Analysis of Longitudinal Studies on Aging and Dementia);
- IGEMS (Interplay of Genes and Environment across Multiple Studies);
- UNITED (Uncovering Neurodegenerative Insights Through Ethnic Diversity).

Projects

"Our goal is to make a major impact on the societal burden due to dementia and related disorders."

Professor Perminder Sachdev AM &
Professor Henry Brodaty AO

Current Projects

A study of the association of acute illness hospitalisation (AIH) on the long-term cognitive trajectory of the Sydney Memory and Aging Study (MAS) participants

(PhD Project submitted Dec 12, 2020 under examination)

CHeBA staff: Lucia Chinnappa-Quinn (PhD Candidate), Perminder Sachdev, Nicole Kochan, John Crawford, Steve Makkar (until Oct 2019), Ben Lam (assistance from Jessica Lo for meta-analysis).

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

Aims:

- to examine the association of AIH exposure and post-hospitalisation cognitive decline (PHCD) in older age adults;
- to characterise the association of recent AIH exposure and PHCD;
- to compare the association of specific types of AIH exposure and PHCD (surgical and non-surgical AIH and AIH complicated by delirium);
- to examine the influence of AIH characteristics such as length of stay on the association with PHCD;
- to examine the influence of patient characteristics (e.g. age, education, sex, comorbidities, Apolipoprotein E ε4 allele (*APOE**4)) on these associations.

Findings:

- The first part of the literature review for this PhD project has been published and summarises studies investigating cognition following surgical, critical care AIH and AIH complicated by delirium: Chinnappa-Quinn L, Bennett M, Makkar SR, Kochan NA, Crawford JD, Sachdev PS. Is hospitalisation a risk factor for cognitive decline in the elderly? Curr Opin Psychiatry. 2019; Published Ahead of Print;
- The second part of the literature review describes a systematic review of peer reviewed papers investigating the association of AIH and post-discharge cognition from Medline, Embase, Psycinfo and CINAHL, screening 6566 titles and abstracts. We synthesized results from 46 papers. Most papers were prone to bias as a result of have no baseline cognition data or appropriate comparison groups. However, eight studies used community cognition data and most of these showed cognitive decline associated with acute hospitalisations. Seven studies were able to be pooled statistically and the meta-analysis also supported this finding that acute hospitalisation increased cognitive decline, in particular conversion to dementia in subsequent years. This meta-analysis has been published: Chinnappa-Quinn L, Makkar SR, Bennett M, Lam BCP, Lo JW, Kochan NA, et al. Is hospitalization a risk factor for cognitive decline in older age adults? International Psychogeriatrics. 2020:1-18;
- Latent growth modelling was used to estimate global cognition latent intercept and slope from neuropsychological data in four biennial waves. Electronically linked hospitalisation data from the New South Wales Admitted Patient Data Collection were computed in time intervals to clarify recency effects. Overall AIH effect, as well as surgical, medical and AIH with delirium exposures were investigated. A novel approach was taken to include concurrent hospitalisation variables in the same model to allow effects to overlap and use continuous variables to quantify effects accurately. The sample (n = 1026) had a mean age of 78.8 years, a mean Mini-Mental State Examination score of 28.7 and was functionally independent. Over ten years, 82% were hospitalised with a mean of 1.7 medical and 1.6 surgical hospitalisations. Their mean global cognition z-score decline per year was -0.105. Recent AIH exposure was associated with an increased rate of decline (-0.014 ▯ 0.005 global cognition z-score per year; p = .008). The number of AIH episodes had a greater association with cognitive decline than length of stay in hospital in days. This association was greater for medical admissions and especially so for AIH complicated by delirium, even for non-neurological AIH. Conversely, surgical AIH were not associated with cognitive decline, when compared to those without hospitalisations. This confirms emerging evidence that post-operative cognitive dysfunction is a mild subset of post-hospitalisation cognitive decline. Delirium, however, emerged as the most potent association with accelerated decline and warrants further investigation and more proactive intervention to reduce its incidence.

Further Analyses:

- To examine the association of AIH exposure and PHCD in older age adults with regards to cognitive domains, subjective cognitive complaints and risk of dementia and MCI;
- To examine the association of the effect of recency of hospitalisation in a short-term context to PHCD, by grouping hospitalisations by timing in relation to subsequent MAS cognitive wave assessments;
- To examine the association of prehospitalisation cognition and risk of AIH.

Funding:
Australian Society of Anaesthetists, DCRC-ABC.

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

CHeBA staff: Anne Poljak (Adjunct), Tharusha Jayasena, 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 Prince of Wales Hospital, Old Age Psychiatry), Dr Bill Giannakopoulos (St George Hospital), Professor Steven Krilis (St George Hospital).

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, post-translational modifications of apolipoproteins (e.g., allosteric disulphide bonds) and dysregulation in neurodegenerative diseases of ageing, including animal models for apolipoproteins APOA1, APOD, APOJ and APOH;
- Interactions between APOH and Aβ peptides, and binding partners of APOH in plasma and cerebrospinal fluid (CSF);

Findings:

- ApoH has some binding affinity for Ab42 and has a variety of protein binding partners in plasma and CSF. The work is ongoing, with a manuscript in preparation;
- An invited book chapter detailing methods of analysis of plasma apolipoproteins has been published (Poljak A, Duncan MW, Jayasena T, Sachdev PS. Quantitative Assays of Plasma Apolipoproteins (Chapter 3). In: *Methods in Molecular Biology (MiMB): Models for Maximising Healthspan: Protocols and Methods* (Ed: Guest PC). 2020; 2138:49-81. DOI: 10.1007/978-1-0716-0471-7_3.

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, St George and Sutherland Medical Research Foundation.

Automatic stratification of patients at risk of post-stroke cognitive impairment using machine learning

CHeBA staff: Perminder Sachdev, Jessica Lo.

Other investigators: Nacim Betrouni, Régis Bordet, Thibaut Dondain, Renaud Lopes (University of Lille).

Aims:

- Some stroke patients develop dementia, several months after their strokes, showing a common pathophysiology. It is therefore important to identify these patients as early as possible, even before the onset of the symptoms, particularly in order to be able to test pharmacological approaches on which the Lille pharmacology team has been working for a long time. An investigation conducted on the T1W MR images acquired with the 72 hours post-stroke and analysed using an original method based on the quantification of textural variations, allowed the construction of a model with 88% accuracy to predict cognitive decline at 6 months. The same approach applied on MRIs of a preclinical stroke rat model showed a correlation between these texture variations and neuronal density;
- The aim for this project is to replicate and to confirm these preliminary results on large data from different centers. The second aim is to build a powerful prediction system, using machine learning methods and combining the two markers (imaging and neuropsychological scores). This system can be used in clinical routine for the detection of patients who will be eligible for clinical trials.

Findings:

- Imaging data have been received in 2020 from five international studies. Nacim has started an initial examination of scans.

Funding:
Vincent Fairfax Family Foundation; NHMRC.

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. Analyses being undertaken include seeking to identify genetic variants associated with a composite measure of brain ageing based on MRI imaging using whole genome sequencing. The relationship between DNA methylation and cerebrovascular disease is also being examined.

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

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: Javier Oltra Cucarella (workgroup leader), Rosario Ferrer Cascales, Miriam Sanchez Sansegundo: University of Alicante, Spain; Juan Carlo Arango Lasprilla, Jesus M. Cortes: Biocruces Health Research Institute, Spain.

Aims:
- 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:
- First draft of manuscript completed.

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

Development and validation of risk models for the prediction of dementia in Low- and Middle-Income Countries: A consortium of population-based cohort studies

CHeBA staff: Darren Lipnicki, Perminder Sachdev.

Other investigators: Eduwin Pakpahan (workgroup leader), Dame Louise Robinson, Blossom Stephan, Newcastle University Institute of Aging; Contributing COSMIC study leaders and associates: Representing cohorts from 6 countries. The project is also being undertaken within the NIHR funded Global Health Group on Dementia Prevention and Enhanced Care (DEPeC).

Aims:
- Within the field of dementia there is an urgent need for data pooling, particularly for undertaking risk stratification analysis, in order to have a sufficient number of outcome events and a sample large enough to undertake model development and validation. The aim of this project is to undertake a detailed program of research into dementia risk prediction modelling from harmonized data across low- and middle-income countries. We will start with the simple risk factors, such as demographic and socioeconomic status, then extend the analysis by including health and cognitive functions, includes lifestyle, medical history, genetics, etc. This project will address the research gap where usually health and its related predictors are limited.

Findings:
- Analyses underway and manuscript in preparation.

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

Development of a general framework for computing new diffusion weighted imaging-based metrics for estimating brain ageing and health

CHeBA staff: Jing Du (PhD Candidate), Wei Wen, Forrest Koch, Jiyang Jiang, Perminder Sachdev.

Other investigators: Aihua Xia, School of Mathematics and Statistics, The University of Melbourne.

Aims:
- The broad aim of this project is to design and establish a general framework for creating and computing novel diffusion weighted imaging (DWI) markers for examining the brain ageing and health.
- DWI is a non-invasive imaging technique and widely used for investigating the microstructural integrity of cerebral white matter in vivo. Fractional

anisotropy (FA) and mean diffusivity (MD) are the two commonly used indexes derived from DWI to depict the directionality and magnitude of diffusion of cerebral white matter. Peak width of skeletonized mean diffusivity (PSMD) is another DWI derived metric introduced in 2016 and has been extensively used in clinical studies, especially in cerebral small vessel disease (CSVD). It is reported that PSMD consistently outperformed traditional imaging markers such as white matter hyperintensity (WMH) volume, lacunes and brain volume and other DWI metrics such as FA and MD, in its correlations with processing speed which is considered the cognitive domain most affected by CSVD. However, PSMD has its own limitations.

Findings:
- This work started in Aug 2019. We used three independent cohorts to develop and validate our general framework. We used UK Biobank for the development of general framework. Reliability and predictive validity of our general framework and metrics arrived at using it were examined using two independent validation cohorts Sydney Memory and Ageing Study (MAS) and Renji Cerebral Small Vessel Disease Corhort Study (RCCS). A research manuscript is now under consideration by a Journal.

Funding:
NHMRC, University International Postgraduate Award (UIPA), and John Holden Family Foundation.

Diet and late-life depression

CHeBA Staff: Karen Mather, Simone Reppermund, Annabel Matison (PhD student), Vibeke Catts, Anbupalam Thalamuthu

Other investigators: Professor Victoria Flood (Sydney University)

Aims:
To examine the associations between dietary measures and late-life depression. To determine the heritability of dietary measures.

Findings:
- Identification of dietary measures, including dietary patterns, and incident depression is being undertaken by reviewing prior literature and undertaking a meta-analysis.

Funding:
NHMRC.

Differential effect of family history on the risk for dementia by sex

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

Other investigators: Jong Bin Bae, Ki Woong Kim (Seoul University Bundang Hospital), investigators from around 7 contributing COSMIC studies.

Aims:
- To investigate if the association between familial history of dementia and dementia risk differs by sex; also to investigate whether the association between a familial history of dementia and dementia risk is different for a history of dementia in the father or brothers compared to a history of dementia in the mother or sisters.

Findings:
- Data from COSMIC studies being analysed.

Funding:
NIH.

Domain-specific cognitive impairments and depression as determinants of post-stroke functional disability

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

Other investigators: Hanna Jokinen and Hanna Laakso (Helsinki University Hospital; University of Helsinki).

Aims:
- Cognitive impairment and depression are frequent consequences of stroke, yet our understanding of their combined effects on functional outcome are unclear. This study investigated the associations of domain-specific cognitive impairments and depression with activities of daily living (ADL) and instrumental ADL (IADL) by using individual participant data (IPD) from the international cohorts of the Stroke and Cognition Consortium (STROKOG).

Findings:
- Domain-specific cognitive impairments and depression are related to post-stroke functional outcome. Subjects with executive dysfunction or global cognitive impairment together with depression are at higher risk of disability. Hanna is working on a revised draft manuscript soon to be circulated with co-authors.

Funding:
Vincent Fairfax Family Foundation; NHMRC.

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.

Aims:
- 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 is undertaking genetic studies examining Alzheimer's disease and related phenotypes. CHeBA has contributed 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 mild cognitive impairment, vascular cognitive impairment and amyloid imaging.

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

Establishing a neuroimaging working group for STROKOG

CHeBA staff: Wei Wen, Jiyang Jiang, Perminder Sachdev, Jessica Lo, John Crawford.

Other investigators: STROKOG collaborators.

Aims:
• To establish a neuroimaging working group for STROKOG;

• To use both FLAIR and T1-weight scans to analyse white matter hyperintensities (WMH) from STROKOG studies.

Findings:
• [project in progress] The project proposal was approved by the research scientific committee at the end of 2019 and 13 studies/PI have agreed to join the workgroup. A protocol for processing MRI using CHeBA's pipeline has been established. Imaging researchers from three international studies worked with CHeBA staff and contributed data to the WMH project. We found that the pipeline, originally developed for healthy ageing participants, tended to segment both WMH and stroke infarcts which overestimate WMH volumes. To address this issue, we propose taking advantage of diffusion-weighted imaging (DWI) sequence which gives a clear intensity contrast for infarcts. We have identified several studies with DWI and a PhD student who would be interested in taking up this project. We plan to begin the second phase of this project when the PhD student is able to commence her studies at UNSW. A progress summary report will be sent out to the workgroup in early 2021.

Funding:
Vincent Fairfax Family Foundation, NHMRC.

Evaluating Maybo training to improve staff response to aggression in people living with dementia.

CHeBA staff: Lynn Chenoweth, Henry Brodaty.

Other investigators: Jacki Wesson.

Aims:
• To evaluate the effectiveness of the Maybo training program on:

• Primary: Front-line staff: 1) confidence; and 2) skill in responding to persons living with severe dementia (PLWD) who show physical aggression in the residential aged care setting;

• Secondary: Front-line staff: 3) attitudes to PLWD, 4) perceived training needs and benefits; 5) staff sickness/ absenteeism/ turnover; 6) type, frequency and severity of physical aggression in PLWD; and 7) use of physical and chemical restraint in PLWD.

Study intervention: Maybo training is a tiered approach to behaviour support, providing education on communication, conflict management and personal safety for both consumers and staff, creating a safer working environment. It includes: 1) Positive Behaviour Support, incorporating risk recognition & reduction, and understanding human behaviour; and 2) Physical Intervention Training, as a last resort when primary & secondary prevention measures have failed. These modules are supported by an e-learning program.

Measurement: This project uses a mixed method research methodology that includes the following data collection method/s: • Staff self-report questionnaires - demographics; and validated measures of confidence in managing aggression in persons living with dementia (residents); attitudes towards persons living with dementia: and perceived training needs and benefits; • Observations of aggression incidents in persons living with dementia and staff responses to preventing and reducing aggression incidents; • Chart audits - resident demographics; recorded aggression incidents in residents; chemical and physical restraint use with residents; staff sick leave, absenteeism and turnover; • Clinical assessments – validated measures of resident dementia stage and severity; and resident behavioural and psychological symptoms.

Progress: All staff in participating units have consented and completed pre-measures. The front-line staff training is progressing using online sessions and face to face training for some modules in small socially distanced groups. Chart audit, clinical assessment and direct observation of staff interaction with residents expressing aggression and other neuropsychiatric symptoms will commence in June, followed by post staff measurement. Follow-up measurement will commence in November.

Funding:
Montefiore Homes.

Examining brain ageing from transcriptomic and epigenomic perspectives

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

Other investigators: A/Professor Nicola Armstrong (Murdoch University, CHeBA Hon. Research Fellow), Associate Professor John Kwok (University of Sydney; 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 has been completed. Both coding and non-coding RNAs and their relationship with age are being examined. Analyses are also being undertaken looking at age-related changes in brain expression from 10 brain regions using publicly available data. In other work, which will enrich the dataset, small RNA sequencing and DNA methylation is being undertaken on the same samples.

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

External validation of dementia risk models in stroke-survivors

CHeBA staff: Perminder Sachdev, Jessica Lo.

Other investigators: 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:
- Dementia risk prediction models developed for the general population do not perform well in individuals with stroke. Their poor performance could have been due to the need for additional and/or different predictors related to stroke and vascular risk factors or methodological differences across studies (e.g., length of follow-up, age distribution). Future work is needed to develop simple and cost-effective risk prediction models specific to post-stroke dementia;
- Dr Tang has completed the project and submitted a manuscript to the journal *Stroke* which is currently under review.

Funding:
Vincent Fairfax Family Foundation; NIHR (UK).

Failure to identify particular odours predicts future dementia and mortality

CHeBA staff: Darren Lipnicki, Nicole Kochan, Katya Numbers, Kristan Kang, John Crawford, Julian Trollor, Henry Brodaty, Perminder Sachdev.

Aims:
- To investigate whether the inability to identify particular odours predicted mortality, and whether similar odours also predicted future dementia.

Findings:
- Lower total BSIT scores significantly predicted both dementia (OR=1.24, 95%CI=1.09-1.41) and mortality (OR=1.16, 95%CI=1.03-1.30), even when accounting for dementia before death and attrition. Dementia was significantly predicted by incorrect responses to smoke, gasoline, and paint thinner, and mortality significantly predicted by incorrect responses to smoke, gasoline and onion. These items retained their significant associations in sensitivity analyses. A manuscript being revised for submission to a new journal.

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

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

CHeBA staff: Perminder Sachdev, Rebecca Koncz (Conjoint Associate Lecturer & PhD Candidate), Wei Wen, Jiyang Jiang, Anbupalam Thalamuthu, Teresa Lee, Vibeke Catts, Julian Trollor, Karen Mather.

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

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 what proportion of the variance of β-amyloid burden is explained by the presence of *APOE ε4* and common vascular risk factors;
- Examine the shared genetic basis between cerebral small vessel disease and β-amyloid burden;
- Investigate the relationship between amyloid burden and aspects of cognitive function;

Findings:
- OATS Wave 4 and 1P recruitment, assessment and scanning completed (n=206; 61 monozygotic and 42 dizygotic twin pairs);
- The heritability of global amyloid burden was moderate (0.41) and ranged between 0.17 and 0.54 across different brain regions;

- There were no significant genetic correlations between global amyloid burden and imaging markers of cerebral small vessel disease;
- These finding were presented by Koncz R et al. at the Alzheimer's Association International Conference in Los Angeles, USA, July 2019, as an oral presentation;
- Manuscripts are currently under 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); 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. The mathematical model of representing curves and trajectories, which is independent of the parametrization, was published in *Journal of the American Statistical Association* (Lafaye de Micheaux et al. 2020. DOI: 10.1080/01621459.2020.1745815). Pending on the new research students' enrolment, we will start using the model to investigate genetic influence on the spatial distribution and density of white matter fibre tracts in 2020.

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

Aims:
- Identify genetic and epigenetic variation associated with longevity and longevity-related phenotypes.

Findings:
- Prior work has identified a list of longevity-related genetic variants (Revelas et al., *Mech Ageing Dev,* 2018). In other work, genetic risk for cardiovascular factors and disease (e.g. low-density lipoproteins, stroke) were not significantly associated with longevity (Revelas et al., Genes, 2019). Research currently being undertaken is looking at the relationships between longevity polygenic risk scores and the health status of UK Biobank participants and replicating the results in the Sydney Memory and Ageing Study.

Funding:
Sachdev Foundation, NHMRC, Thomas Foundation.

Genetics of white matter hyperintensities

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

Other investigators: A/Professor Nicola Armstrong (Murdoch University, CHeBA Hon. Research Fellow), Professor Paul Nqyuist (John Hopkins, USA), Professor David Ames (National Ageing Research Institute, Royal Melbourne Hospital), Associate Professor John Kwok (University of Sydney; UNSW), Professor Peter Schofield (NeuRA; UNSW), Professor Margaret J. Wright (University of Queensland), and other external collaborators.

Aims:
- 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. We undertook a genome-wide association study looking at these two sub-classifications using data from over 24,000 participants from around the world.

- We identified common genetic variants significantly associated with both deep and periventricular WMHs and found unique variants for periventricular WMH alone. The results confirm that these two sub-classifications of WMH have distinct but also overlapping aetiology. This work has now been published in the highly respected journal, *Stroke* (Armstrong, Mather et al., 2020). Extension of this work is being undertaken, including looking at other types of genetic variation that may influence deep and periventricular WMHs.

Funding:
NHMRC, Thomas Foundation.

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

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

Other investigators: A/Professor Nicola Armstrong (Murdoch University, CHeBA Hon. Research Fellow), Professor David Ames (National Ageing Research Institute, Royal Melbourne Hospital), Associate Professor John Kwok (University of Sydney, UNSW), Professor Peter Schofield (NeuRA, UNSW), Professor Margaret J. Wright (University of Queensland).

Aims:
- Identify single nucleotide polymorphisms (SNPs) and differentially methylated regions for various brain measures, such as subcortical volume.

Findings:
- A number of genetic and epigenetic projects are underway, of which both the Sydney Memory and Ageing Study and the Older Australian Twins Study have contributed data. In 2020, a large study with over 50,000 individuals was published in the highly regarded journal, Science, reporting nearly 200 SNPs associated with cortical surface area and thickness (Grasby et al., 2020), highlighting that different genes are involved in the development of distinct cortical regions.

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 investigators: Assoc Prof Nicola Armstrong (Murdoch University) (CHeBA Hon. Research Fellow), Professor David Ames (National Ageing Research Institute, Royal Melbourne Hospital), Associate Professor John Kwok (Sydney Univ UNSW), Professor Peter Schofield (NeuRA, UNSW), Professor Margaret J. Wright (Queensland Brain Institute, University of Queensland).

Aims:
- 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 22,000 individuals identified 160 genetic loci for brain cortical measures (Hofer et al., Nature Communications, 2020). In another study, 27 significant genetic variants were identified for white matter volume in over 50,000 adults (Sargurupremraj et al., Nature Communications, 2020).

Funding:
NHMRC, Thomas Foundation.

High value imaging data storage and publishing scheme

The NeuroImaging Lab (NiL) at Centre for Healthy Brain Ageing (CHeBA), School of Psychiatry, Medicine is tasked with the cleaning, formatting, storing and distributing (to our proved research collaborators) of raw brain MRI scans.

NiL takes care MRI scans of about 1500 participants, totalling over 10,000 scans (multiple scans for a participant). We also have around 220 participants who had amyloid-PET scans. Our plan included the following tasks:

- Remove sensitive information from each scan (e.g. participant's name/study ID, date of the scan, referring doctor etc);
- Convert the de-IDed scans into a file format commonly accepted/used by neuroimaging community;
- Remove the facial features (a user of the MRI

could do a surface rendering to reveal the facial features otherwise) by running some neuroimaging processing program;

- Establish an easy-to-use data structure BIDS format (see: ***https://bids.neuroimaging.io/***), so that the scans (including MRI scans of different modality, e.g., various structural and functional MRI scans; amyloid-PET scans) will be organised in a systematic fashion;
- Carry out visual QC so that the scans with poor quality can be identified, indexed, and recorded;
- All the prepared scans will then be uploaded to the long-term data storage: ***www.dataarchive.unsw.edu.au/***
- We will have a copy of these data on our server stationed in the basement of AGSM.

Status of the project:
- We have completed the first 4 tasks;
- Visual QC is ongoing;
- We have uploaded all the raw scans to the long-term data storage: ***https://www.dataarchive.unsw.edu.au/***
- The part of BIDS format data that are visually QC'ed are also uploaded to the long-term data storage and we will keep uploading them;
- A SharePoint account has been created with 5TB of space to store scans that are to be shared with collaborators and approved users;
- The use of SharePoint has been approved by UNSW for storing sensitive data. Briefly, a link for downloading the data is sent to the recipient. The data are only accessible by the person receiving the email with the link. Thereby, the security of the data is assured.

Funding:
UNSW High Value Data Collections Publishing Scheme Seed Grant.

History of skin cancer is associated with better late-life cognition

CHeBA staff: Darren Lipnicki, Perminder Sachdev, Katya Numbers, John Crawford, Nicole Kochan, Henry Brodaty, Julian Trollor.

Aims:
- To investigate how skin cancer, including non-melanoma skin cancer, is associated with cognition, and with the development of dementia and Alzheimer's disease within six years of follow-up.

Findings:
- History of any cancer was reported by 33% of participants, with 12% reporting NMSC. After adjusting for age, sex, education and APOE*4, any cancer was associated with better memory, and NMSC was associated with better memory and global cognition. Across all participants, dementia developed in 15%, and AD in 6%. Cancer other than NMSC was associated with lower odds of dementia or AD within 6 years. Basal cell carcinoma was associated with better global cognition and memory, and melanoma was associated with better global cognition and language scores. Gastrointestinal cancer was associated with better memory. No particular cancer type was statistically associated with dementia or AD, but there were no AD cases among those reporting gastrointestinal cancer. Cancer other than NMSC and melanoma were both associated with greater chances of mortality after 6 years.

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

Identifying expression quantitative trait loci (eQTLS) in older adults

CHeBA staff: Anbupalam Thalamuthu, Toyin Abdulsalam (Scientia PhD student), Karen Mather, Perminder Sachdev.

Other 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 (Sydney University; UNSW), Professor Peter Schofield (NeuRA; UNSW).

Aims:
- 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 has been extended to the OATS cohort, which is being 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.

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 (Adjunct), 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°C and vapour phase storage;

- Setup of a biobanking subcommittee and preparation of a Biobank Ethics submission, which is now enacted.

Findings:

- Aliquoting of MAS samples (all waves which have plasma) has largely been completed, although ongoing plasma collections will require processing. Aliquoting of all waves of OATS has been completed, except the OATS2 (PET study). 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: Ms Claudia Woolf (University of Sydney), Zara Page (UNSW Neuroscience Honours Student).

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. The work has been published in the Journal of the American Geriatric Society (Bentvelzen et al. *J Am Geriatr Soc*. 2019 Oct; 67(10): 2108-2115. DOI: 10.1111/jgs.16033). An online normative data calculator is available for clinicians and researchers https://cheba.unsw.edu.au/research-groups/neuropsychology.

- As our Neuroscience (Hons) student, Zara Page achieved a First-Class Honours for her thesis titled *Performance of older Australians from culturally and linguistically diverse backgrounds on pencil-and-paper and computerised neuropsychological assessments.* The study used data from the Sydney Memory and Ageing study and observed that CALD individuals (n=164) performed more poorly than native English speakers (n=873) on neuropsychological tests in general. However, the difference was larger on pencil-and-paper tests than computerised measures, and specific language and acculturation factors strongly influenced test performance over and above demographic characteristics and health factors. Accounting for identified language and acculturation variables may improve the accuracy of neuropsychological assessments in CALD individuals. A manuscript has been submitted to a peer-reviewed journal and is currently under review;

- As a part of Zara's PhD project, a systematic review is currently in progress titled *Methods of bias reduction for the neuropsychological assessment of culturally, ethnically, or linguistically diverse adults: A systematic review*, which aims to identify current statistical and/or methodological approaches to reduce systematic CALD disadvantage identified in her honours work.

Funding:
DCRC – Assessment and Better Care, UNSW.

Instrumental activities of daily living and cognitive decline in older adults

CHeBA Staff: Simone Reppermund, Sujin Jang (Honours student), Katya Numbers, Ben Lam, Perminder Sachdev, Henry Brodaty.

Aims:

- The aims of the present study were to examine differences in informant-reported and performance-based measures of instrumental activities of daily living (IADL) and to assess whether a performance-based IADL measure out-performs informant-reports in predicting incident dementia over 4 years.

Findings:

- Performance-based IADL impairment at baseline and decline in performance-based IADL function predicted incident dementia over 4 years, with the prediction provided by the STAM being statistically significant over and above the B-ADL. Performance-based measures of IADL can predict progression to dementia over 4 years beyond that provided by an informant-report of IADL. Performance based IADL measures are promising tools for clinical practice to identify individuals at greater risk of developing dementia.

Funding:
NHMRC, UNSW Scientia Fellowship.

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.

Other investigators: STROKOG collaborators.

Aims:
- Examine the longitudinal course of post-stroke cognitive function in a diverse group of international post-stroke cohorts;
- Investigate the rates of cognitive decline in stroke patients and what are the risk factors for post-stroke cognitive decline.

Findings:
- [project is in progress] Data were received from nine studies and data cleaning and harmonisation was completed by the end of 2019. Analyses was completed in 2020 and a first draft was sent out to co-authors in early 2021. We found that stroke patients experience cognitive decline that is faster than that of stroke-free control subjects from one to three years after onset. An increased rate of decline is associated with older age and recurrent stroke.

Funding:
Vincent Fairfax Family Foundation.

Longitudinal investigation of the inter-relationships between depression, vascular disease and cognition in older adults.

CHeBA Staff: Simone Reppermund, Ben Lam, Louise Mewton, Wei Wen, Perminder Sachdev.

Other investigators: Professor Kaarin Anstey (UNSW Sydney).

Aims:
- This project aims to further examine the longitudinal associations among late-life depression, vascular factors and disease (e.g., history and onset of stroke/TIA, hypertension, diabetes, hypercholesterolemia, smoking, BMI, white matter hyperintensities), and cognition using data from three longitudinal studies, Memory and Ageing Study (MAS) (> 8 years follow up), Older Australian Twin Study (OATS) (> 10 years) and Personality & Total Health (PATH) Through Life (> 16 years). We will extend the outcomes by including more neuropsychological domains (i.e., executive function, memory, attention, language and visuo-spatial) in addition to global cognition.

Findings:
- Findings from this research will provide evidence on the vascular mechanisms linking depression and cognition, and inform recommendations on managing depression, vascular disease, and neurocognitive disorder in late-life.

Funding:
NHMRC, UNSW Scientia Fellowship.

Limbic-Predominant Age-Related TDP-43 Encephalopathy (LATE) in specimens from the Sydney Brain Bank

CHeBA staff: Anne Poljak (Adjunct), Rene Jezewski (Scientia PhD candidate), Perminder Sachdev, Karen Mather, John Crawford.

Other investigators: Claire Shepherd (NeuRA).

Aims:
- Explore the neuropathology of LATE in individuals over the age of 85 years;
- To potentially explore mechanisms underlying the formation of TDP-43 inclusions, identify proteins which associate with TDP-43 using laser capture microdissection and proteomic LCMSMS analysis (fixed tissues);
- Compare proteomic profiles of pure LATE vs LATE with other types of pathology and control samples (fresh tissues).

Findings:
- Individuals aged 85 years and older were >4 times more likely to have LATE neuropathologic change (LATE-NC), most with intermediate/high AD neuropathology. Only ~11% of cases over the age of 85 years had pure LATE-NC;
- Pure LATE-NC could only be attributed to ~9% of dementias in cases over 85 years. Advanced LATE-NC stage and more severe TDP-43 pathological burden may contribute to a disease threshold;
- Other age-related pathologies were also present in cases with pure LATE-NC but did not appear to influence the clinical phenotype;
- Methods development for the laser capture microdissection and proteomic LCMSMS analysis are being established, to optimise quantity of inclusions and maximising the numbers of proteins that can be extracted and identified.

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

Maintain Your Brain

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

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

- Main trial commenced June 2018 and the first annual assessments were completed at the end of 2019. A final sample of 6,236 people were recruited and enrolled in the study. In 2020 2 -year follow-up data was collected. Final data collection will commence in 2021.

Publications:

- Ginige, J. A., Boulamatsis, C., Heffernan, M., San Jose, J. C., Chuprov, I., Chau, T., Maeder, A., Valenzuela, M., Fiatarone Singh, M., Mavros, Y., Noble, Y., Radd-Vagenas, S., Guerrero, Y., Jain, N., O'Leary, F., Kochan, N., & Brodaty, H. (2020). Fully-Online, Interoperable Clinical Trial Management System for Multi-Interventional RCT: Maintain Your Brain Digital Platform. Studies in health technology and informatics, 268, 97–112. ***https://doi.org/10.3233/SHTI200009***
- Kivipelto, M, Mangialasche, F, Snyder, HM, et al. World-Wide FINGERS Network: A global approach to risk reduction and prevention of dementia. Alzheimer's Dement. 2020; 16: 1078– 1094. ***https://doi.org/10.1002/alz.12123***
- Lancaster, R, Radd-Vagenas, S, Fiatarone Singh, M, et al. Electronic food records among middle-aged and older people: A comparison of self-reported and dietitian-assisted information. Nutrition & Dietetics. 2020; 1– 9. ***https://doi.org/10.1111/1747-0080.12606***

Funding:
NHMRC Dementia Team Research Grant.

Maximizing dementia risk reduction: the impact of demographic/diversity factors on a modifiable dementia risk score

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

Other investigators: Kay Deckers, Sebastian Köhler, Martin van Boxtel, Stephanie van Asbroeck (Maastricht University), investigators from around 15 contributing COSMIC studies.

Aims:

- To investigate whether there are differences in dementia risk factor profiles (LIBRA scores) based on important demographic/diversity factors such as sex, educational level, ethnicity/race and socioeconomic status.

Findings:

- Data from COSMIC studies being obtained and harmonised.

Funding:
NIH.

Metabolomic screening for discovery of small metabolite/lipid blood-based biomarkers

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

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

Aims:

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

Findings:

- 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, along with a significant age-dependent decline in the levels of L-alanine, and L-threonine. In human plasma, concentrations of L-alanine, methylserine, glycine, D-serine and L-serine and several lipids were significantly altered in plasma from participants with dementia. Using a series of NMR based plasma metabolite measures (48 compounds identified in 30 subjects), principle components analysis showed a clear separation of dementia from normal control subjects based on features in the NMR spectra. Separation of subjects with mild cognitive impairment vs normal controls was much less pronounced and did not reach statistical significance.
- Eight manuscripts have been published with 3 manuscripts contributing to Matthew Wong's PhD thesis. Another 2 manuscripts formed part of Yue Liu's PhD thesis.

Publications:

- Wong MWK, Braidy N, Crawford J, Pickford R, Song F, Mather KA, Schofield P, Attia J, Brodaty H, Sachdev P, Poljak A. *APOE* genotype differentially modulates plasma lipids in healthy older individuals. *J Alzheimers Dis.* 2019; 72(3): 703-716;
- Wong MWK, Braidy N, Pickford R, Sachdev P, Poljak A. Comparison of single phase and biphasic extraction protocols for lipidomic studies using human plasma. *Front Neurol.* 2019; 10: 879;
- Wong MWK, Braidy N, Pickford R, Vafaee F, Crawford J, Muenchhoff J, Schofield P, Attia J, Brodaty H, Sachdev P, Poljak A. Plasma lipidome variation during the second half of the human

lifespan is associated with age and sex but minimally with BMI. *PLoS One.* 2019; 13(8): e0201968;

- Braidy N, Zarka M, Jugder B-E, Welch J, Jayasena T, Chan DKY, Sachdev P, Bridge W. The precursor to glutathione (GSH), γ-glutamylcysteine (GGC), can ameliorate oxidative damage and neuroinflammation induced by $A\beta_{40}$ oligomers in human astrocytes. *Front Aging Neurosci.* 2019; 11: 177;

- Chen Z, Jiang R, Chen M, Zheng J, Chen M, Braidy N, Liu S, Liu G, Maimaitiming Z, Shen T, Dunaief JL, Vulpe CD, Anderson GJ, Chen H. Multi-copper ferroxidase deficiency leads to iron accumulation and oxidative damage in astrocytes and oligodendrocytes. *Sci Rep*. 2019; 9(1): 9437;

- Liu Y, Chan DKY, Thalamuthu A, Wen W, Jiang J, Paradise M, Lee T, Crawford J, Wong MWK, Xu YH, Poljak A, Pickford R, Sachdev PS, Braidy N (2020). Plasma lipidomic biomarker analysis reveals distinct lipid changes in vascular dementia. *Computational and Structural Biotechnology*. 18:1613-1624;

- Liu, Y., Chen, Z., Li, B., Yao, H., Zarka, M., Welch, J., Sachdev, P., Bridge, W., Braidy, N (. *Supplementation with gamma-glutamylcysteine (gamma-GC) lessens oxidative stress, brain inflammation and amyloid pathology and improves spatial memory in a murine model of AD* Neurochem Int (2021) 144 104931;

- Liu, Y, Thalamuthu, A, Mather, K. A., Crawford, J, Ulanova, M, Wong, M. W. K., Pickford, R., Sachdev, P., Braidy, N (2021). *Plasma lipidome is dysregulated in Alzheimer's Disease and is associated with disease risk genes* Transl. Psychiatry [Accepted for Publication].

Funding:
Thomas Foundation, Australian Research Council Discovery Early Career Research Fellowship to Dr Nady Braidy.

Nutrition and cognitive health in the older population: emphasis on food groups consumption and dietary patterns

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

Other investigators: Costas Anastasiou (workgroup leader), Nikolaos Scarmeas, Mary Yannakoulia: Greece; Contributing COSMIC study leaders and associates: Representing cohorts from around 10 countries.

Aims:
- To examine the association between consumption of food groups, in isolation or in their combination into specific dietary patterns, and cognitive function in the older population (>60 years).

Findings:
- Data being harmonised and analysed.

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

Plasma proteomics biomarkers

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

Other investigators: Dr Julia Muenchhoff (CHeBA Hon. Research Fellow), Professor John Attia (University of Newcastle), Dr Mark Duncan (TargetDiscovery, USA), Laureate Professor Colin Masters (University of Melbourne), Professor Ralph Martins (Edith Cowan University), Dr Mark McEvoy (University of Newcastle), Associate Professor Mark Raftery (BMSF, UNSW), Dr Ling Zhong, Associate Professor Peter W. Schofield (University of Newcastle), Laureate Professor.

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. Dysregulation of protein members from these same protein family groups (though not always identical proteins) has been observed across a number of independent cohorts (Sydney MAS, Hunter Community Study and a preliminary study of the DIAN cohort):

  - Kaur et al. CSF and blood protein biomarkers and *APOE* genotype status of early-onset Alzheimer's disease variants: A systematic review and meta-analysis. *J Alzheimers Dis*. 2020; 75(3):827-843. DOI: 10.3233/JAD-200052;

  - A plasma pre-analysis fractionation method has been developed which allows identification of >3000 plasma proteins, and this work has now been published; Kaur *et al* Extending the Depth of Human Plasma Proteome Coverage Using Simple Fractionation Techniques J. Proteome Res. 2021,

20, 1261–1279. Analysis of two cohorts (MAS and AIBL) has been performed using an adaptation of this method, and two additional manuscripts are in progress: (a) longitudinal analysis of plasma proteomic changes in MCI and AD using plasma from the Sydney MAS cohort (waves 1 and 4); (b) exploring plasma proteomic expression differences between control and AD plasma, in *APOEε4* carriers and non-carriers, using plasma from the AIBL cohort.

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

Poststroke anxiety: a domain-specific cognitive impairments characterization from the STROKOG Consortium

CHeBA staff: Perminder Sachdev, Jessica Lo.

Other investigators: Thibaut Dondaine, Nacim Betrouni, Regis Bordet, Renaud Lopes (University of Lille).

Aims:
The aim of the study is i) to evaluate the influence of post-stroke anxiety on the cognitive disorders observed in patients, ii) to observe the consequences of a stroke on brain structures involving anxiety (in particular the amygdala and the dorsolateral prefrontal cortex) iii) to identify a marker predicting the occurrence of anxiety disorders at a distance from the stroke in the chronic phase (from 6 to 12 months after the index stroke). We will examine whether clinical features such as cognitive disorders, demographic variables and localisation of lesion could explain PSA.

Findings:
- Data request was completed in December 2020 with three studies contributing data. Thibaut has begun data harmonisation in early 2021.

Funding:
Vincent Fairfax Family Foundation; NHMRC.

Post-stroke neuropsychiatric symptoms: apathy and psychosis

CHeBA staff: Michael Connors, Perminder Sachdev, Jessica Lo, Henry Brodaty, John Crawford, Nicole Kochan.

Other investigators: Armando Teixeira-Pinto (University of Sydney).

Aims:
- We aim to examine post-stroke apathy and psychosis using the STROKOG data. In particular, we seek to address questions of prevalence; incidence; time to onset of symptoms; clinical correlates and predictors (including demographics; cognition; medical history; other neuropsychiatric symptoms, such as depression and anxiety); neuroanatomical correlates; and ethnic and geographical variation. Based on previous research, it is expected that patients with these symptoms will show worse clinical outcomes.

Findings:
- Data requested was completed in 2020 with data received from five studies. Michael has begun initial data harmonisation in early 2021.

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), Dr Gelareh Mohammadi (Computer Science & Engineering, UNSW).

Aims:
- To develop machine learning models to identify risk factors that could predict the onset of dementia, using data from the Sydney Memory and Ageing Study and the Older Australian Twins Study.
Awards: Awarded the Norman Foo Memorial Prize for Best Research Paper in the School of Computer Science & Engineering in 2020.

Findings:
- Our work on machine learning models using baseline data from the MAS study to predict dementia was published in *Nature Scientific Reports* in November 2020. These models were designed for survival analysis of high dimensional data. As such they examined over 250 variables and predicted survival to dementia with a concordance index of up to 0.82;

- Further work has focussed on identifying risk factors from these models. High dimensional models can produce unstable results for a variety of reasons, so our work has been in stabilising these results using ensembling techniques. To date, the most predictive variables are the neuropsychological test scores, other cognitive test scores and the Brief Smell Identification Test score;

- In addition, work has begun on analysing the longitudinal data from all available waves of MAS and OATS. The technique we are using is temporal pattern mining with temporal abstraction. Temporal pattern mining looks for common patterns in the data over time amongst all study participants. Temporal abstraction transforms the data into a higher level, more abstract form, that is easier for machine learning models to work with. Instead of working with raw values, the models work with labels such as *low, normal* and *high*, *rising, falling* and *steady*.

Funding:
• Annette Spooner was supported by the Australian Government RTP Scholarship and Women in Engineering Scholarship.

Quantification of fatty acid levels in MAS plasma

CHeBA staff: Tharusha Jayasena, Anne Poljak (Adjunct), Mahboobeh Hosseini, Perminder Sachdev.

Other investigators: Sonia Bustamante (BMSF, UNSW), Laureate Professor Colin Masters (University of Melbourne).

Aims:
• Develop a quantitative mass spectrometric quantitative assay for analysis of fatty acids in plasma;

• Quantitate levels of fatty acids in wave 1 MAS plasma;

• Explore changes to fatty acids levels with cognition and share data with FORCE consortium to explore changes with other disease factors.

Findings:
• A reliable and sensitive GC/MS mass spectrometry-based method has been established for the quantification of 27 fatty acids using 50ul of human plasma. Optimising sample preparation protocols from previously published studies allowed us to detect levels of both free and bound fatty acids. Analysis of MAS Wave 1 cohort samples were completed by December 2020. We found significant differences in levels of fatty acids between the free and bound compartments in plasma including EPA, DHA and Arachidonic acid, which were elevated in the bound fraction. Statistical analysis of data is currently underway, statistical results will be sent to FORCE in April for inclusion into their meta-analysis investigating fatty acids and chronic kidney disease. We will then work on completing statistical analysis for our manuscripts investigating fatty acid level changes with cognition in MAS wave 1 samples, with the aim of completing statistical analysis and manuscript write-up by May 2021;

• We also performed a meta-analysis of plasma fatty acids in cross-sectional case-control studies of MCI and AD and found that total fatty acids were ~30% lower in AD than controls, and also lower in MCI though not quite as markedly. In particular the fatty acid docosahexaenoic acid was significantly lower in both MCI and AD and may be a driver of pathology. This work was published in Ageing Research Reviews (Hosseini *et al.* Blood fatty acids in Alzheimer's disease and mild cognitive impairment: a meta-analysis and systematic review. *Ageing Res Rev*. 2020 Jul; 60:101043. DOI: 10.1016/j.arr.2020.101043). A book chapter reviewing the role of lipids was published (Sachdev PS, Poljak A. Lipidomics for Biomarkers and Biomechanisms in Brain Ageing and Dementia (Chapter 12). In: *Neuroscience of Dementia* (Eds: Martin CR, Preedy VR). Elsevier BV: 2020.

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

Rates of progression to dementia in diverse ageing populations, using different dementia harmonisation methods

CHeBA staff: Ben Lam, John Crawford, Darren Lipnicki, Louise Mewton, Perminder Sachdev.

Other investigators: Contributing COSMIC study leaders and associates: Representing cohorts from 10 studies.

Aims:
• A previous COSMIC paper examined longitudinal decline in continuous measures of cognition, as well as the effects of demographic characteristics and APOE e4 carrier status. This project will complement that work by examining rates of progression to dementia in such populations and how they vary with the same characteristics examined earlier. A challenge will be to harmonise dementia diagnoses across COSMIC cohorts. Recently, continuous measures considered to be "homologues" or "proxies" for dementia have been developed. Royal et al. used structural equation modelling to define a latent variable (delta) representing the dementia-relevant shared variance between cognitive and functional measures. Similarly, Jutten et al. formed a novel cognitive-functional composite (CFC) using item response theory, which was subsequently shown to improve the detection of early stages of dementia;

• The current project will explore the use of continuous proxies for dementia like delta and CFC to form harmonised dementia classifications across COSMIC cohorts. Dementia will be classified from the continuous measures by applying appropriate cut-points. Levels of agreement between such dementia classifications and those derived from consensus diagnoses will be examined. We will also examine how measures like delta and CFC vary with demographic characteristics and APOE e4 carrier status.

Findings:
• The latent dementia factor was estimated longitudinally using structural equation modelling in 10 participating COSMIC cohorts. Initial evidence has demonstrated the validity of this factor in associating with MMSE scores ($b = -0.78$, $p < .001$), CDR Sum-of-boxes scores ($b = 0.21$, $p < .001$), and the propensity of developing dementia (OR = 37.11, $p < .001$) over time. Preliminary findings were presented at AAIC 2020 and the COSMIC symposium held in August 2020.

Funding:
Direct donations to The Dementia Momentum Fund,

NIH grant, NHMRC grant.

Relationship between body mass index and cognitive decline

CHeBA staff: Darren Lipnicki, John Crawford, Ben Lam, Nicole Kochan, Henry Brodaty, Perminder Sachdev.

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

Aims:
- Examine associations between body mass index (BMI), cognition and dementia in diverse ethno-regional groups.

Findings:
- The project is being re-designed in consideration of recent literature and may include additional COSMIC studies that have joined recently.

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

Aims:
- 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);

- 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: (a) 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 (b) To evaluate the impact of clustering and patterns of clusters on imaging measures.

Findings:
- There were 11,928 eligible individuals drawn from 10 cohorts across the Americas, Europe, Asia and Australia. Mean age 70 years (SD=6.7, range:54-100), 54% female, mean follow-up 2.5 years (SD=1.4, range: 0.5-15). Mean baseline MMSE was 28.1 (SD=1.7) and 8% (965) had incident cognitive decline. There were 651 (5.5%) participants identified with high lifestyle and cardiovascular risk, 38% with high cardiovascular risk only, 5% with high lifestyle risk only, 51% were low risk. Only the cardiovascular group was associated with greater rates of decline in MMSE scores (B=-0.13,95%CI=-0.24:-0.02). Neither the lifestyle (OR=1.03(95%CI=0.77:1.38)), nor the cardiovascular (OR=1.07(95%CI=0.93:1.24)) group was associated with an increased risk of incident cognitive decline compared to the low risk group. Having both lifestyle and cardiovascular risk resulted in an OR=1.10 (95%CI=0.83:1.46). The impact of risk factor clusters varied by outcome, region, study, and key socio-demographic groups (age, sex). In conclusion, there were no robust relationships between a priori defined modifiable risk factor clusters and cognitive decline.

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

Risk factors for post-stroke depression

CHeBA staff: Ben Lam, Jessica Lo, Perminder Sachdev, Louise Mewton, Simone Reppermund, John Crawford, Henry Brodaty.

Other investigators: Lena Oestreich, Michael O'Sullivan, STROKOG collaborators.

Aims:
- To investigate and identify the risk factors that predict the first onset and development of post-stroke depression using STROKOG data.

Findings:
- Preliminary findings in six STROKOG studies showed that being impaired in global cognition (HR = 1.35, p = .041) and function (HR = 1.73, p < .001) at baseline assessment predicted higher risk of incident depression post-stroke, after controlling for demographic variables, stroke severity, and history of stroke. Moreover, impairment in function (OR = 2.02, p < .001) at baseline predicted higher propensity of developing post-stroke depression over time, after controlling for covariates. These findings were presented in the STROKOG symposium in September 2020. A manuscript is being prepared.

Funding:
Vincent Fairfax Family Foundation, NHMRC.

Sex differences in risk factors for dementia and cognitive decline

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

Other investigators: Jessica Gong, Mark Woodward, Maree Hackett, Sanne Peters, Katie Harris (The George Institute), investigators from around 18 contributing COSMIC studies.

Aims:
- To provide a complete, systematic and comprehensive analysis of sex differences in risk factors for dementia using standardised methods, as opposed to examining a single risk factor and its association with dementia at a time.

Findings:
- Data from COSMIC studies being harmonised.

Funding:
NIH.

Sex differences in white matter hyperintensities (WMH) in non-demented individuals

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

Aims:
- To examine the risk factors for WMHs in non-demented individuals, the possible differential trajectories for WMH progressions for men and women in mid-life and ageing process. WMHs are generally considered to be associated with cerebral small vessels disease. They are commonly found in the brains of older individuals. Significant sex differences have been reported in the severity of WMH, but there are many unknown factors for such differences, e.g. it is not yet known if the risk factors for WMH differ in men and women; are the trajectories of WMH progression for men and women different; are the major risk factors that are associated with men and women different; and how these risk factors have differential impact on men and women?

Findings:
- Our first studies of this research theme has just appeared in *Neurobiology of Aging* (2021: ***https://doi.org/10.1016/j.neurobiolaging.2020.11.001***). Examining the trajectories of WMH progress due to ageing in men and women and investigation of the dynamics of the trajectories and how these trajectories will be influenced by risk factors will be our next work. We will take advantage of a large sample of UK Biobank for this work. We have processed FLAIR and T1-weighted scans from UK Biobank (~17000), all three waves of Sydney Memory and Ageing Study (~1200) and Older Australian Twins Study (~1000) and analysis is underway.

Funding:
NHMRC, John Holden Family Foundation and a PhD scholarship provided by Saudi government.

Sleep, Mild Cognitive Impairment, and Dementia in Elderly Cohorts with Ethnoracial Diversity

CHeBA staff: Darren Lipnicki, Perminder Sachdev.

Other investigators: Seung Wan Suh (workgroup leader), Ki Woong Kim: South Korea; Contributing COSMIC study leaders and associates: Representing cohorts from around 8 countries.

Aims:
- To identify subjective sleep parameters at baseline which have significant associations with cognitive decline at follow-up.
- To investigate the association between a specific pattern of changes of sleep parameters over follow-up period and cognitive decline.

Findings:
- Analyses underway.

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

Social relationships as protective factors and modifiable risk factors for cognitive decline in the Sydney Memory and Ageing Study

CHeBA staff: Anne-Nicole Casey (Postdoctoral Researcher), Nicole Kochan, Perminder Sachdev, Henry Brodaty, John Crawford.

Other investigators: Zhixin Liu (Statistical consultant, UNSW Stats Central).

Aims:
- Investigate the size of social networks (number of friends/relatives contacted monthly) and qualities of social relationships as modifiable lifestyle factors that impact cognitive function over time.

Findings:
- Researchers used data from the first four waves of the Sydney Memory and Ageing Study to assess whether reciprocal relationships exist between social network size and cognitive performance in each of seven domains including a global score;
- Average performance declined in all domains of cognitive function over time as did the average size of social networks;
- Although both cognition and network size declined over time, slower than expected decline in language ability predicted less than expected contraction in social network size;
- Similar influence of social network size on executive functioning indicated that relationships with friends and family outside of the home contributed significantly to maintenance of higher order cognitive abilities in older late life;
- Diverse patterns of influence between cognitive domains and social network size over six years underscore the importance of assessing the complex and nuanced interplay between brain health and social relationships in older age;
- Anne-Nicole S Casey, Zhixin Liu, Nicole A Kochan, Perminder S Sachdev, Henry Brodaty. Cross-Lagged

modeling of cognition and social network size in the Sydney Memory and Ageing Study, *The Journals of Gerontology: Series B*, 2020; ***https://doi-org.wwwproxy1.library.unsw.edu.au/10.1093/geronb/gbaa193***

Funding:
Thomas Foundation.

Social Health and Reserve in the Dementia patient journey (SHARED)

CHeBA staff: Suraj Samtani (Study Co-ordinator), Henry Brodaty (Work Package leader), Ashley Stevens, Darren Lipnicki, Perminder Sachdev. Other investigators: Contributing COSMIC study leaders and associates.

Aims:
- Examine the variance in cognitive function explained by social health (marital status; social network size; frequency of interactions; social support received and provided; independence in daily functioning; loneliness; quality of relationships), beyond that explained by APOE*4, demographic variables, baseline cognitive function, and physical health;
- Study the trajectory of social health as individuals progress from MCI to dementia (latent growth class analysis);
- Investigate the pathways that mediate the relationship between social and cognitive health (brain reserve as indicated through MRI, health behaviours, physiological factors, psychological factors) using structural equation modelling;
- Examine the variance in social health explained by cognitive function, physical health, and APOE*4;
- Findings: Data being obtained from COSMIC studies.

Funding:
- Direct donations to The Dementia Momentum Fund, NIH grant, NHMRC grants, European Union Joint Programme - Neurodegenerative Disease Research grant.

Social Orientation of Care in Aged Living (SOCIAL) Study: Meaningful relationships for people with (dementia-associated) changed behaviours 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).

Aims:
- Identify the occurrence of meaningful relationships for people with changed behaviours and dementia in residential aged care;
- Identify the contexts associated with the occurrence of meaningful relationships for people with changed behaviours and dementia in residential aged care.

Findings:
- Residents with the highest Australian Aged Care Funding Index behaviour rating, including in end-of-life care were capable of initiating and contributing to meaningful relationships;
- Residents' approach in relationships reflected how they were related to, expected to be related to and / or sought to be related to, by the other party;
- In a care home culture that valued relationships, a resident's changed behaviours were accepted as an important form of communication. The resident felt valued and was enabled to pursue their interests in an environment where their agency was respected;
- Residents' relationship networks reflected the number and diversity of the participants that residents encountered in care, the degrees of relationship that occurred and the potential to enhance the degree of relatedness;
- Residents recognised names of people in their network, confirming one aspect of short-term memory;
- Even in difficult situations, residents showed evidence of resilience and ingenuity;
- When staff and visiting personnel were asked to describe their understanding of a resident's 'quality of care,' they referred to the value of developing relationships among each other, the resident and with the resident's family;
- Staff's approach to residents reflected the care home's organisation culture, associated processes and its architectural design;
- The care home that most designed for and adopted systems and processes to support meaningful relationships was profitable;
- Data collection and analysis aspects of the project completed in 2020;
- Thesis currently being written up due to be ready for examination end 2021, with publications and presentations continuing.

Funding:
Self-funded.

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

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

Other investigators: Clare Flach and Majed Obaid (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:
- Dr Flach found that individuals who were cognitively impaired three months after stroke were at significantly increased risk of depression and disability in long-term follow-up. A manuscript draft is completed and has been circulated with collaborators in late 2019. Dr Flach is to conduct additional analyses and circulate a revised draft in early 2020. Dr Flach has since left the university and colleague Dr Majed Obaid has taken up the project in early 2020. A number of drafts have been circulated with co-authors. Majed has been working on co-authors' comments, revising the manuscript, and plans to submit to a journal soon.

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:
- The hydrodynamic diameter of nanoparticles, determined by dynamic light scattering (DLS) using the Malvern Zetasizer Nano Particle Characterisation System, demonstrated the stability of our nanoparticles in different biological media. Both the DMSA coated nanospheres and nanocubes showed expected changes to diameter and low polydispersity;
- The cytotoxicity of our functionalised nanoparticles was assessed in astrocytes and neurons using the lactate dehydrogenase assay and caspase-3 expression. Our nanoparticles showed no significant increases in toxicity relative to control at all concentrations up to 1mm;
- The internalisation of the nanoparticles and their localisation within the cellular organelles have been assessed using electron microscopy. After 6 hours of incubation, the nanoparticles appeared to localise on the plasma membrane and within multivesicular bodies. After 24 hours of incubation, the nanoparticles were observed to have moved into the lysosomes;
- We also demonstrated, using immunohistochemistry and electron microscopy, that these functionalised nanoparticles indeed bind to Aβ fibrils, suggesting selectivity to bind plaque deposits in AD transgenic mouse and post-mortem human probable AD brain tissue sections;
- Our nanoparticles were shown to be safe and well tolerated in AD transgenic mice (APP/PS1) and wild type mice with no changes in liver and renal function tests and no observable changes in behaviour even at repeatedly high doses of 10 ng per kg weight of mouse.

Publications:
- Ulanova M, Poljak A, Wen W, Bongers A, Gloag L, Gooding J, Tilley R, Sachdev P, Braidy N. Nanoparticles as contrast agents for the diagnosis of Alzheimer's disease: A systematic review. *Nanomedicine* 2020 Mar; 15(7):725-743. DOI: 10.2217/nnm-2019-0316;
- Gloag L, Mehdipour M, Ulanova M, Mariandry K, Nichol MA, Hernández-Castillo DJ, Gaudet J, Qiao R, Zhang J, Nelson M, Thierry B, Alvarez-Lemus MA, Tan TT, Gooding JJ, Braidy N, Sachdev PS, Tilley RD. Zero valent iron core-iron oxide shell nanoparticles as small magnetic particle imaging tracers. *Chem Commun*. 2020 Mar 25; 56(24):3504-3507. DOI: 10.1039/c9cc08972a.

Funding:
Sachdev Foundation, The Yulgilbar 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 (Adjunct), 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. We also found the significant relation of global, old, acute/subacute and regional cerebral vascular pathologies, but not white matter rarefaction, to the onset and severity of Alzheimer's dementia. We also showed that late-life risk factors were found to have no relation with Alzheimer's dementia, and the increased risk of dementia with APOE ε4 is not mediated by CVD. The best interpretation of these findings is that CVD has a potential additive effect with AD pathologies in the development and progression of what is clinically diagnosed as Alzheimer's dementia. There are two publications reporting on these findings and 2 more are under preparation for submission.

Publications:

- Liu Y, Chan DKY, Thalamuthu A, Wen W, Jiang J, Paradise M, Lee T, Crawford J, Wong MWK, Xu YH, Poljak A, Pickford R, Sachdev PS, Braidy N (2020). Plasma lipidomic biomarker analysis reveals distinct lipid changes in vascular dementia. *Computational and Structural Biotechnology*. 18:1613-1624;
- Liu Y, Chan DKY, Crawford J, Sachdev P, Braidy N (2020). The contribution of cerebral vascular disease to mild stage of Alzheimer's dementia using the NACC database. Current Alzheimer Research. 17(13):1167-1176.

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

The association between cardiovascular risk factor variability with dementia risk and cognitive impairment

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

Other investigators: Phillip Tully, Andrew Vincent (University of Adelaide), Rianne de Heus (Radboud University), investigators from around 16 contributing COSMIC studies.

Aims:

- To examine whether variability in cardiovascular risk factors is independently associated with dementia and cognitive impairment.

Findings:

- Data being obtained from COSMIC studies.

Funding:
NIH.

The associations among education, occupational complexity, and late-life cognition

CHeBA staff: Darren Lipnicki, Perminder Sachdev.

Other investigators: Jinshil Hyun (workgroup leader), Charles B. Hall, Mindy J. Katz, Richard B. Lipton from the Albert Einstein College of Medicine; Contributing COSMIC study leaders and associates: Representing cohorts from around 11 countries.

Aims:

- Our overall aim is to examine the unique and interactive effects of occupational complexity and education on late-life cognition (cognitive impairment and normal cognitive aging, including levels and rates of change). Our specific aims are to examine:
    - Whether occupational complexity is associated with late-life cognition over and above the effect of education. High occupational complexity is associated with lower likelihood of developing

cognitive impairment. High occupational complexity is also associated with higher levels of cognition and slower rates of cognitive decline at earlier stages of cognitive aging;

- Whether occupational complexity is the mechanism though which early-life education is associated with late-life cognition. The association between education and cognitive impairment is mediated by occupational complexity. The association between education and cognitive aging (i.e., levels, rates of change) is mediated by occupational complexity;

- How education and occupational complexity interact. There is an incremental effect of these factors on cognitive impairment. Being low in either education or occupation conveys greater risk for cognitive impairment than being high on both; being low in both conveys the greatest incidence risk. There is an incremental effect of education and occupation on levels and rates of change in cognition;

- We will also examine whether these effects are over and above the effects of late-life cognitive activities and whether they vary by APOE e4 status, gender, and race/ethnicity.

Findings:
- First draft of manuscript being revised.

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

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.

Publications:
- Braidy N, Liu Y. NAD+ therapy in age-related degenerative disorders: A benefit/risk analysis. *Exp Gerontol*. 2020 Apr; 132: 110831. DOI: 10.1016/j.exger.2020.110831;

- Jayasena T, Bustamante S, Clement J, Welschinger R, Caplan GA, Sachdev PS, Braidy N. Clinical Assessment of the NADome as biomarkers for healthy ageing. *Methods Mol Biol.* 2020; 2138: 207-216. DOI: 10.1007/978-1-0716-0471-7_13;

- Grant R, Berg J, Mestayer R, Braidy N, Bennett J, Broom S, Watson J. A pilot study investigating changes in the human plasma and urine NAD+ metabolome during a 6 hour intravenous infusion of NAD+. *Front Aging Neurosci.* 2019 Sep 12; 11: 257. DOI: 10.3389/fnagi.2019.00257;

- Clement J, Wong M, Poljak A, Sachdev P, Braidy N. The plasma NAD+ metabolome is dysregulated in 'normal' ageing. *Rejuvenation Res.* 2019 Apr; 22(2):121-130. DOI: 10.1089/rej.2018.2077;

- Braidy N, Berg J, Clement J, Poljak A, Sachdev P, Grant R (2019). Role of nicotinamide adenine dinucleotide and related precursors as therapeutic targets for age-related degenerative diseases: rationale, biochemistry, pharmacokinetics, and outcomes. *Antioxid Redox Signal.* 2019 Jan 10;30(2):251-294. doi: 10.1089/ars.2017.7269;

- Braidy N, Liu Y (2020). Can nicotinamide riboside protect against cognitive impairment? *Current Opinion in Nutrition and Metabolic Care*. 23(6):413-420;

- Braidy N, Villalva MD, Van Eeden S (2020). Sobriety and satiety: Is NAD+ the answer? *Antioxidants* 14;9(5):E425;

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

The Global burden of dementia

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

Other investigators: Emma Nichols, Jaimie Adelson (Institute for Health Metrics and Evaluation), investigators from around 34 contributing COSMIC studies.

Aims:
- Describe prevalence and incidence of dementia by age and sex for each contributing study. For those studies that have included the Clinical Dementia Rating Scale (CDR) or other markers of severity, describe the severity of dementia by age and sex for each contributing study and investigate whether this varies across countries;
- Using mortality records (date of death), investigate excess mortality attributable to dementia and how this may vary across countries. For the subset of studies that have included the CDR, investigate what proportion of mortality among people with dementia occurs in those with severe disease and can therefore be assumed to be due to dementia as an underlying cause of death;
- Calculate relative risks and population attributable fractions for risk factors previously included in the GBD analyses (BMI, fasting plasma glucose, and smoking), as well as several additional dementia risk factors that have not previously been estimated within the GBD study, including education, alcohol consumption, physical inactivity and blood pressure.

Findings:
- Data from COSMIC studies being obtained.

Funding:
NIH, Vincent Fairfax Family Foundation.

The Older Australian Twins Study (OATS)

CHeBA staff: Perminder Sachdev, Henry Brodaty, John Crawford, Teresa Lee, Karen Mather, Anne Poljak (Adjunct), Amanda Selwood, Anbu Thalamuthu, Julian Trollor, Wei Wen.

Aims:
- Find out what influences memory and thinking as we age;
- Investigate environmental influences such as lifetime physical and mental activity, socioeconomic environment and nutrition;
- Investigate how biological factors such as hypertension and antioxidant levels interact with genes to influence brain ageing;
- Determine which influences on the ageing process are genetic, which are environmental, and how the two interact.

Findings:
OATS data contributed to a significant number of publications in 2020, including:

- Wong, M.W.K., et al., Genetic and environmental determinants of variation in the plasma lipidome of older Australian twins. Elife, 2020. 9;
- Weston, S., et al., *Is Healthy Neuroticism Associated with Chronic Conditions? A Coordinated Integrative Data Analysis.* Collabra: Psychology, 2020. 6(1): p. 42;
- Turiano, N.A., et al., *Is Healthy Neuroticism Associated with Longevity? A Coordinated Integrative Data Analysis.* Collabra: Psychology 2020. 6(1): p. 33;
- Sonderby, I.E., et al., *Dose response of the 16p11.2 distal copy number variant on intracranial volume and basal ganglia.* Molecular Psychiatry, 2020. 25: p. 584-602;
- Shin, J., et al., *Global and regional development of the human cerebral cortex: molecular architecture and occupational aptitudes.* Cerebral Cortex, 2020. 30(7): p. 4121–4139;
- Parker, N., et al., *Corticosteroids and Regional Variations in Thickness of the Human Cerebral Cortex across the Lifespan.* Cerebral Cortex, 2020. 30(2): p. 575-586;
- Nabais, M.F., et al., *Significant out-of-sample classification from methylation profile scoring for amyotrophic lateral sclerosis.* Npj Genomic Medicine, 2020. 5(1);
- Liu, Y., et al., *Plasma lipidomic biomarker analysis reveals distinct lipid changes in vascular dementia.* Computational and Structural Biotechnology Journal, 2020. 18: p. 1613 - 1624;
- Li, S., et al., *Genetic and environmental causes of variation in epigenetic aging across the lifespan.* Clinical Epigenetics, 2020. 12(1);
- Jia, T. and K. Mather, *Epigenome-wide meta-analysis of blood DNA methylation and its association with subcortical volumes: findings from the ENIGMA Epigenetics Working Group.* Molecular Psychiatry, 2020;
- Iacoangeli, A., et al., *Genome-wide Meta-analysis Finds the ACSL5-ZDHHC6 Locus Is Associated with ALS and Links Weight Loss to the Disease Genetics.* Cell Reports, 2020. 33(4);
- Grasby, K.L., et al., *The genetic architecture of the human cerebral cortex.* Science, 2020. 367: p. eaay6690;
- Graham, E.K., et al., *Is Healthy Neuroticism Associated with Health Behaviors? A Coordinated Integrative Data Analysis.* Collabra: Psychology 2020. 6: p. 32;

- Ciobanu, L.G., et al., *Downregulated transferrin receptor in the blood predicts recurrent MDD in the elderly cohort: A fuzzy forests approach.* Journal of Affective Disorder, 2020. 267: p. 42-48;
- Beaudet, G., et al., *Age-Related Changes of Peak Width Skeletonized Mean Diffusivity (PSMD) Across the Adult Lifespan: A Multi-Cohort Study.* Frontiers in Psychiatry, 2020. 11;
- Armstrong, N. and K. Mather, *Common genetic variation indicates separate etiologies for periventricular and deep white matter hyperintensities.* Stroke, 2020. 51: p. 2111-2121;
- Hofer, E., et al., *Genetic correlations and genome-wide associations of cortical structure in general population samples of 22,824 adults.* Nature Communications, 2020. 11:4796.

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. Results showed that centenarians without diagnosis of dementia had more synchronised activation of bilateral parietofrontal control networks compared to young-old participants. Stronger functional connectivity between bilateral parietofrontal control networks was associated with better performance in visuospatial ability in centenarians. The paper has been published in *Neuroimage*: ***https://doi.org/10.1016/j.neuroimage.2020.116855***

Funding:
John Holden Family Foundation, NHMRC.

The prevalence of poor mobility in older adults

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

Other investigators: Caterina Rosana, Briana Sprague (University of Pittsburgh), Joe Verghese (Albert Einstein College of Medicine), Kim Delbaere (NeuRA), investigators from around 14 contributing COSMIC studies.

Aims:
- Is the prevalence of poor mobility (via objective measure of gait speed and self-reported measures of physical disability such as ADL/IADLs) similar across countries, and;
- What are the most common predictors of poor mobility across countries?

Findings:
- Data from COSMIC studies being harmonised.

Funding:
NIH.

The relationship between alcohol use trajectories and health, mortality and cognition in older adults

CHeBA staff: Louise Mewton, Darren Lipnicki, Perminder Sachdev, Nicholas Hoy, Rachel Visontay.

Other investigators: Contributing COSMIC study leaders and associates: Representing cohorts from around 12 countries.

Aims:
- To examine inter-individual variation in the relationship between drinking trajectories and a range of variables related to health, mortality and cognition in adults aged 60+ years.

Findings:
- Analyses complete and manuscript in draft.

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

The relationship between blood pressure and risk of cognitive decline

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

Other investigators: Ruth Peters (NeuRA); Contributing COSMIC study leaders and associates: Representing cohorts from around 14 countries

Aims:
- To examine the effect of BP and antihypertensives on cognitive function in late life. Specifically:
    - The relationship of hypertension (including systolic and diastolic) with cognitive decline and all cause dementia;

- The relationship of hypotension with cognitive decline and all cause dementia and Alzheimer's disease;
- Differences in late life BP trajectories among those who maintain normal cognition or develop MCI/dementia;
- If antihypertensive treatment and type are related to risk of cognitive decline, including within BP groups;
- Ethno-regional differences in hypertension as a risk for cognitive decline and dementia;
- If the genetic determinants of hypertension are correlated with the genetic determinants of cognitive decline (if possible);
- Investigate associations between BP and small vessel disease using MRI data (if possible).

Findings:
- Data being obtained from COSMIC studies.

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

The hormetic and toxic effects of common dietary components on cultured neuronal cells

CHeBA staff: Anne Poljak (Adjunct), Fatemeh Khorshidi (APA PhD candidate), Tharusha Jayasena, Perminder Sachdev.

Other investigators: Sonia Bustamante.

Aims:
- Determine if several commonly ingested dietary constituents (including ethanol, resveratrol, nicotinamide, etc) show typical dose response curves in a cultured astrocyte cell line, including a hormetic effect at lower dose levels and toxicity at higher dose levels;
- Explore cellular proteomic and metabolomics changes associated with the hormetic and toxic levels of the dose response curves. From this data determine if specific cellular pathways are altered as a response to exposure to compounds and dose levels;
- Use electron microscopy to identify potential changes in cellular morphology in response to exposure to compounds and dose levels.

Findings:
- We performed a meta-analysis of clinical trials using resveratrol and/or foods containing resveratrol (i.e., wine and grapes) on cognition in humans, and reviewed the literature, including that using animal models. The main findings were that; (a) resveratrol and resveratrol containing foods generally showed beneficial effects on cognition in animal studies but not in human studies; (b) clinical efficacy of resveratrol in humans appears to be of negligible effect and (c) the difference between the results reported in animal models to those reported in human clinical trials may be related to the substantially higher dose levels normally using in animal models. Caution is therefore advised to pharmaceutical companies seeking to utilise resveratrol as an approach to treatment of cognitive/memory disorders. This work has now been published; Khorshidi *et al* Resveratrol: A "miracle" drug in neuropsychiatry or a cognitive enhancer for mice only? A systematic review and meta-analysis, Ageing Research Reviews 65 (2021) 101199;
- Experimental work to establish dose response curves and proteomics analysis using each of ethanol, resveratrol, nicotinamide and NAD, are now close to completion. Fatemeh is currently finalising her PhD experimental work and writing her thesis chapters.

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

The Sydney Centenarian Study (SCS)

CHeBA staff: Perminder Sachdev, Henry Brodaty, John Crawford, Wei Wen, Nicole Kochan, Karen Mather, Catherine Browning, Kristan Kang, Fleur Harrison, Julia Riches, Suzi Artiss, Anbupalam Thalamuthu, Jiyang Jiang.

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:
- CHeBA's Genetics and Epigenomic Group whole genome sequenced 101 SCS participants who had reached 100 years of age, which provides us with detailed information about the genetic makeup of these long-lived SCS participants. 74% of the sample sequenced were women, which reflects the gender difference in reaching 100 years or over. This newly acquired data allows us to look at different types of genetic variants, including genomic repeats - sections of DNA that can vary in their copy number and even to estimate telomere length. Telomeres are the DNA caps found at the ends of our chromosomes that have a protective function, which shorten as we age. Our preliminary results, yet to be published, suggest that centenarians do have shorter telomeres compared to younger individuals aged in their 70s.

Funding: NHMRC.

The Sydney Memory and Ageing Study (MAS)

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

Other staff: Josephine Bigland (UNSW).

Aims:

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

Findings:

- MAS data contributed to a significant number of publications in 2020, including:
    - Röhr S, Sachdev PS et al. Estimating prevalence of subjective cognitive decline in and across international cohort studies of aging: A COSMIC study. *Alzheimers Res Ther*. 2020 Dec 18;12(1):167. DOI: 10.1186/s13195-020-00734-y. PMID: 33339532 / PMCID: PMC7749505;
    - Casey AS, et al. Cross-lagged modeling of cognition and social network size in the Sydney Memory and Ageing Study. *J Gerontol B Psychol Sci Soc Sci*. 2020 Nov 7. DOI: 10.1093/geronb/gbaa193. PMID: 33159521 [Epub 2020 Nov 8];
    - Strutt PA et al. Hearing loss, cognition, and risk of neurocognitive disorder: evidence from a longitudinal cohort study of older adult Australians. *Neuropsychol Dev Cogn B Aging Neuropsychol Cogn*. 2020; Dec 28:1-18. DOI: 10.1080/13825585.2020.1857328. PMID: 33371769 [Epub 2020 Dec 30];
    - Alqarni A et al. Sex differences in risk factors for white matter hyperintensities in non-demented older individuals. *Neurobiol Aging*. 2020 Nov 10; 98:197-204. DOI: 10.1016/j.neurobiolaging.2020.11.001. PMID: 33307330 [Epub 2020 Dec 12];
    - Spooner A et al. A comparison of machine learning methods for survival analysis of high-dimensional clinical data for dementia prediction. *Sci Rep*. 2020 Nov 23; 10(1):20410. DOI: 10.1038/s41598-020-77220-w. PMID: 33230128;
    - Hofer E, Sachdev PS, et al. Genetic correlations and genome-wide associations of cortical structure in general population samples of 22,824 adults. *Nat Commun*. 2020 Sep 22; 11(1):4796. DOI: 10.1038/s41467-020-18367-y. PMID: 32963231 [Epub 2020 Sep 24];
    - Zhang Q, et al. Risk prediction of late-onset Alzheimer's disease implies an oligogenic architecture. *Nat Commun*. 2020 Sep 23; 11(1):4799. DOI: 10.1038/s41467-020-18534-1. PMID: 32968074. [Epub 2020 Sep 25];
    - Affleck AJ et al. Antihypertensive medications ameliorate Alzheimer's disease pathology by slowing its propagation. *Alzheimers Dement (N Y)*. 2020; 6(1):e12060. DOI: 10.1002/trc2.12060. PMID: 32802934. [Epub 2020 Aug 12];
    - Samaras K, Sachdev PS et al. Metformin Use Is Associated With Slowed Cognitive Decline and Reduced Incident Dementia in Older Adults With Type 2 Diabetes: The Sydney Memory and Ageing Study. *Diabetes Care*. 2020 Nov;43(11):2691-2701. DOI: 10.2337/dc20-0892. PMID: 32967921 [Epub 2020 Sep 25];
    - Grasby KL, Sachdev PS, et al. The genetic architecture of the human cerebral cortex. *Science*. 2020 Mar 20; 367(6484): 1-14. DOI: 10.1126/science.aay6690. PMID: 32193296 [Epub 2020 Mar 21];
    - Lennon MJ et al. Does antihypertensive use moderate the effect of blood pressure on cognitive decline in older people? *J Gerontol A Biol Sci Med Sci.* 2020 Oct 12: glaa232. DOI: 10.1093/gerona/glaa232. PMID: 33225353;
    - Makkar SR, Lipnicki DM et al. APOE ε4 and the influence of sex, age, vascular risk factors, and ethnicity on cognitive decline. *J Gerontol A Biol Sci Med Sci*. 2020 Sep 25; 75(10):1863-1873. DOI: 10.1093/gerona/glaa116. PMID: 32396611 [Epub 2020 May 12];
    - Chander RJ, Sachdev PS, et al. Development of a short-form version of the reading the mind in the eyes test for assessing theory of mind in older adults. *Int J Geriatr Psychiatry.* 2020 Nov; 35(11):1322-1330. DOI: 10.1002/gps.5369. PMID: 32584445 [Epub 2020 Jun 25];
    - Graham EK, Broday H, et al. Is Healthy Neuroticism Associated with Health Behaviors? A Coordinated Integrative Data Analysis. *Collabra Psychol*. 2020; 6(1). DOI: 10.1525/collabra.266. PMID: 33354649. [Epub 2020 Dec 24];
    - Numbers K, et al. Participant and informant memory-specific cognitive complaints predict future decline and incident dementia: Findings from the Sydney Memory and Ageing Study. *PLoS ONE*. 2020 May 12; 15(5):e0232961. DOI: 10.1371/journal.pone.0232961. PMID: 32396544;
    - Shin J, Sachdev PS, et al. Global and regional development of the human cerebral cortex: molecular architecture and occupational aptitudes. *Cereb Cortex.* 2020 Jun 1;30(7):4121-4139. DOI: 10.1093/cercor/bhaa035. PMID: 32198502 [Epub 2020 Mar 22];

Funding:
NHMRC Program Grants (ID350833; ID568969; APP1093083).

Towards understanding the role of gene expression in ageing

CHeBA staff: Anbupalam Thalamuthu, Karen Mather, Perminder Sachdev, Sri Chandana Kanchibhotla, Toyin Abdulsalam (Scientia PhD student).

Other investigators: Professor Bernhard Baune (University of Adelaide), Dr Liliana Ciobanu (University of Adelaide), A/Professor Nicola Armstrong (Murdoch University) (CHeBA Hon. Research Fellow), A/ProfessorJohn Kwok (University of Sydney; UNSW), Professor Peter Schofield (NeuRA; UNSW).

Aims:
- 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. Heritability of gene expression in older adults using twins from the Older Australian Twins Study has been undertaken and is being written up for publication.

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. Two manuscripts are currently under preparation for this project.

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

White matter lesions and their neuropsychological correspondence using data from COSMIC

CHeBA staff: Jiyang Jiang, Wei Wen, John Crawford, Darren Lipnicki, Perminder Sachdev, Henry Brodaty, Nicole Kochan.

Other investigators: Investigators from around 5 contributing studies.

Aims:
- To examine effects of age, sex, and ethnicity on WML measures;
- To study how WML measures and changes in WML measures over time are associated with cognitive domain scores;
- To study how WML measures and their changes over time are associated with MCI and dementia;
- To examine how WML measures are associated with neuropsychological disorders (e.g. depression, anxiety) and motion disorders;

Findings:
- Data from studies being obtained and analysed.

Funding:
NIH, Vincent Fairfax Family Foundation.

Completed Projects

A cross-national study of depression in pre-clinical Alzheimer's disease: a COSMIC collaboration study

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

Other investigators: Karen Ritchie (workgroup co-leader), Isabelle Carriere, Sophie Carles, Marie-Laure Ancelin: 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:

- Depression incidence varied across the 8 included studies from 3.5 to 15.5 cases per 100 person years. Taking into account methodological differences between studies, an increase in the incidence of depression was observed as the time to dementia diagnosis decreased despite cross-national variability in depression rates. The results support the hypothesis that depression occurring in the pre-clinical phases of dementia is more likely to be attributable to brain changes than environmental risk factors or reverse causality;
- Our findings were published in *Alzheimer's and Dementia:* Carles S, Carrière I, Reppermund S, Davin A, Guaita A, Vaccaro R, Ganguli M, Jacobsen EP, Beer JC, Riedel-Heller SG, Roehr S, Pabst A, Haan MN, Brodaty H, Kochan NA, Trollor JN, Kim KW, Han JW, Suh SW, Lobo A, la Camara C, Lobo E, Lipnicki DM, Sachdev PS, Ancelin ML, Ritchie K; for Cohort Studies of Memory in an International Consortium (COSMIC). A cross-national study of depression in preclinical dementia: A COSMIC collaboration study. Alzheimers Dement. 2020 Nov;16(11):1544-1552. doi: 10.1002/alz.12149

Funding:
Direct donations to The Dementia Momentum Fund, NIH grant, NHMRC grant. Dr Simone Reppermund is supported by a UNSW Scientia Fellowship.

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.

Aims:

- 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, and 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 Findings: APOE ε4 and the Influence of Sex, Age, Vascular Risk Factors, and Ethnicity on Cognitive Decline. Makkar SR, Lipnicki DM, Crawford JD, Kochan NA, Castro-Costa E, Lima-Costa MF, Diniz BS, Brayne C, Stephan B, Matthews F, Llibre-Rodriguez JJ, Llibre-Guerra JJ, Valhuerdi-Cepero AJ, Lipton RB, Katz MJ, Wang C, Ritchie K, Carles S, Carriere I, Scarmeas N, Yannakoulia M, Kosmidis M, Lam L, Chan WC, Fung A, Guaita A, Vaccaro R, Davin A, Kim KW, Han JW, Suh SW, Riedel-Heller SG, Roehr S, Pabst A, Ganguli M, Hughes TF, Snitz B, Anstey KJ, Cherbuin N, Easteal S, Haan MN, Aiello AE, Dang K, Pin Ng T, Gao Q, Zin Nyunt MS, Brodaty H, Trollor JN, Leung Y, Lo JW, Sachdev P. J Gerontol A Biol Sci Med Sci. 2020 Sep 25;75(10):1863-1873.

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

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

CHeBA staff: Lynn Chenoweth, Henry Brodaty.

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

Aims:

- 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 with an influence on family-staff relationships were assessed using 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;

- Our findings were published in *Medical Research Archives* (Chenoweth L, Cook J, Wesson J, Brodaty H. Evaluating an education program promoting positive family and staff relationships and collaboration in aged care services: Pre/post/follow-up pilot study. *Medical Research Archives*. 2019 Aug 17; 7(7): 1-26. DOI: 10.18103/mra.v7i7.1958). The Staff and Family Relationship training program is also available at the DCRC website: Collaboration between family members and direct care staff in quality improvement of residential care services - DCRC (***dementiaresearch.org.au***)

Funding:
Montefiore.

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)***, with recommendations only applying to individuals already taking one of the described medications (donepezil, rivastigmine, galantamine and/or memantine). The main points of this guideline are as follows:

    - There is considerable uncertainty in the benefits and harms of both prescribing and deprescribing in the individual who has used these medications for over 12 months. Cessation may have minimal, clinically relevant negative consequences, but in some individuals, discontinuation of ChEIs and/or memantine may lead to a worsening of cognitive function. With regard to quality of life and function, these outcomes may not be altered by discontinuation;

    - Good communication between clinicians and people with dementia and/or carers/family on the benefits and harms of continuing versus discontinuing, in the context of their values and preferences, is necessary when discussing a potential trial of deprescribing, since individuals

may feel that deprescribing is 'giving up', or a signal that they are no longer worth treating;

- The cost implications of deprescribing may include reduced medication costs, reduced costs of treating adverse drug effects, and an uncertain benefit or cost if there is a change in function that increases or decreases health service utilisation.

These findings were also published in the *Medical Journal of Australia* (Reeve et al. *Med J Aust*. 210(4): 174-179).

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

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

CHeBA staff: Lynn Chenoweth.

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

Aims:

- Evaluate the clinical and cost-effectiveness of Dementia Care Mapping (DCM) in supporting the implementation of person-centred care training (PCCT);
- Evaluate its effectiveness as a process for improving care quality and quality outcomes for people with dementia, compared with usual dementia care;
- DCM-EPIC was conducted as a pragmatic, cluster randomised controlled trial with cost-effectiveness analysis. Follow-up at 6- and 16-months. Stratified randomisation of 50 care homes to intervention (n=31) or control (n=19). Care home eligibility included recruitment of ≥10 residents; not subject to improvement notices; not used DCM. At baseline and 16-months, 726 and 261 residents were recruited, respectively. Resident eligibility included: permanent residence; diagnosis of dementia/ probable dementia; not at end-of-life. Clusters were not blinded to allocation. Three DCM cycles delivered by two trained care home staff were scheduled; cycle one supported by a DCM expert. Agitation (Cohen-Mansfield Agitation Inventory (CMAI)) at 16-months was the primary outcome.

Findings:

- DCM was not superior to control on any outcomes (n=675 residents: 287 control, 388 intervention). The adjusted mean CMAI score difference intervention versus control was -2.11 points) (95% CI -4.66 to 0.44, p = 0.104, adjusted ICC control=0, intervention 0.001). Sensitivity analyses supported the primary analysis. Intervention adherence was problematic. Incremental cost per unit improvement in CMAI and QALYs (intervention versus control) for baseline recruited residents (n=726, 418 intervention, 308 control) was £289 and £60,627 respectively. 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).

Publications:

- Surr CA, Holloway I, Walwyn RE, Griffiths AW, Meads D, Kelley R, Martin A, McLellan V, Ballard C, Fossey J, Burnley N, Chenoweth L, Creese B, Downs M, Garrod L, Graham EH, Lilley-Kelley A, McDermid J, Millard H, Perfect D, Robinson L, Robinson O, Shoesmith E, Siddiqi N, Stokes G, Wallace D, Farrin AJ. Dementia Care Mapping (DCM™) to reduce agitation in care home residents with dementia: The DCM™ EPIC cluster RCT. Monograph. *National Institute for Health Research - Health Technology Assessment (NIHR-HTA) Repository*. 2019: UK;
- Griffiths AW, Surr CA, Creese B, Garrod L, Chenoweth L. The development and use of the Assessment of Dementia Awareness and Person-centred Care Training (ADAPT) tool in long-term care. *Dementia (London)*. 2019 Oct-Nov; 18(7-8):3059-3070. DOI: 10.1177/1471301218768165. PMID: 29631493;
- Surr C, Griffiths A, Kelley R, Holloway I, Walwyn R, Martin A, McDermid J, Chenoweth L, Farrin AJ. The implementation of Dementia Care Mapping™ in a randomised controlled trial in long-term care: results of a process evaluation. *Am J Alzheimers Dis Other Demen*. 2019 Sep; 34(6):390-398. DOI: 10.1177/1533317519845725. PMID: 31056923 / PMCID: PMC6676338;
- Surr C, Woodward-Carlton B, Griffiths AW, the DCM-EPIC team. Does DCM Improve Care in Care Homes? The EPIC trial. *Journal of Dementia Care*. 2019; 27(5): 24-27.

Parity and the risk of incident dementia: a COSMIC collaboration cohort study

CHeBA staff: Darren Lipnicki, Perminder Sachdev.

Other investigators: Jong Bin Bae (workgroup leader), Ki-Woong Kim: South Korea; Contributing COSMIC study leaders and associates: Representing cohorts from 6 countries.

Aims:
- To investigate the association between parity and risk of incident dementia.

Findings:
- Of 9,756 women dementia-free at baseline, 7,010 completed one or more follow-up assessments. The number of parities was associated with the risk of incident dementia (Hazard ratio [HR] = 1.07, 95% CI = 1.02 – 1.13). Grand multiparity increased the risk of dementia by 30% compared to 1 – 4 parities (HR = 1.30, 95% CI = 1.02 – 1.67). Parity and the risk of incident dementia: a COSMIC study. Bae JB et al.; for Cohort Studies of Memory in an International Consortium (COSMIC). *Epidemiology and Psychiatric Sciences*. 2020 Oct 20;29:e176.

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: 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.

Aims:
- Examine whether years of education is associated with a reduced risk of cognitive impairment;
- Further explore the nature of this relationship, namely: (a) whether the association between education and attenuated risk of cognitive impairment is nonlinear; and (b) 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:
- Makkar SR et al; for Cohort Studies of Memory in an International Consortium (COSMIC). *Archives of Gerontology and Geriatrics*. 2020 Nov/Dec; 91:104112. doi: 10.1016/j.archger.2020.104112.

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

Relationship between metabolic syndrome and inflammatory protein clusters on cognitive decline and dementia: the Sydney Memory and Ageing Study

CHeBA staff: Darren Lipnicki, Perminder Sachdev, Ben Lam, John Crawford, Nicole Kochan, Henry Brodaty, Julian Trollor.

Other investigators: Kathy Samaras (UNSW).

Aims:
- To investigate whether the level of inflammation moderates the association between metabolic syndrome and cognitive decline and dementia, and whether these associations are driven by specific clusters of inflammatory proteins.

Findings:
- Confirmatory factor analysis results showed that each of the metabolic syndrome components loaded significantly on the metabolic syndrome factor, indicating the validity of the metabolic syndrome construct in this older-aged sample. Principal components analysis yielded two distinct clusters of inflammatory proteins: IL6/SAA and IL-1β/TNF-α which were used as the primary markers of inflammation. Results showed that IL6/SAA and IL-1β/TNF-α, but not CRP, uniquely moderated the relationship between metabolic syndrome and cognitive decline. In addition, IL6/SAA was a unique moderator of the relationship between metabolic syndrome and dementia incidence. Specifically, at elevated levels of these inflammatory protein clusters, metabolic syndrome was associated with more rapid cognitive decline (for IL6/SAA and IL-1β/TNF-α) and heightened risk of dementia (for IL6/SAA). A manuscript is under preparation.

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

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, Alexander Pabst, Steffi Riedel-Heller; Contributing COSMIC study leaders and associates: Representing cohorts from around 15 countries.

Aims:

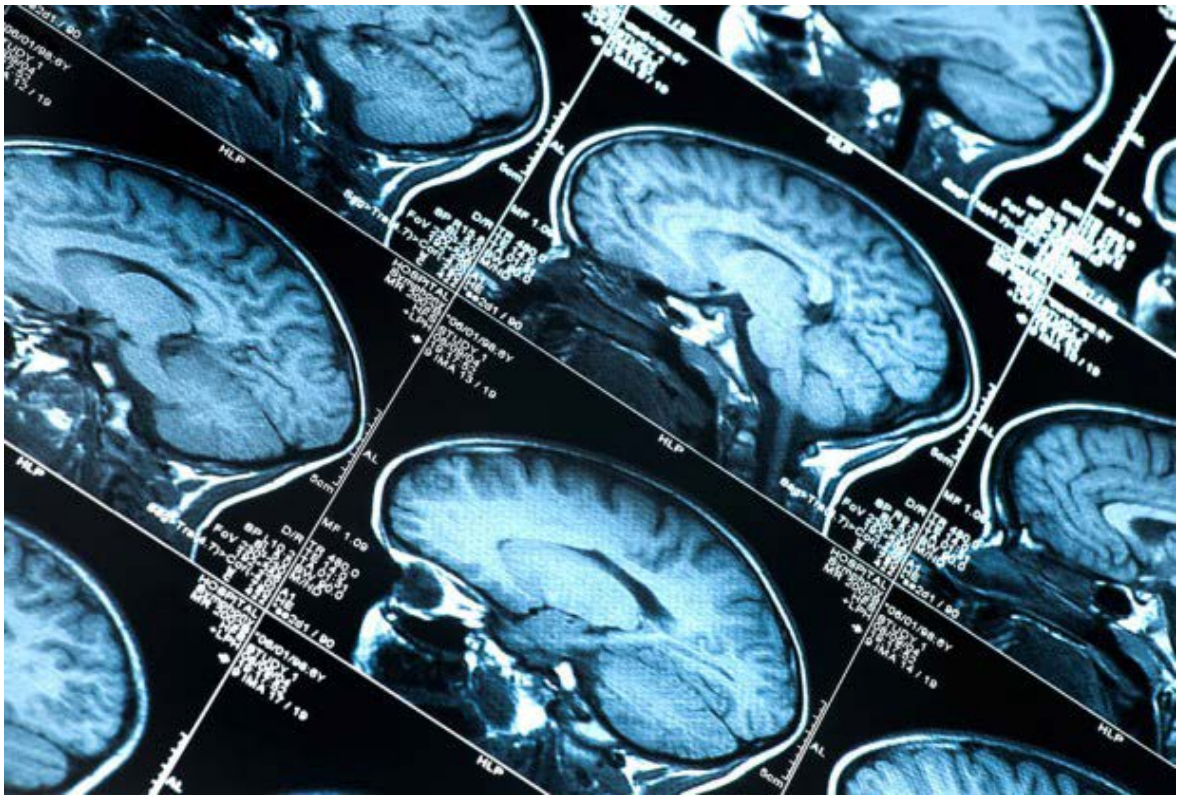
- Establish the prevalence of subjective cognitive decline (SCD) in and across different geographical and ethno-cultural regions.

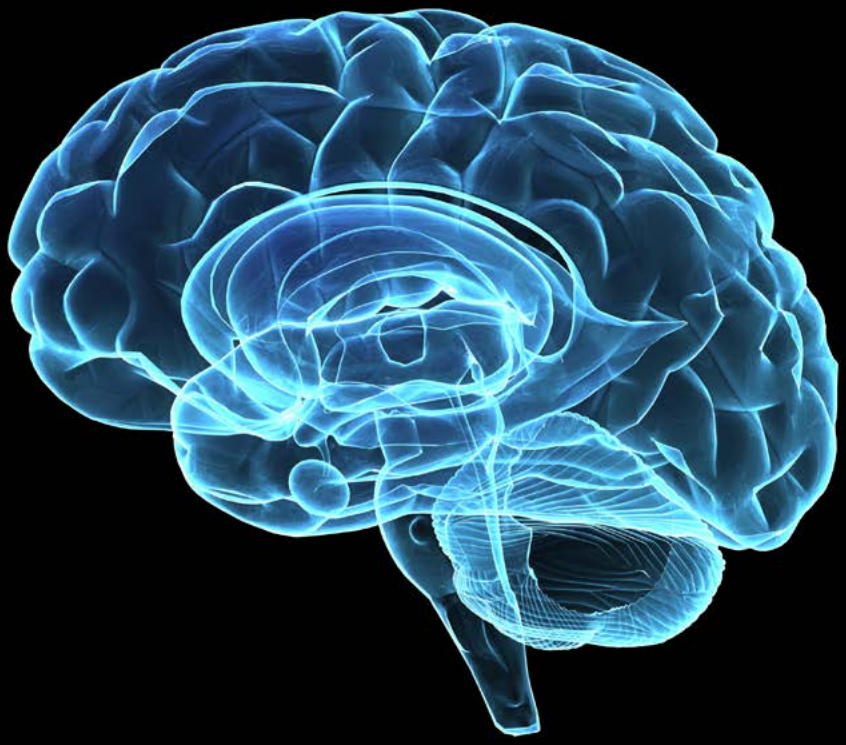
Findings:

- 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 (Estimating prevalence of subjective cognitive decline in and across international cohort studies of aging: a COSMIC study. Röhr S et al; for Cohort Studies of Memory in an International Consortium (COSMIC). *Alzheimers Res Ther*. 2020 Dec 18;12(1):167).

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





Appendices

"Living to 100 or 150 may be possible, but what we need to ensure is that we're adding life to our years and not just years to our life."

Professor Henry Brodaty AO

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, Leader Neuropsychiatry Group Co-Leader Epidemiology Group

Angela (Angie) Russell
Centre Manager

Academic Staff

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

Catherine Browning
Postdoctoral Fellow, Sydney Centenarian Study (SCS) Co-ordinator (until 30 October 2020)

Anne-Nicole Casey
Postdoctoral Fellow (until 31 December 2020)

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

Lynn Chenoweth
Professor of Nursing

Meredith Gresham
Research Fellow, COGNISANCE Project Co-ordinator

Megan Heffernan
Postdoctoral Fellow, Maintain Your Brain Trial 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

Chun Pan (Ben) Lam
Postdoctoral Fellow, STROKOG Project Co-ordinator

Darren Lipnicki
Postdoctoral Fellow, COSMIC Consortium Co-ordinator

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

Karen Mather
Senior Research Fellow, Leader Genetics & Epigenomics Group

Louise Mewton
Senior Research Fellow, UNSW Scientia Program of Research

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

Suraj Samtani
Postdoctoral Fellow, SHARED Project Co-ordinator

Anbupalam (Anbu) Thalamuthu

Postdoctoral Research Fellow

Stephanie Ward
Senior Research Fellow, Clinical Leader, ADNet Project (ADNet-CQR Initiative)

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

Professional & Technical Staff – Research

Professional & Technical Staff – Research

Karen Allison
Research Officer, CogSCAN Study Co-ordinator (until 31 December 2020)

Valerie Arsenova
Research Officer, ADNet Project (ADNet-MC & ADNet-CQR Initiatives)

Suzanne (Suzi) Artiss
Data Manager

Adam Bentvelzen
Research Assistant, Memory & Ageing Study (MAS) (until 31 December 2020)

Josephine (Josie) Bigland
Research Assistant (Casual), CHeBA longitudinal studies

Russell Chander
Research Assistant (Casual), CHeBA Longitudinal Studies

Tiffany Chau
Research Assistant, Maintain Your Brain Trial

Rhiagh Cleary
Research Assistant, SocCog Study Co-ordinator (until 31 December 2020)

John Crawford
Senior Statistician

Karen Croot
Research Officer, CogSCAN Study

Jing Du
Student Assistant (Casual), Neuroimaging Group

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

Elizabeth Haris
Research Assistant, COSMIC Alcohol Study (until 19 February 2020)

Fleur Harrison
Research Assistant, Sydney Centenarian Study (SCS) (until 31 December 2020)

Mahboobeh (Mabi) Hosseini
Research Assistant (Casual), CHeBA Biobank (until 25 September 2020)

Nicholas (Nick) Hoy
Research Assistant, COSMIC Alcohol Study

Sri Chandana Kanchibotla
Research Assistant, Genetics & Epigenomics Group

Kristan Kang
Research Manager (until 16 January 2020)

Lauren King
Research Assistant, COGNISANCE Project (until 2 September 2020)

Yue Liu
Student Assistant (Casual), Neuroimaging Group (until 5 September 2020)

Inga Mehrani
Project Manager, The Australian Dementia Network (ADNet) Project

Naga Sowjanya Mutyala
Research Officer (Casual), Genetics & Epigenomics Group (until 4 December 2020)

Min Yee Ong
Research Assistant, CogSCAN Study (until 30 November 2020)

Julia Riches
Research Assistant, Sydney Centenarian Study (SCS) (until 15 December 2020)

Matilda Rossie
Research Assistant, CogSCAN Study

Juan Carlo San Jose
Health Informatics Specialist

Amanda Selwood
Research Assistant, Older Australian Twins Study (OATS)

Jessica Turner
Research Officer, CogSCAN Study (until 31 December 2020)

Maria Villalva
Research Assistant, Nanotechnology for the diagnosis and treatment of neurodegenerative disorders project

Rachel Visontay
Research Assistant, COSMIC Alcohol Study

Virginia (Ginny) Winter
Research Assistant, Memory & Ageing Study (MAS) (until 31 December 2020)

Professional & Technical Staff – Support

Kim Babbage
Event & Engagement Officer (until 25 August 2020)

Sophia Dean
Administrative Officer

Heidi Douglass
Marketing, Communications & Project Officer

Celia Falato
Administrative Assistant (until 25 August 2020)

Suzanne (Suzy) Forrester
Administrative Assistant, OATS (until 31 December 2020)

Laurie Mock
Digital Communications Officer

Michelle Savignano
Web Coordinator (until 6 January 2020)

UNSW Adjunct & Conjoint Staff

Gavin Andrews
Emeritus Professor, Chief Investigator, NHMRC Program Grant ID1093083 (until 31 December 2020)

Brian Draper
Professor, Associate Investigator, Sydney Memory & Ageing Study (until 31 December 2020)

Rebecca Koncz
Adjunct Senior Lecturer

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

Yvonne Leung
Adjunct Associate Lecturer

Anne Poljak
Adjunct Senior Lecturer, Protein Chemist, Leader Proteomics Group

Julian Trollor
Professor, Leader Neuroinflammation Group

UNSW Honorary Academics

Catherine Browning
Honorary Associate Lecturer

Kristan Kang
Honorary Senior Lecturer

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

Michael Valenzuela
Honorary Professor

UNSW Visiting Fellows

Helen Lapsley
Visiting Professorial Fellow

Steve Makkar
Visiting Fellow

Jacki Wesson
Visiting Fellow

CHeBA Honorary Research Fellows

Nicola Armstrong

Simone Reppermund

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 in the following journals: *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 the following journals: *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)

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 Vibeke Catts

• Member, Behavior Genetics Association (since 2019) and Australian Society for Medical Research (since 2006)

Professor Lynn Chenoweth

• Adjunct Professor, the University of Notre Dame Australia, 2017-2019, continuing

• Adjunct Professor, School of Nursing, Macau, China

• Editorial board for *Older People Nursing, International Journal of Older People Nursing, Worldviews on Evidence-based Nursing, Annals of Alzheimer's and Parkinson's Disease, Neurodegenerative Disease Management*

• Board Member, Australian Multicultural Aged Nursing Pty Ltd. (AMAN), Lebanese Muslim Association

• Expert group membership:

• Optimising an evidence-based intervention to improve care for Ambulatory Care Sensitive conditions in nursing homes. CIA Downs M (Bradford University, UK)

• Clinical Guidelines for evidence-based deprescribing for acetylcholinesterase inhibitors and memantine in people with dementia. CIA Hilmer S (University of Sydney), CIB Rockwood K (Dalhousie University)

• Mapping the journey in residential aged care for residents with dementia. CIA Scherer S (NARI/Royal Freemasons, Victoria)

• Non-drug care pathway (for behaviours in dementia). CIA Vickers J (Wicking Dementia Research Centre Tasmania), in collaboration with Care Visions China

• Dementia Clinical Quality Indicators Registry Project. CIA McNeill J (School of Public Health and Preventive Medicine, Monash University)

• The Notre Dame University Australia, Sydney. Primary Health Care Curriculum Committee.

Dr Nicole Kochan

• Honorary Associate, Department of Psychology, Macquarie University (2007-present)

• Australian Psychological Society Approved Supervisor (College of Clinical Neuropsychologists)

• Member, APS College of Clinical Neuropsychologists (CCN)

• Member, American Association for the Advancement of Science (AAAS)

• Member, International Society to Advance Alzheimer Research and Treatment (ISTAART)

• Member, Women in Research Network, UNSW

Dr Rebecca Koncz

• Senior Lecturer, Concord Clinical School, Sydney Medical Program, University of Sydney (2018-present)

• Clinical Academic Neuropsychiatrist, Sydney Local Health District (2017-present)

• Adjunct Senior Lecturer, School of Psychiatry, UNSW Sydney (Aug 2020-present)

• Fellow, Royal Australian and New Zealand College of Psychiatrists (RANZCP) (2017-present)

• Member, "Motivation" taskforce, The Human Affectome Project (2017-present)

• Member, Physical Health in Mental Health expert group, NSW Ministry of Health (2019-ongoing)

• Member, COVID-19 Disability Community of Practice, NSW Ministry of Health (2020-present)

Dr Mari Kondo

• Visiting Fellow at the Australian National University (2018-present)

• Member of Australasian Neuroscience Society (2019-present)

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 Matthew Lennon

• Member, Australian and New Zealand Association of Neurologists

• Member, Australian Medical Association

• Conjoint associate lecturer, University of New South Wales

• Editorial Board, Journal of Alzhiemer's Disease

Dr Karen Mather

• Visiting Senior Research Officer, Neuroscience Research Australia (NeuRA)

• Member, Australian Association Gerontology

• Member, ISTAART (Alzheimer's Association of the International Society to Advance Alzheimer Research & Treatment)

Dr Louise Mewton

• University of Sydney Honorary Senior Lecturer (2019-present)

• Member, Research Society on Alcoholism (2019-present)

• Editorial Board *Mental Health and Prevention* (2019-present)

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 Katya Numbers

• Associate Investigator, Ageing Futures Institute (AFI) (2019-present)

• Member, Alzheimer's Association International Society to Advance Alzheimer's Research and Treatment (ISTAART) (2019-present)

Dr Matthew Paradise

• Clinical appointments as a VMO Psychogeriatrician (Campbelltown 1day/week; Tamworth 2days/month; Coffs Harbour 2days/month)

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 the following journals: *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

• Convenor of the XXIV World Congress of Neurology (WCN2019). 27-31 Oct 2019; Dubai, UAE

Professor Julian Trollor

• Chair, Intellectual Disability Mental Health, School of Psychiatry, UNSW Sydney (2009-present)

• Senior Medical Practitioner (Academic): Professor in Neuropsychiatry and Intellectual Disability, South Eastern Sydney Local Health District, Sydney (2009-present)

• Appointed to NSW Institute of Psychiatry Board (2012-present)

• Unconditional Registration, the New South Wales Medical Board, currently Australian Health Practitioner Regulation Agency

• Fellow, the Royal Australian and New Zealand College of Psychiatrists (RANZCP)

• Founder, Neuropsychiatry Section, RANZCP

• Co-Founder & Executive Member, Section of Psychiatry of Intellectual and Developmental Disability, RANZCP

• Executive Committee Member, NSW Health Agency for Clinical Innovation, Intellectual Disability Health Network

• Expert consultant for ASD Health Pathways Development

• Member, Research and Development Committee, NSW Health Agency for Clinical Innovation, Intellectual Disability Health Network

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

• NSW Ombudsman Panel of Expert Advisers

• Visiting Senior Research Fellow, Neuroscience Research Australia

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

• International Member, Neuroleptic Malignant Syndrome Information Service

• Member in the following organisations: Australasian Society for the Study of Intellectual Disability; Faculty of Psychiatry of Old Age & Faculty of Adult Psychiatry, RANZCP; National Association for the Dually Diagnosed; Joint Mental Health and Disability Committee, NSW Health and Ageing Disability and Home Care, NSW Government Family and Community Services; NSW Council for Intellectual Disability; Society for the Study of Behavioural Phenotypes; Australian Medical Association; Australian Salaried Medical Officers Federation; International Association for the Scientific Study of Intellectual Disability; Intellectual Disability Advisory Committee; Health Education and Training Institute Higher Education Governing Council HETI

• Vice President & Member, Australian Association of Developmental Disability Medicine

• Neurocognitive Disorder Working Group, Diagnostic Manual for Intellectual Disability

• Committee Member, RANZCP, New National Guideline for the Assessment and Diagnosis of Autism Spectrum Disorders in Australia

• Past & Current Reviewer for the following journals: *Acta Neuropsychiatrica, Alzheimer Disease & Associated Disorders, Archives of General Psychiatry, Australasian Psychiatry, Australian and New Zealand Journal of Psychiatry, BMC Psychiatry, BMJ Open, Brain, British Journal of Developmental Disabilities, British Journal of Psychiatry, Comprehensive Psychiatry, Current Psychiatry Reviews, European Journal of Neurology, International Journal of Geriatric Psychiatry, International Psychogeriatrics, JARED, Journal of Attention Disorders, Journal of*

Geriatric Psychiatry and Neurology, Journal of Intellectual Disability Research, Neurology, Neuro-Psychopharmacology & Biological Psychiatry, Psychiatry Research – Neuroimaging, The Journal of Psychosomatic Research, The Medical Journal of Australia, Therapeutic Advances in Chronic Disease

- Associate Editor for *Journal Intellectual & Developmental Disability*
- Editorial Board of *Advances in Mental Health and Intellectual Disabilities Journal*
- Reviewer for the following funding bodies: NHMRC, Australia Research Council, Alzheimer's Australia, Alzheimer's USA, Welcome Trust, Neuroscience Research Grants, Pfizer, Rotary Health Foundation, The Dunhill Medical Trust
- Reviewer & Contributor for the following bodies policy documents: NSW Health; NSW Health, The NSW Strategic Framework and Workforce Plan for Mental Health 2018-2022; NSW Agency for Clinical Innovation; Clinical Care of People who might be Suicidal Education and Training Initiative (COPSETI); Podcasts 2017; Health Education and Training Institute (HETI)
- Expert Consultant for Mental Health Regulation 2019
- Expert Consultant on the Royal Commission into Violence, Abuse, Neglect and Exploitation of People with Disability

APPENDIX C: Postgraduate Students

CURRENT

Toyin Abdulsalam
Scientia PhD student
Bioinformatics using multi-omics data integration strategies to predict age-related phenotypes and longevity
School of Psychiatry, Faculty of Medicine, UNSW
Supervisors: Prof Perminder Sachdev, Dr Karen Mather, Dr Anbu Thalamuthu, Dr Anne Poljak, Prof Marc Wilkins (School of Biotechnology and Biomolecular Sciences)

Andrew Affleck
PhD student
Effects of anti-hypertensive medications on Alzheimer and cerebrovascular disease brain pathology
School of Psychiatry, Faculty of Medicine, UNSW
Supervisors: Prof Perminder Sachdev, Prof Glenda Halliday (USyd)

Abdullah Alqarni
PhD student
Sex differences in white matter hyperintensities
School of Psychiatry, Faculty of Medicine, UNSW
Supervisors: A/Prof Wei Wen, Dr Jiyang Jiang, Prof Perminder Sachdev

Russell Chander
Scientia PhD student
Social cognition in the older adult lifespan
School of Psychiatry, Faculty of Medicine, UNSW
Supervisors: Prof Perminder Sachdev, Prof Julie Henry (UQ)

Xi (Sophie) Chen
PhD student
The relationship between dietary patterns and cognitive health among older adults
School of Psychiatry, Faculty of Medicine, UNSW
Supervisors: Prof Henry Brodaty, Dr Fiona O'Leary (USyd)

Lucia (Premilla) Chinnappa-Quinn
PhD student
The association of acute illness hospitalisation with cognitive trajectory in the Sydney Memory and Ageing Study
School of Psychiatry, Faculty of Medicine, UNSW
Supervisors: Prof Perminder Sachdev, Prof Michael Bennett (Prince of Wales Clinical School), Dr Nicole Kochan, Dr John Crawford, Dr Steve Makkar (until Oct 2019), Dr Ben Lam (from Oct 2019)

Chao Dong
Scientia PhD student
Investigation of genetic risk factors related to ageing
Supervisors: A/Prof Wei Wen, Dr Jiyang Jiang, Dr Karen Mather, Dr Anbu Thalamuthu, Prof Perminder Sachdev

Jing Du
PhD Student
Examination of cerebrovascular burden using neuroimaging techniques in ageing brains
School of Psychiatry, Faculty of Medicine, UNSW
Supervisors: Prof Wei Wen, Dr Jiyang Jiang

Heidi Foo
Scientia PhD student
Risk factors and biomarkers of Alzheimer's disease and vascular dementia
School of Psychiatry, Faculty of Medicine, UNSW
Supervisors: Prof Perminder Sachdev, A/Prof Wei Wen

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

Rene Jezewski
PhD student
The neuropathology of ageing
School of Psychiatry, Faculty of Medicine, UNSW
Supervisors: Prof Perminder Sachdev, Dr Claire Shepherd, Dr Karen Mather, Dr Anne Poljak

Fatemeh Khorshidi
PhD student
Pharmacological promotion of NAD+ anabolism to reduce ad pathology and delay cognitive decline
School of Psychiatry, Faculty of Medicine, UNSW
Supervisors: Prof Perminder Sachdev, Dr Anne Poljak

Chulkyu Kim
PhD student
Nutrigenomic activators: A target for neurocognitive disorders and healthy brain ageing
School of Psychiatry, Faculty of Medicine, UNSW
Supervisors: Dr Nady Braidy

Rebecca Koncz
PhD student
The relative genetic and environmental contributions to amyloid deposition in the brains of older adults: amyloid

imaging using the twin design
School of Psychiatry, Faculty of Medicine, UNSW
Supervisors: Prof Perminder Sachdev, Prof Christopher Rowe (Austin Health, Melbourne), A/Prof Wei Wen, Dr Anbu Thalamuthu

Jessica Lazarus
PhD student
Epigenetics and longevity
Department of Anatomy, School of Medical Sciences, Faculty of Medicine, UNSW
Supervisors: Dr Karen Mather

Matthew Lennon
PhD student
Risk and preventive factors in Dementia – An international harmonization of longitudinal studies
School of Psychiatry and St Vincents Clinical School, Faculty of Medicine, UNSW
Supervisors: Prof Perminder Sachdev, Dr Anbu Thalamuthu, Dr John Crawford, Dr Ben Lam

Annabel Matison
PhD student
Examining the relationship between diet, depression and nutrigenomics
School of Psychiatry and St Vincents Clinical School, Faculty of Medicine, UNSW
Supervisors: Dr Karen Mather, Dr Simon Reppermund, Prof Vicki Flood (USYD)

Janet Mitchell
PhD student
Meaningful relationships with care – The Social Orientation of Care in Aged Living (SOCIAL)
School of Psychiatry, Faculty of Medicine, UNSW
Supervisors: Prof Henry Brodaty, Prof Jeffrey Braithwaite (Macquarie University), Professor Lynn Chenoweth

Adith Mohan
PhD student
Influence of ageing on the human brain transcriptome
School of Psychiatry, Faculty of Medicine, UNSW
Supervisors: Dr Karen Mather, Prof Perminder Sachdev, Dr Anbu Thalamuthu

Zara Page
PhD Student
Towards achieving culture-fair neuropsychological assessment for Mild Cognitive Impairment and dementia in culturally and linguistic diverse (CALD) School of Psychiatry, Faculty of Medicine, UNSW
Supervisors: Dr Nicky Kochan, Prof Henry Brodaty

Matthew Paradise
PhD student
Neuroimaging of cerebrovascular disease
School of Psychiatry, Faculty of Medicine, UNSW
Supervisors: Prof Perminder Sachdev, A/Prof Wei Wen

Mary Revelas
PhD student
The genetics of exceptional longevity and successful ageing
School of Psychiatry, Faculty of Medicine, UNSW
Supervisors: Dr Karen Mather, Prof Perminder Sachdev, Dr Anbu Thalamuthu

Annette Spooner
PhD student
Early detection of Alzheimer's disease using machine learning
School of Computer Science and Engineering, Faculty of Engineering, UNSW
Supervisors: Prof Arcot Sowmya, Prof Perminder Sachdev, A/Prof Gelareh Mohammadi

Marina Ulanova
PhD student
Superparamagnetic iron oxide nanoparticles as contrast agents for mr imaging of amyloid beta plaques in Alzheimer's disease
School of Medical Sciences, Faculty of Medicine, UNSW
Supervisors: Dr Nady Braidy

Gurjeet Kaur Virk
Scientia PhD student
Development of blood biomarkers for early onset Alzheimer's disease using discovery proteomics
School of Psychiatry, Faculty of Medicine, UNSW
Supervisors: Dr Anne Poljak, Prof Perminder Sachdev

Heidi Welberry
PhD student
Using big data to understand health related trajectories for older Australians at risk of dementia
School of Psychiatry, Faculty of Medicine, UNSW
Supervisors: Prof Henry Brodaty

Jacqueline Wesson
PhD student
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
Faculty of Health Sciences, University of Sydney
Supervisors: Prof Lindy Clemson, Prof Henry Brodaty, Dr Simone Reppermund

Mark Yates
PhD student
The impact of the Dementia Care in Hospitals Program in improving the quality of life and adverse events in acute hospital patients with cognitive impairment: a stepped wedge cluster randomized trial
School of Psychiatry, Faculty of Medicine, UNSW
Supervisors: Prof Henry Brodaty

COMPLETED

Yue Liu, PhD
Contribution of cerebrovascular and Alzheimer-type pathology in the aetiology of neurocognitive disorders
School of Psychiatry, Faculty of Medicine, UNSW
Supervisors: Dr Nady Braidy, Prof Perminder Sachdev, Dr Anne Poljak, A/Prof Wei Wen
PhD conferred: 2020

Anne Wand, PhD
Understanding self-harm in the very old: A qualitative study with implications for clinical care and wider society
School of Psychiatry, Faculty of Medicine, UNSW
Supervisors: Prof Carmelle Peisah, Prof Brian Draper and Prof Henry Brodaty
PhD conferred: May 2020

Appendix D: Awards & Promotions

Dr Jiyang Jiang
Recipient of the 2020 CHeBA Publication Award (Early Career Category) for the paper "Stronger bilateral functional connectivity of the frontoparietal control network in near-centenarians and centenarians without dementia" published in *NeuroImage*

Dr Rebecca Koncz
Adjunct Senior Lecturer, School of Psychiatry, UNSW Sydney (Aug 2020)

Jess Lo
Recipient of the 2020 CHeBA Publication Award (Professional Staff Category) for the paper "Association of Pre-Diabetes and Type 2 Diabetes With Cognitive Function After Stroke: A STROKOG Collaboration Study" published in *Stroke*

Dr Karen Mather
Recipient of the 2020 CHeBA Publication Award (Mid Career Category) for the paper "Common Genetic Variation Indicates Separate Causes for Periventricular and Deep White Matter Hyperintensities" published in *Stroke*

Mary Revelas
Recipient of the 2020 CHeBA Publication Award (Student Category) for the paper "Exceptional Longevity and Polygenic Risk for Cardiovascular Health" published in *Genes*

Dr Anbu Thalamuthu
Senior Research Fellow, School of Psychiatry, UNSW (July 2020)

Appendix E: Research Grants & Funding

Grants

Healthier drinking choices and cognitive decline in older risky drinkers

Funding Source:	NHMRC / DCRC
Project ID:	RG180842-D
Investigator/s:	Dr Louise Mewton
Duration:	4 years: 2020-2023
Total Funds:	$598,209

Towards achieving culture-fair neuropsychological assessment for mild cognitive impairment and dementia in culturally and linguistic diverse (CALD) older Australians

Funding Source:	NHMRC / DCRC
Project ID:	RG180842-C
Investigator/s:	Dr Nicole Kochan, Ms Zara Page (PhD Candidate)
Duration:	4 years: 2020-2023
Total Funds:	$90,000

Unravelling human brain ageing – a multi-omics approach

Funding Source:	Rebecca L Cooper Medical Research Foundation
Project ID:	Dr Karen Mather
Investigator/s:	Dr Nicole Kochan, Ms Zara Page (PhD Candidate)
Duration:	2 years: 2020-2021*
Total Funds:	$100,000

*Extended to 31 March 2023

Improving psychological wellbeing for older adults during and after the COVID-19 outbreak

Funding Source:	UNSW/PLuS Alliance Collaborative Research Seed Grant
Project ID:	RG202503
Investigator/s:	Prof Henry Brodaty, Dr Katya Numbers
Duration:	1 year: June 2020-June 2021
Total Funds:	$19,500

Clarifying the relationship between alcohol use and dementia

Funding Source:	NHMRC/DCRC & Dementia Australia Research Foundation (DARF)
Project ID:	RG180842-A / RG200724-A
Investigator/s:	Dr Louise Mewton
Duration:	1 year: 2020
Total Funds:	$75,000

The APPLE Tree programme: Active Prevention in People at risk of dementia through Lifestyle bEhaviour change and Technology to build REsiliEnce

Funding Source:	Economic & Social Research Council (ESRC)-NIHR Dementia Research Initiative Shared Grant (University College London/ CHeBA)
Project ID:	RG191662
Investigator/s:	Prof Claudia Cooper, Prof Helen Kales, Prof Henry Brodaty**, Dr Penny Rapaport, Dr Miguel Rio, Prof Anne Matie Minihane, Prof Irene Petersen, Dr Julie Barber, Dr Iain Lang, Ms Rachael Hunter, Dr Zuzana Walker, Dr Nicholas Bass, Dr Natalie Marchant, Dr Jonathan Huntley, Dr Jennifer Wenborn, Dr Joanne Rodda, Prof Paul Higgs, Dr Kate Walers, Dr Sarah Morgan-Trimmer, Dr Elisa Aguirre, Prof Karen Ritchie, Ms Alexandra Burton
Duration:	5 years: 2019-2023
Total Funds:	£3,884,409 (**AUD12,603)

UNSW Scientia Fellowship Research Support Program

Funding Source: UNSW Sydney
Project ID: PS416170-A
Investigator/s: Dr Louise Mewton
Duration: 4 years: January 2019-January 2023
Total Funds: $160,000

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: 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

*Extended to 31 July 2022

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

*Extended to 31 August 2022

Online alcohol prevention for older adults: adapting an effective and scalable solution

Funding Source: UNSW-USYD Mental Health & Wellbeing Grants
Project ID: RG192547
Investigator/s: Dr Louise Mewton
Duration: 1 year: 1 July 2019-30 June 2020
Total Funds: $20,000

Lipids in brain ageing and cognitive disorders

Funding Source: Rebecca L Cooper Foundation
Project ID: RG182333
Investigator/s: Dr Anne Poljak, Prof Perminder Sachdev
Duration: 2 years: 2019-2020
Total Funds: $100,000

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: 2019*
Total Funds: $10,000

*Extended to 31 December 2021

Towards a better understanding of the mechanisms of ageing and longevity in C.elegans and humans

Funding Source: UNSW/Chinese Academy of Sciences (CAS) Collaborative Research Seed Program – Mobility Grant
Project ID: RG192635
Investigator/s: Dr Karen Mather, Dr Shi-Qing Cai
Duration: 1 year: 2019*
Total Funds: $5,000

*Extended to 30 October 2021

High value data collections publishing scheme

Funding Source: UNSW Sydney / High Value Data Collections Publishing Scheme
Project ID: RG192941-A
Investigator/s: Dr Kristan Kang, A/Prof Wei Wen
Duration: 1 year: 2019*
Total Funds: $14,000

*Extended to 30 December 2020

Ageing – development and validation of emerging magnetic resonance imaging (MRI) methods for measuring cerebrovascular disease (CVD) burden in the ageing brain

Funding Source: UNSW Sydney/UNSW-Tsinghua University Collaborative Research Fund – Seed Grants
Project ID: RG193804
Investigator/s: A/Prof Wei Wen, A/Prof Hua Guo, Prof Perminder Sachdev, Dr Jiyang Jiang, Dr Xihai Zhao, Dr Huijun Chen
Duration: 1 year: 2019*
Total Funds: $15,000

*Extended to 30 November 2021

The Australian Dementia Network (ADNet): Bringing together Australia's dementia stakeholders

Funding Source: NHMRC

Project ID: RG181548 / RG191015

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 (**$732,439 / $183,109 – total $915,548)

Clarify risk and protective factors for dementia with the Interplay of Genes and Environment in Multiple Studies (IGEMS) Consortium

Funding Source: National Institutes of Health (NIH)

Project ID: RG182556

Investigator/s: Prof Nancy Pedersen, Dr Margaret Gatz, Dr Vibeke Catts, Prof Perminder Sachdev

Duration: 5 years: July 2018-June 2021

Total Funds: USD40,534.34

BRAIN-MEND: biological resource analysis to identify new mechanism and phenotypes in neurodegenerative diseases

Funding Source: 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: 2018-2020

Total Funds: $849,967 (**$42,154)

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: 3 years: 2018-2020

Total Funds: $12,818,309 (**$4,272,769)

The long-term effectiveness of a combined prevention model for anxiety, depression, and substance use in adolescents

Funding Source: Australian Rotary Health

Project ID: RG180380

Investigator/s: Dr Louise Mewton, A/Prof Tim Slade, Prof Maree Teesson, A/Prof Nicola Newton, Dr Cath Chapman, Dr Louise Birrell

Duration: 3 years: 2018-2020

Total Funds: $209,829*

*Project closed January 2020

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: April 2018-April 2019

Total Funds: $20,000

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 2022

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

*Extended to 31 October 2021

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: 3 years: July 2017-June 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: 2017-2019

Total Funds: $50,000

Risk factors, early diagnosis and effective interventions for neurocognitive disorders

Funding Source: 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

Understanding the molecular control of human neurogenesis in health and in schizophrenia

Funding Source: UNSW Sydney Vice-Chancellor's Postdoctoral Fellowship – Research Support

Project ID: RG152485

Investigator/s: Dr Mari Kondo

Duration: 3 years: 2016-2018*

Total Funds: $30,000

*Extended to 22 October 2021

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

Investigator/s: 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

*Extend to 31 December 2020

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

Investigator/s: 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 2020

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*

*Extended to 31 December 2023

Evaluating the effectiveness and cost effectiveness of Dementia Care Mapping (DCM) to enable person-centred care for people with dementia and their carers: a UK cluster randomised controlled trial in care homes (DCM EPIC trial)

Funding Source: Leeds Beckett University

Project ID: RG172452

Investigator/s: Prof Lynn Chenoweth

Duration: 2 years: 2016-2018*

Total Funds: $9,716

*Extended to 30 June 2021

Philanthropic

Retinal Biomarkers in Dementia

Funding Source: Sachdev Foundation

Project ID: PS61657_PS61604

Awardee/s: Prof Perminder Sachdev

Total Funds: $52,534

The Diet Gut Microbiome and Exceptional Ageing

Funding Source: The Mostyn Family Foundation

Project ID: PS58977_PS58998

Awardee/s: Prof Perminder Sachdev Dr Yvonne Leung/ Dr Karen Mather

Total Funds: $17,000

The Blood Brain Barrier and Integrity in the Ageing Brain

Funding Source: The Mostyn Family Foundation

Project ID: PS58698_PS58830

Awardee/s: Prof Perminder Sachdev, A/Prof Wei Wen, Dr Jiyang Jiang, Dr Vibeke Catts

Total Funds: $30,000

Mapping Neuropathology in Centenarians with Dementia

Funding Source: Sachdev Foundation

Project ID: PS55062_PS55172

Awardee/s: Prof Perminder Sachdev

Total Funds: $45,000

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
Total Funds: $25,000

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 CHeBA Cerebral Small Vessel Disease (SVD) Fund

Funding Source: John Holden Family Foundation
Project ID: PS41604_PS41625
Awardee/s: 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
Awardee/s: Prof Perminder Sachdev, Prof Henry Brodaty
Duration: 5 years: 2016-2020
Total Funds: $90,000

Funding Source: Sachdev Foundation
Project ID: PS38235_PS38252
Awardee/s: Prof Perminder Sachdev, Prof Henry Brodaty
Duration: 3 years: 2016/17-2018/19
Total Funds: $124,000

Funding Source: Vincent Fairfax Family Foundation
Project ID: PS42069_PS42074
Awardee/s: Prof Perminder Sachdev, Prof Henry Brodaty
Duration: 5 years: July 2015- June 2019*
Total Funds: $500,000

*Acquittal March 2021

The Thomas Foundation Grant

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 (*$36,144)

*As at 31 December 2020

Other

The Healthy Brain Ageing Fund

Funding Source: Miscellaneous Donor Contributions
Project ID: PS22384_PS41631
Awardee/s: Prof Henry Brodaty, Prof Perminder Sachdev
Duration: Ongoing
Total Funds: $379,108*

*As at 31 December 2020

Centre for Healthy Brain Ageing Event & Sponsorship Fund

Funding Source: Miscellaneous
Project ID: PS33379_PS33397
Awardee/s: Prof Henry Brodaty, Prof Perminder Sachdev
Duration: Ongoing
Total Funds: $2,314*

*As at 31 December 2020

The Kwan & Yuet Ying Fung Health Brain Ageing Research Award

Funding Source: Kwan & Yuet Ying Fung Estate
Project ID: PS36983_PS37138
Awardee/s: Prof Henry Brodaty, Prof Perminder Sachdev
Duration: Ongoing
Total Funds: $107,286*

*As at 31 December 2020

The Josh Woolfson Memorial Scholarship Fund

Funding Source: Woolfson Family
Project ID: PS42978_PS42948
Awardee/s: Prof Henry Brodaty, Prof Perminder Sachdev
Duration: Ongoing
Total Funds: $118,821*

*As at 31 December 2020

Appendix F: Statement of Financial Performance

Statement of Financial Performance for the year ended 31 December 2019

	Notes	2020	2019
Funds			
Research Revenue		4,588,028	4,713,144
Donations		549,129	684,568
Fees		-	-
Faculty Funds	3	-	-
UNSW Contribution - Competitive	1	92,336	388,199
UNSW Contribution - Strategic	2	-	-
Sundry Other Revenue		(4,703)	13,012
Total Funds		5,224,790	5,798,923
Costs			
People Costs		4,985,618	4,375,008
Scholarship Stipends		58,886	56,717
Contract & Consulting Services		129,982	159,927
Repairs and Maintenance		423	-
Consumables		94,053	130,607
Travel		8,839	87,583
Equipment		75,940	165,446
Entertainment		-	3,571
Marketing		9,784	3,644
Overheads		2,403	1,805
Other Expenses		374,311	361,924
Interest Expense		-	-
Other Expenses		386,498	370,944
Internal Expense		178,179	208,211
Total Costs		5,918,418	5,554,442
Operating result		(693,628)	244,481
Opening Balance		3,262,934	3,018,453
Closing Balance		2,569,306	3,262,934

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 G: Publications

BOOK CHAPTERS

1. Chenoweth L, Williams A. Situating Nursing, Contexts of Care: Working in the aged care sector. Adapting Nursing: Contexts of Care (Part 5, Chapter 37). In: Crisp J, Douglas C, Rebeiro G, Waters D (Eds) *Potter & Perry's Fundamentals of Nursing, 6th edition*. 2020 Nov; 1379-1412. ISBN: 9780729544139.

2. Chenoweth L, Lapkin, S. Considering the older person. Adapting nursing: Life stages and transitions (Part 5, Chapter 32). In: Crisp J, Douglas C, Rebeiro G, Waters D (Eds) *Potter & Perry's Fundamentals of Nursing, 6th edition*. 2020 Nov; 1252-1290. ISBN: 9780729544139.

3. Finucane G, Mohan A, Sachdev PS. Neuropsychiatric services in Australia and New Zealand (Chapter 45). In: Agrawal N, Faruqui R, Bodani M (Eds) *Oxford Textbook of Neuropsychiatry:* Oxford University Press: Oxford, UK. 2020 Aug. DOI: 10.1093/med/9780198757139.003.0045. ISBN: 9780198757139. eISBN: 9780191817038.

4. Jayasena T, Bustamante S, Clement J, Welschinger R, Caplan GA, Sachdev PS, Braidy N. Clinical assessment of the nadome as biomarkers for healthy aging (Chapter 13). In: Guest PC (Ed) *Clinical and Preclinical Models for Maximizing Healthspan: Methods in Molecular Biology*. Springer: New York, NY, USA. 2020 Mar 29; 2138: 207-216. DOI: 10.1007/978-1-0716-0471-7_13. PMID: 32219750. ISBN: 978-1-0716-0470-0 / 978-1-0716-0471-7.

5. Ozdemir B, Selamoglu Z, Braidy N. Absolute Quantification of Plasma Apolipoproteins for Cardiovascular Disease Risk Prediction (Chapter 27). In: Guest PC (Ed) *Clinical and Preclinical Models for Maximizing Healthspan: Methods in Molecular Biology*. Springer: New York, NY, USA. 2020; 2138: 373-9. DOI: 10.1007/978-1-0716-0471-7_27. PMID: 32219764. ISBN: 1064-3745.

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7. Poljak A, Nady B, Wong MWK, Liu Y, Housseini M, Sachdev PS. Lipids, brain ageing, dementia, and lipidomics (Chapter 12). In: Martin CR, Preedy VR (Eds) *Diagnosis and Management in Dementia. The Neuroscience of Dementia Vol 1*. Academic Press; 2020; 183-205. DOI: 10.1016/B978-0-12-815854-8.00012-4. ISBN: 978-0-12-815854-8.

8. Sachdev P, Mohan A. Neuropsychiatry and key clinical competencies (Chapter 13). In: Agrawal N, Faruqui RA, Bodani M (Eds) *Oxford Textbook of Neuropsychiatry*. Oxford University Press: Oxford, UK. 2020 Aug. DOI: 10.1093/med/9780198757139.003.0013 ISBN: 9780198757139. eISBN: 9780191817038.

JOURNAL ARTICLES

1. Affleck AJ, Sachdev PS, Stevens J, Halliday GM. Antihypertensive medications ameliorate Alzheimer's disease pathology by slowing its propagation. *Alzheimers Dement (NY)*. 2020; 6(1):e12060. DOI: 10.1002/trc2.12060. PMID: 32802934. [Epub 2020 Aug 12].

2. Alqarni A, Jiang J, Crawford JD, Koch F, Brodaty H, Sachdev P, Wen W. Sex differences in risk factors for white matter hyperintensities in non-demented older individuals. *Neurobiol Aging*. 2020 Nov 10; 98:197-204. DOI: 10.1016/j.neurobiolaging.2020.11.001. PMID: 33307330 [Epub 2020 Dec 12].

3. Anstey KJ, Peters R, Zheng L, Barnes DE, Brayne C, Brodaty H, Chalmers J, Clare L, Dixon RA, Dodge H, Lautenschlager NT, Middleton L, Qiu C, Rees G, Shahar S, Yaffe K. Future Directions for Dementia Risk Reduction and Prevention Research: An International Research Network on Dementia Prevention Consensus. *J Alzheimers Dis*. 2020 Sep 8. DOI: 10.3233/jad-200674. PMID: 32925063. [Epub 2020 Sep 15].

4. Armstrong NJ, Mather KA, Sargurupremraj M, Knol MJ, Malik R, Satizabal CL, ..., Wen W, ..., Brodaty H, ..., Jiang J, ..., Thalamuthu A, Trollor J, ..., Sachdev PS et al. Common genetic variation indicates separate causes for periventricular and deep white matter hyperintensities. *Stroke*. 2020 July; 51(7): 2111-2121. DOI: 10.1161/strokeaha.119.027544. PMID: 32517579 [Epub 2020 Jun 10].

5. Ayton D, Gardam M, Ward S, Brodaty H, Pritchard E, Earnest A, Krysinska K, Banaszak-Holl J, McNeil J, Ahern S. How can quality of dementia care be measured? The development of clinical quality indicators for an Australian Pilot Dementia Registry. *J Alzheimers Dis*. 2020; 75(3):923-36. DOI: 10.3233/jad-191044. PMID: 32390616 [Epub 2020 May 12].

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7. Bae JB, Lipnicki DM, Han JW, Sachdev PS, 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, Skoog I, Najar J, Sterner TR, Scarmeas N, Yannakoulia M, Dardiotis E, Riedel-Heller S, Roehr S, Pabst A, Ding D, Zhao Q, Liang X, Lobo A, De-la-Cámara C, Lobo E, Kim KW. Parity and the risk of incident dementia: a COSMIC study. *Epidemiol Psychiatr Sci*. 2020; Oct 20; 29:e176. DOI: 10.1017/s2045796020000876. PMID: 33077022. [Epub 2020 Oct 21].

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11. De Erausquin GA, Brusco I, Zamponi H, Sachdev P, Arroyo GR, Sanos JM, et al. Alzheimer's Association International Cohort Study of Chronic Neuropsychiatric Sequeale of SARS-Cov-2 (CNS-SARS-CoV-2) [Poster]. *Alzheimer's Association International Conference (AAIC 2020)*. 2020 July 29; online. *Alzheimers Dement*. 2020 Dec; 16(Suppl. 6):e047721. DOI: 10.1002/alz.047721.

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13. Khorshidi F, Poljak A, Jayasena T, Sachdev PS. Hormetic effects of alcohol in an astroglial cellular model and its proteomics signature [Poster]. *Alzheimer's Association International Conference (AAIC 2020)*. 2020 July 27; online. *Alzheimers Dement*. 2020 Dec; 16(Suppl. 3):e041665. DOI: 10.1002/alz.041665.

14. Lam BCP, Crawford JD, Lipnicki DM, Number KT, Kochan NA, Draper B, Trollor JN, Brodaty H, Sachdev PS. The latent construct of dementia phenotype: Validation and longitudinal examination in the Sydney Memory and Ageing Study [Poster]. *Alzheimer's Association International Conference (AAIC 2020)*. 2020 July 30; online.

15. Lennon MJ, Lam BCP, Crawford JD, Brodaty H, Kochan NA, Trollor JN, Numbers KT, Draper B, Thalamuthu A, Sachdev PS. Does antihypertensive use moderate the effect of blood pressure on cognitive decline in the elderly? [Abstract SO4-03-06]. *Alzheimer's Association International Conference (AAIC 2020)*. 2020 July 30; online.

16. Mansour H, Whitty E, Aguirre E, Palomo M, Charlesworth G, Ramjee S, Poppe M, Brodaty H, Kales HC, Morgan-Trimmer S, Nyman S, Lang IA, Walters K, Petersen I, Wenborn J, Minihane A-M, Ritchie K, Huntley JD, Walker Z, Cooper C. Effectiveness of lifestyle and psychosocial interventions in reducing cognitive decline in older people: systematic review [Abstract SO4-01-01]. *Alzheimer's Association International Conference (AAIC 2020)*. 2020 July 30; online. *Alzheimers Dement*. 2020 Dec; 16(Suppl. 7):e042843. DOI: 10.1002/alz.042843.

17. Mohan A, Thalamuthu A, Mather KA, Sachdev PS. Towards a better understanding of human brain ageing – An RNA sequencing study of neuroinflammatory, neurotransmission-related and synaptic genes in 2 key brain regions over the lifespan [Poster]. *Alzheimer's Association International Conference (AAIC 2020)*. 2020 July 27; online. *Alzheimers Dement*. 2020 Dec; 16(Suppl. 2):e045746. DOI: 10.1002/alz.045746.

18. Nguyen TA, Dang TH, Tran K, Kim GB, Brodaty H, Pham T, Le Pham T, Crotty M, Kurrle S, Hinton L, Esterman A, Nguyen TA, Roughead EE. Dementia in Vietnam: a situational analysis [Poster]. *Alzheimer's Association International Conference (AAIC 2020)*. 2020 July 30; online. *Alzheimers Dement*. 2020 Dec; 16(Suppl. 10): e039252. DOI: 10.1002/alz.039252.

19. Numbers KT, Lam BCP, Crawford JD, Kochan NA, Sachdev PS, Brodaty H. Patterns of Change in Subjective Cognitive Complaints are Associated with Cognitive Decline and Dementia Risk: Findings from the Sydney Memory and Ageing Study [Abstract ODO3-10-01]. *Alzheimer's Association International Conference (AAIC 2020)*. 2020 July 29; online.

20. Numbers KT, Lam BCP, Crawford JD, Kochan NA, Sachdev PS, Brodaty H. Patterns of change in subjective cognitive complaints are associated with cognitive decline and dementia risk: findings from the Sydney Memory and Ageing Study [Abstract SCR3-05-01]. *Alzheimer's Association International Conference (AAIC 2020)*. 2020 July 29; online.

21. Poole M, Wilcock J, Rait G, Brodaty H, Robinson L. Policy, Practice and Public Awareness: A review of national and international approaches to improve diagnosis and post-diagnostic support for people living with dementia [Abstract ODO4-07-01]. *Alzheimer's Association International Conference (AAIC 2020)*. 2020 July 30; online. *Alzheimers Dement*. 2020 Dec; 16(Suppl. 7): e040918. DOI: 10.1002/alz.040918.

22. Poole M, Wilcock, Rait G, Brodaty H, Robinson L. Policy, Practice and Public Awareness: A review of national and international approaches to improve diagnosis and post-diagnostic support for people living with dementia [Abstract SCR4-14-01]. *Alzheimer's Association International Conference (AAIC 2020)*. 2020 July 31; online. *Alzheimers Dement*. 2020 Dec; 16(Suppl. 7): e040918. DOI: 10.1002/alz.040918.

23. Rossie M, Croot K, Allison KC, Brodaty H, Crawford JD, Lee T, Henry JD, Draper B, Close J, Ong MY, Lam BCP, Sachdev PS, Kochan NA. Predictors of acceptability and emotional response to computerized neuropsychological assessments in older adults: The CogSCAN study [Poster]. *Alzheimer's Association International Conference (AAIC 2020)*. 2020 July 29; online. *Alzheimers Dement*. 2020 Dec; 16(Suppl. 6): e044730. DOI: 10.1002/alz.044730.

24. Samaras K, Makkar S, Crawford JD, Kochan NA, Wen W, Brian D, Trollor JN, Brodaty H, Sachdev PS. Metformin-use is associated with slowed cognitive decline and reduced incident dementia in older adults with type 2 diabetes mellitus: The Sydney Memory and Ageing Study [Abstract SAT-LB115]. *Annual Meeting of the Endocrine Society*. 28-31 March 2020; San Francisco, CA, USA. *J Endocrine Soc*. 2020 April-May; 4 (Suppl.1):A1035. DOI: 10.1210/jendso/bvaa046.2055.

25. Sisakhti M, Sachdev P, Batouli SAH. The effect of cognitive load on the retrieval of long term memory: an fMRI study. *26th Annual Meeting of the Organization on Human Brain Mapping (OHBM2020)*. 23 June – 3 July 2020; virtual meeting.

26. Ulanova M, Gloag L, Bongers A, Gooding J, Biazil J, Tilley R, Sachdev PS, Braidy N. Magnetic nanoparticles as MRI contrast agents for the diagnosis of Alzheimer's Disease [Poster]. *Alzheimer's Association International Conference (AAIC 2020)*. 2020 July 28; online. *Alzheimers Dement*. 2020 Dec; 16(Suppl. 5):e041609. DOI: 10.1002/alz.041609.

Appenidx H: Conference Presentations

Virtual Conferences

1. Brodaty H. Socialization as an approach to reduce risks of cognitive decline. *Alzheimer's Association International Conference (AAIC 2020)*. 2020 July 19; online.

2. Brodaty H, Heffernan M, Andrews G, Anstey KJ, Fiatorone Singh MA, Jorm L, Lautenschlager NT, Maeder A, McNeil J, Sachdev PS, Valenzuela M. Internet based multicomponent interventions to prevent cognitive decline: The Maintain Your Brain Trial [Poster]. *Alzheimer's Association International Conference (AAIC 2020)*. 2020 July 30; online. *Alzheimers Dement*. 2020 Dec; 16(Suppl. 10): e044180. DOI: 10.1002/alz.044180.

3. Brodaty H. Invited Plenary Speaker. Debate: That nursing homes should be abolished. *International Psychogeriatrics Association Conference*. 2020 Sep 1; online.

4. Brodaty H. Invited Plenary Speaker. Cognisance – Post diagnostic care. *Alzheimer's Association International Conference (AAIC 2020)*. 19 Oct 2002.

5. Brodaty H. Invited Plenary/Keynote Speaker. The importance of socialisation for people to prevent dementia, for people who have dementia and in the time of corona. *National Dementia Conference*. 16 Oct 2020; Melbourne, Australia and online.

6. Brodaty H. Invited Plenary Speaker. Carers and dementia. Where to next? *Alzheimer Disease International Conference*. 4 Dec 2020; Singapore and online.

7. Brodaty H. Maintain your brain. *International Psychogeriatric Association Conference*. 4 Dec 2020; Lisbon and online.

8. Burley CV, Livingston G, Knapp MR, Wimo A, Norma R, Brodaty H. Time to invest in nonpharmacological interventions for behaviours and psychological symptoms associated with dementia [Poster]. *Alzheimer's Association International Conference (AAIC 2020)*. 2020 July 30; online. *Alzheimers Dement*. 2020 Dec; 16(Suppl. 10):e042281. DOI: 10.1002/alz.042281.

9. Casey A-N, Liu Z, Kochan NA, Sachdev P, Brodaty H. Social network size, cognition, and incident dementia in the Sydney Memory and Ageing Study. *Alzheimer's Disease International (ADI) 34th Conference*. 10-12 Dec 2020; Singapore and online.

10. Casey A-N, Kochan NA, Liu Z, Crawford JD, Sachdev P, Brodaty H. Social relationship quality is associated with cognition in the Sydney Memory and Ageing Study [Poster Abstract]. *Australian Dementia Forum (ADF2020-21)*. 31 May 2020; Adelaide, SA.

11. Chander RJ, Numbers KT, Grainger SA, Cleary R, Das D, Mather KA, Kochan NA, Brodaty H, Henry JD, Sachdev PS. Social cognitive abilities in older adults with mild cognitive impairment and dementia [Abstract ODO3-07-04]. *Alzheimer's Association International Conference (AAIC 2020)*. 2020 July 29; online. *Alzheimers Dement*. 2020 Dec; 16(Suppl. 6): e044231. DOI: 10.1002/alz.044231.

12. Chander RJ, Numbers KT, Grainger SA, Cleary R, Das D, Mather KA, Kochan NA, Brodaty H, Henry JD, Sachdev PS. Social cognitive abilities in older adults with mild cognitive impairment and dementia [Abstract SCR3-02-04]. *Alzheimer's Association International Conference (AAIC 2020)*. 2020 July 29; online.

13. Casey A-NS, Kochan NA, Crawford JD, Sachdev PS, Brodaty H. Quality of connections counts: social relationships and global cognition in the Sydney Memory and Ageing Study [Poster]. *Alzheimer's Association International Conference (AAIC 2020)*. 2020 July 30; online. *Alzheimers Dement*. 2020 Dec; 16(Suppl. 7): e044192. DOI: 10.1002/alz.044192.

14. XS Chen, O'Leary F, Liu Z, Brodaty H. Dietary Patterns and Cognitive decline among Older Adults: Findings from Sydney Memory and Aging Study [Abstract ODO4-14-01]. Alzheimer's *Association International Conference (AAIC 2020)*. 2020 July 30; online. *Alzheimers Dement*. 2020 Dec; 16(Suppl. 10): e042450. DOI: 10.1002/alz.042450.

15. Cheng A, Leung Y, Crawford J, Harrison F, Sachdev P, Brodaty H. A psychological profile of near-centenarians and centenarians with and without dementia from the Sydney Centenarian Study [Abstract 339]. *2020 Virtual IPA International Congress*. 2-3 Oct 2020; virtual meeting. *Int Psychogeriatr*. 2020 Oct; 32(S1):99. DOI: 10.1017/S1041610220002392.

16. Croot K, Allison KC, Sachdev PS, Brodaty H, Crawford JD, Lam BCP, Lee T, Henry JD, Draper B, Close J, Ong MY, Rossie M, Kochan NA. Development of The Computer and Technology Attitude Questionnaire (CaTAQ) to inform performance on computerised cognitive testing in older adults in the CogSCAN Study [Poster]. *Alzheimer's Association International Conference (AAIC 2020)*. 2020 July 29; online. *Alzheimers Dement*. 2020 Dec; 16(Suppl. 6): e045676. DOI: 10.1002/alz.045676.

17. De Erausquin GA, Brusco I, Zamponi H, Sachdev P, Arroyo GR, Sanos JM, et al. Alzheimer's Association International Cohort Study of Chronic Neuropsychiatric Sequeale of SARS-Cov-2 (CNS-SARS-CoV-2) [Poster]. *Alzheimer's Association International Conference (AAIC 2020)*. 2020 July 29; online. *Alzheimers Dement*. 2020 Dec; 16(Suppl. 6): e047721. DOI: 10.1002/alz.047721.

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22. Lo J. STROKOG overview and update. *STROKOG Collaborators' Forum*. 17 Sep2020; online.

23. Lo J. Cognitive decline after stroke across diverse ethno-regional groups. *STROKOG Collaborators' Forum*. 17 Sep 2020; online.

24. Mansour H, Whitty E, Aguirre E, Palomo M, Charlesworth G, Ramjee S, Poppe M, Brodaty H, Kales HC, Morgan-Trimmer S, Nyman S, Lang IA, Walters K, Petersen I, Wenborn J, Minihane A-M, Ritchie K, Huntley JD, Walker Z, Cooper C. Effectiveness of lifestyle and psychosocial interventions in reducing cognitive decline in older people: systematic review [Abstract SO4-01-01]. *Alzheimer's Association International Conference (AAIC 2020)*. 2020 July 30; online. *Alzheimers Dement*. 2020 Dec; 16(Suppl. 7):e042843. DOI: 10.1002/alz.042843.

25. Mitchell J, Brodaty H, Chenoweth, L. Person-centred care: how is it practiced today? *34th International Conference of Alzheimer's Disease International*. 10-12 Dec 2020; Singapore and online.

26. Mohan A, Thalamuthu A, Mather KA, Sachdev PS. Towards a better understanding of human brain ageing – An RNA sequencing study of neuroinflammatory, neurotransmission-related and synaptic genes in 2 key brain regions over the lifespan [Poster]. *Alzheimer's Association International Conference (AAIC 2020)*. 2020 July 27; online. *Alzheimers Dement*. 2020 Dec; 16(Suppl. 2): e045746. DOI: 10.1002/alz.045746.

27. Nguyen TA, Dang TH, Tran K, Kim GB, Brodaty H, Pham T, Le Pham T, Crotty M, Kurrle S, Hinton L, Esterman A, Nguyen TA, Roughead EE. Dementia in Vietnam: a situational analysis [Poster]. *Alzheimer's Association International Conference (AAIC 2020)*. 2020 July 30; online. *Alzheimers Dement*. 2020 Dec; 16(Suppl. 10): e039252. DOI: 10.1002/alz.039252.

28. Numbers KT, Lam BCP, Crawford JD, Kochan NA, Sachdev PS, Brodaty H. Patterns of Change in Subjective Cognitive Complaints are Associated with Cognitive Decline and Dementia Risk: Findings from the Sydney Memory and Ageing Study [Abstract ODO3-10-01]. *Alzheimer's Association International Conference (AAIC*

2020). 2020 July 29; online. *Alzheimers Dement*. 2020 Dec; 16(Suppl. 6): e040685. DOI: 10.1002/alz.040685.

29. Numbers KT, Lam BCP, Crawford JD, Kochan NA, Sachdev PS, Brodaty H. Patterns of change in subjective cognitive complaints are associated with cognitive decline and dementia risk: findings from the Sydney Memory and Ageing Study [Abstract SCR3-05-01]. *Alzheimer's Association International Conference (AAIC 2020)*. 2020 July 29; online. *Alzheimers Dement*. 2020 Dec; 16(Suppl. 6): e040685. DOI: 10.1002/alz.040685.

30. Peters R, Ying X, Cherbuin N, Sachdev PS, Anstey KJ. Higher diastolic blood pressure aged 40-44 is associated with declining cognition and increasing white matter lesions over 8-12 year follow up [Abstract]. *Alzheimer's Association International Conference (AAIC 2020)*. 2020 July 30; online. *Alzheimers Dement*. 2020 Dec; 16(Suppl.10): e045569. DOI: 10.1002/alz.045569.

31. Poole M, Wilcock J, Rait G, Brodaty H, Robinson L. Policy, Practice and Public Awareness: A review of national and international approaches to improve diagnosis and post-diagnostic support for people living with dementia [Abstract ODO4-07-01]. *Alzheimer's Association International Conference (AAIC 2020)*. 2020 July 30; online. *Alzheimers Dement*. 2020 Dec; 16(Suppl. 7): e040918. DOI: 10.1002/alz.040918.

32. Poole M, Wilcock, Rait G, Brodaty H, Robinson L. Policy, Practice and Public Awareness: A review of national and international approaches to improve diagnosis and post-diagnostic support for people living with dementia [Abstract SCR4-14-01]. *Alzheimer's Association International Conference (AAIC 2020)*. 2020 July 31; online. *Alzheimers Dement*. 2020 Dec; 16(Suppl. 7): e040918. DOI: 10.1002/alz.040918.

33. Rossie M, Croot K, Allison KC, Brodaty H, Crawford JD, Lee T, Henry JD, Draper B, Close J, Ong MY, Lam BCP, Sachdev PS, Kochan NA. Predictors of acceptability and emotional response to computerized neuropsychological assessments in older adults: The CogSCAN study [Poster]. *Alzheimer's Association International Conference (AAIC 2020)*. 2020 July 29; online. *Alzheimers Dement*. 2020 Dec; 16(Suppl. 6): e044730. DOI: 10.1002/alz.044730.

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35. Ulanova M, Gloag L, Bongers A, Gooding J, Biazil J, Tilley R, Sachdev PS, Braidy N. Magnetic nanoparticles as MRI contrast agents for the diagnosis of Alzheimer's Disease [Poster]. *Alzheimer's Association International Conference (AAIC 2020)*. 2020 July 28; online. *Alzheimers Dement*. 2020 Dec; 16 (Suppl. 5):e042628. DOI: 10.1002/alz.041609.

Seminars/Lectures

1. Brodaty H. Invited Plenary Speaker. Preventing dementia and enhancing brain health. *TEDX Presentation*. 26 Feb 2020; Sydney and also live-streamed in YouTube.

2. Brodaty H. Invited Speaker. Supporting older people in time of crisis. *Wolper Hospital Public Forum*. 16 June 2020; Sydney.

3. Brodaty H. Global Debate: Nursing Homes should be abolished. *International online webinar hosted by Capacity Australia*. 2 Sep 2020; online webinar.

4. Brodaty H. Invited Plenary Speaker. Reducing the risk and early intervention of dementia. *Jiao Tang University Shanghai*. 29 July 2020; online webinar.

5. Brodaty H. Invited Plenary Speaker. Mental Health of Older People. *Ageing Positively Forum*. 29 Oct 2020; Sydney and online.

6. Brodaty H. Invited Plenary Speaker. Preventing dementia and cognitive decline. In webinar *Dementia Research and Risk Reduction – Together Looking Toward the Future* hosted by Qatar Biomedical Research Institute. 30 Sep 2020; Qatar and online.

7. Brodaty H. Keynote Speaker. Maintain your brain: can we prevent dementia? In webinar *Dementia Research and Risk Reduction – Together Looking Toward the Future*. Hosted by Qatar Biomedical Research Institute QBRI. 30 Sep 2020; Qatar and online.

8. Brodaty H. Behaviours and dementia. *Dementia Australia*. 15 Dec 2020; online webinar.

9. Casey A-N. Reciprocal influence between social networks and healthy brain ageing. *CHeBA Stitch Lecture Series. Stitch Online Community*. 15 Sep 2020; online.

10. Chenoweth L. Person-centred dementia care for the acute care setting. Modules 1, 2 and 3 x 22, for St Vincent's Public Hospital. Jan–March 2020; Sydney.

11. Chenoweth L. Person-centred responses to dementia-related behaviour. Online learning modules x 10, for NPS Medicine Wise. Mar–Apr 2020; online.

12. Koncz R. Invited speaker. Cerebral PET in the Clinic and Research. *Masters of Brain and Mind Sciences Program, Brain and Mind Centre, University of Sydney*. 7 April 2020.

13. Koncz R. Invited speaker. Neuroimaging for Psychiatrists. *Masters of Medicine (Psychiatry) Program, University of Sydney*. 12 May 2020.

14. Koncz R. Invited speaker. Seminar in Intellectual Disability Mental Health. *Masters in Psychiatric Medicine Program, Health Education & Training Institute (HETI)*. 21 May 2020.

15. Numbers K. Change in Subjective Cognitive Complaints are Associated with Cognitive Decline and Dementia Risk: Findings from the Sydney Memory and Ageing Study. *Older Person Mental Health (OPMH) Dementia Showcase*. Dec 2020; Sydney.

16. Numbers K. Change in Subjective Cognitive Complaints are Associated with Cognitive Decline and Dementia Risk. *CHeBA Seminar Series*. Nov 2020; online.

17. Numbers K. Not at your age: Challenging negative stereotypes of ageing. *CHeBA Stitch Lecture Series. Stich Online Community*. Oct 2020.

18. Numbers K. The Relationship Between Objective and Subjective Sleep and Memory in Ageing. *Centre for Sleep and Chronobiology, Woolcock Institute of Medical Research, University of Sydney*. June 2020; Sydney.

19. Sachdev P. Keynote Speaker. Can we really prevent dementia? *Inaugural Healthy Ageing Forum*. Hosted by The Little Bay Coast Centre for Seniors in partnership with the Centre for Healthy Brain Ageing (CHeBA). 19 Mar 2020; The Little Bay Coast Centre, Little Bay, Sydney.

20. Sachdev P. Keynote Speaker. A biomarker approach to diagnosing dementia. *Master Class in Psychiatry*. 6 Mar 2020; Edith Cowan University, Perth WA & UNDA Fremantle.

21. Sachdev P. Invited Speaker. Classification of neurocognitive disorders: the DSM-5 approach. *Neuropsychiatry Education Series*. 12 May 2020; Concord Hospital, Sydney. Also video conferenced to the Royal Melbourne and the Alfred Hospitals, VIC.

22. Sachdev P. Invited Speaker. The classification of vascular cognitive disorders. *INA Webinar on Vascular Cognitive Dysfunction*. 17 June 2020; online via Zoom.

23. Sachdev P. Invited Speaker. Vascular cognitive disorders. *Training Seminar for Early and Mid Career Dementia Researchers (CBCR Fellowship Program)*. 29 June 2020; online via Zoom.

24. Sachdev P. Invited Keynote Speaker. The centenarian brain as a model of resilience. *Brain's Resilience And Intelligence Networks (B.R.A.I.N. lecture) – Virtual keynote lectures on Cognitive Resilience/Reserve*. 3 Sep 2020; online via Zoom and live-streamed in YouTube.

25. Sachdev P. Chair. ADNeT Screening for Trials and Memory Clinics. 10 Sep 2020, 4pm AEST; online webinar via Zoom.

26. Sachdev P. Invited Speaker. "Nanotechnology for the theranostics of dementia". *BioNetwork 3rd Annual Research Symposium on Dementia*. Hosted by Macquarie Uni "Dementia Hackathon". 14 Sep 2020; online via Zoom.

27. Sachdev P. Invited Speaker. The current status of tardive dyskinesia. *Grand Rounds at the Cumberland Hospital*. 16 Sep 2020.

28. Numbers K, Ong MY. Subjective experience of Ageing. *CHeBA Seminar Series*. 9 Nov 2020; online via Zoom.

29. Samtini S, Casey A-N, Stevens A. Social health and social network analyses in dementia. *CHeBA Seminar Series*. 12 Oct 2020; online via Zoom.

30. Kochan NA. Issues related to traditional and computerised neuropsychological methods. *CHeBA Seminar Series*. 14 Sep 2020; online via Zoom.

31. Jiang J, Du J. Neuroimaging Measures and Current Projects at the Neuroimaging Lab. *CHeBA Seminar Series*. 18 May 2020; online via Zoom.

32. Kochan NA, Croot K, Rossie M. Evaluating computerised neuropsychological assessment in older Australians; Findings and lessons learned from the CogSCAN Study. *Online seminar hosted by the School of Population Health*. 7 Oct 2020; online via Microsoft Teams.

33. Braidy N. Current Projects Within the Brain Ageing Research Laboratory. *CHeBA Seminar Series*. 13 July 2020; online via Zoom.

34. Mather KA. Current Projects Within the Genetics Group. *CHeBA Seminar Series*. 15 June 2020; online via Zoom.

35. Sachdev PS. Research at CHeBA: now and into the future. *CHeBA Seminar Series*. 24 Feb 2020; Colonial Bank Theatre, AGSM Building, UNSW Sydney.