

Centre for Healthy Brain Ageing (CHeBA) Annual Report 2021



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Co-Directors' Report

2021 was another unpredictable year, providing a variety of challenges for us all.

Undaunted by microbial threats and movement restrictions, the CHeBA staff and students inspired us with their drive to create new opportunities, and support each other through several activities that kept us socially connected, including the CHeBA Lockdown Challenge which took us virtually from London to the foothills of the Himalayas.

As a group, we recognise that people with dementia are more vulnerable to COVID with higher risks of serious illness and death. We know that dementia takes no heed of a pandemic, which helped harness our attention on finding ways to counter the challenges and to ensure our research continued.

2021 marked the ninth anniversary of CHeBA, with some more extraordinary achievements:

- ✧ a \$3 million National Health & Medical Research Council (NHMRC) Grant awarded to Professor Perminder Sachdev to fund the establishment of the Centre for Research Excellence for Vascular Contributions to Dementia;
- ✧ a prestigious NHMRC Investigator Grant awarded to Dr Nady Braidy to develop a new strategy to improve cognition and quality of life for people living with cognitive impairment and dementia;
- ✧ the launch of a number of new studies and significant projects including Dementias Platform AU, Rethink My Drink, Older Australian Twins Study Online and Forward With Dementia;
- ✧ continuing significant success in research output across two major CHeBA-led consortia – STROKOG and COSMIC.

We were humbled by the commitment made by KPMG to continue its support as an in-kind partner of The Dementia Momentum and were fortunate to hold an event for our donors and Wipeout Dementia supporters in June at their offices – chaired by Senior Partner Eileen Hoggett. We thank Spokesman for The Dementia Momentum, Richard Grellman AM, who led the launch of the CHeBA Change Makers initiative with Ambassadors Mr PJ Lane, Mr Ed Caser and Ms Keri Kitay, and whose unwavering dedication to CHeBA has seen this initiative continue to expand and remain a major philanthropic driver for CHeBA's research.

The COVID pandemic has demonstrated what international collaboration, strategic public and private funding, and the concentration of scientific minds can achieve to meet a global health challenge. Let us apply these lessons to defeat the dementia pandemic.

Professor Henry Brodaty AO & Professor Perminder Sachdev AM

We extend our thanks to all our donors who have supported us in an uncertain time, notably Montefiore, the Vincent Fairfax Family Foundation, the John Holden Family Foundation, the Sachdev Foundation, the Mostyn Family Foundation and the Idle Acres Foundation.

We are also very grateful to all our community supporters who donated to CHeBA staff and students through the Lockdown Challenge, and the commitment from those members who ran the Virtual Blackmores Sydney Running Festival and raised funds for The Dementia Momentum.

This enduring support from an engaged community has ensured that CHeBA continues to expand its critical research in the fields of Alzheimer's disease and other dementias, as well as healthy ageing.

We gratefully acknowledge our colleagues and other supporters for their enthusiastic connection to CHeBA, without which our work would not occur. Our highly skilled group of researchers continue to provide new insights into brain ageing and we thank them for their devotion to a valuable research cause. We would also like to thank our highly committed Centre Manager, Angie Russell and the research support team at CHeBA, as well as congratulate Heidi Douglass on receiving the 2021 UNSW Values in Action Award for Innovation.



2022 promises to be another big year for CHeBA. The results of the *Maintain Your Brain* trial will become available, the Metformin trial for the prevention of dementia will begin, the Dementias Platform Australia will begin to mature, and the Centre for Research Excellence will make CHeBA the hub for vascular dementia research.

Our community engagement will continue to blossom and we will resume the much-loved Wipeout Dementia, with an event in March, all leading to CHeBA's 10th anniversary celebrations in October.

Sincerely

**Professor
Henry Brodaty AO**

**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 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;
- ⦿ Improving diagnosis, post-diagnostic care and long-term community and residential care;
- ⦿ Improving quality of practice for GPs, memory clinics and hospitals through research and through setting up Australian Dementia Network and Registry.

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 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



“As a research group, we are acutely aware that although we are living in a complex time with the worldwide pandemic, dementia remains one of our biggest global public health challenges.”

**Professor Perminder Sachdev AM &
Professor Henry Brodaty AO**

CHeBA Funding Success to Transform 'Preventable Dementia'

In September, the National Health & Medical Research Council (NHMRC) awarded Co-Director Professor Perminder Sachdev AM \$3 million to lead a team of experts from eight universities and three research institutes to improve our understanding of vascular dementia, the second most common form of dementia.

The grant will fund the establishment of the Vascular Contributions to Dementia Centre for Research Excellence, with a vision of reducing the overall health burden of vascular dementia.

"Cerebral vascular disease makes a contribution to 50 – 70% of all dementia cases, and in 15 – 20% of cases, it is the predominant cause," Professor Sachdev said.

Research into vascular cognitive impairment and dementia has lagged behind that of Alzheimer's disease research, and the development of this Centre seeks to remedy this.

The team of leading researchers will address the most critical questions relating to the diagnosis and epidemiology of vascular dementia and develop strategies for its prevention and treatment.

"It will be the Australian hub of an international consortium of Centres that plan to make dementia prevention a reality," Professor Sachdev said.

"Our new Centre hopes to place vascular dementia research at the forefront of dementia research, alongside that of Alzheimer's disease, and meet the promise of vascular dementia as a truly preventable dementia."

Professor Perminder Sachdev AM



Professor Perminder Sachdev AM

Effect of COVID-19 Greatest on People Living with Dementia

The COVID-19 global pandemic is affecting people with Alzheimer's disease and other dementias in a unique way, with researchers from CHeBA calling for increased caregiver support and skilled staff to provide extra support for people living with dementia.

Not only does evidence suggest that people with dementia are more likely to contract COVID-19 than people without dementia, but also that older adults with dementia are more likely to have severe disease outcomes from the virus, including increased risk of death.

An opinion piece written for *Nature Reviews Neurology* by Study Coordinator of CHeBA's Sydney Memory and Ageing Study, Dr Katya Numbers, noted that safeguarding procedures - such as physical distancing and wearing of masks - are extremely difficult for people with dementia to follow, which increases their risk of infection.

The article, co-authored by Co-Director of CHeBA Scientia Professor Henry Brodaty, also highlighted the fact that living arrangements within aged care facilities increase viral propagation.

Not only is this population group more susceptible to the virus and its effects, but they are also more impacted by the negative effects of the measures taken worldwide to control its spread. Forced social isolation during lockdown periods has led to an increase in anxiety and depression for persons living with dementia, who are more likely to have pre-existing anxious and depressive symptoms.



"In aged care homes, where infection rates are disproportionately high, over half the residents have dementia and they are even more vulnerable to COVID."

Professor Henry Brodaty AO

DOI: [10.1038/s41582-020-00450-z](https://doi.org/10.1038/s41582-020-00450-z)



Dr Katya Numbers

Can Fluid-Filled Spaces in the Brain Predict Dementia?

People with enlarged fluid-filled spaces in the brain around small blood vessels may be more likely to develop dementia than people whose perivascular spaces are smaller, according to a CHeBA study published in *Neurology*.

The study, led by Research Fellow Dr Matt Paradise, involved 400 people with an average age of 80. Participants took tests of thinking and memory skills at the beginning of the study and again four years later. Researchers evaluated participants for dementia at the beginning of the study and again eight years later. The participants also had MRI brain scans to check for enlarged perivascular spaces in two areas of the brain. The top quarter of the people with the largest number of enlarged perivascular spaces, or the severe cases, were compared to those with fewer or no enlarged spaces, or the mild or absent cases.



"Severe perivascular space disease may be a marker for an increased risk of cognitive decline and dementia."

Dr Matt Paradise

"More research is needed to understand how these enlarged spaces develop, as they could be an important potential biomarker to help with early diagnosis of dementia."

Researchers found that people with severe cases in both areas of the brain were nearly three times more likely to develop dementia during the study than people with fewer or no enlarged spaces.

Co-author and Co-Director of CHeBA, Professor Perminder Sachdev, said that vascular abnormalities play a central role in the development of dementia in a large proportion of patients.

"Vascular abnormalities can manifest in many forms, and this study highlights the importance of looking at perivascular spaces, which have often been dismissed in the past as being simply normal age-related changes," said Professor Perminder Sachdev.

DOI: [10.1212/WNL.0000000000011537](https://doi.org/10.1212/WNL.0000000000011537)

The study was supported by the Australian National Health and Medical Research Council and the Josh Woolfson Memorial Scholarship.



CHeBA Launches Dementias Platform Australia to Make Study of Ageing 'Truly Global'

With dementia affecting all populations globally, in 2021 CHeBA launched Dementias Platform Australia (DPAU) in partnership with the already established Dementias Platform UK (DPUK), with a collective vision of accelerating new discoveries in the understanding and diagnosis of dementia.

The collaboration, which allows for access to research data from multiple dementia studies carried out in Australia, the Asia-Pacific region and beyond to all six continents, will enable new insights into ageing, age-related diseases and risk of Alzheimer's disease and other dementias.

"The aim is to transform the study of the epidemiology of brain ageing and dementia and make it truly global."

Professor Perminder Sachdev AM

The challenges posed by dementia are complex. Addressing them requires many smaller pieces of a puzzle to come together to increase our understanding of brain function and of the risks that genetic, environmental and lifestyle factors pose to healthy brain ageing.

While the contribution of one research participant, one researcher or one study is often modest, the ability to combine data across many studies has a potential not yet fully realised.

The DPAU platform, which uses secure technology deployed at Monash University, will house data on physical and brain health from studies conducted around the world.

Monash SeRP is a secure, trusted and scalable environment for data sharing, governance, control and management services for researchers.

According to Dr Vibeke Catts, Research Manager at CHeBA and project leader of DPAU, dementia research will be reshaped through the hosting of data from international longitudinal and cross-sectional studies of brain ageing.

"The impact that health and medical research has on society cannot be underestimated," says Dr Catts.

"DPAU allows for critical information about disease trends and risk factors, outcomes of treatment or public health interventions as well as methods of care and associated costs."

DPAU is funded by a grant from the National Institute of Health (NIH) to the Cohort Studies of Memory in an International Consortium (COSMIC) led by CHeBA Co-Director Professor Perminder Sachdev. COSMIC aims to identify risk and protective factors and biomarkers of cognitive ageing and dementia in diverse ethno-racial groups and geographical settings and currently comprises data from 44 studies across the globe.



Researching Aged Care, Policy and Education

Professor Lynn Chenoweth, who is one of Australia's most eminent Professors of Nursing, has been researching aged care, health and aged care policy, and contributing to aged care nursing education and practice since 1987.

CHeBA is extremely privileged to have Professor Chenoweth as part of the team, with an important outcome of her research being the potential to influence policy decisions on how best to enable and support the health, emotional and social needs of older people – including family carers and persons living with dementia.

This position at CHeBA is funded by Montefiore with Professor Chenoweth gaining significant success across a number of research grants in 2021, including being awarded a DCRC (Dementia Australia) World Class Dementia Grant aimed at improving hospital care for people with dementia.

Through 2021 Professor Chenoweth led a research project to improve staff response to aggression in aged care residents living with dementia. The 'Maybo' project has been a significant collaboration with Montefiore and CHeBA is grateful for their funding and in-kind support for research.

Professor Chenoweth's research also includes projects looking at improving health outcomes, wellbeing and care for people living with dementia in the hospital setting, carer end of life planning intervention in people living with dementia, dementia medicines and consumer priorities.



"My hope is that my research not only provides robust evidence of the benefits of implementing safe person-centred systems of treatment and care, but that the evidence is accepted and applied across local, state and national health jurisdictions."

Professor Lynn Chenoweth



Our Groups



“Our goal is to make a major impact on the societal burden imposed by Alzheimer’s disease and other dementias, in Australia and internationally.”

**Professor Perminder Sachdev AM &
Professor Henry Brodaty AO**

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 a 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.

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.



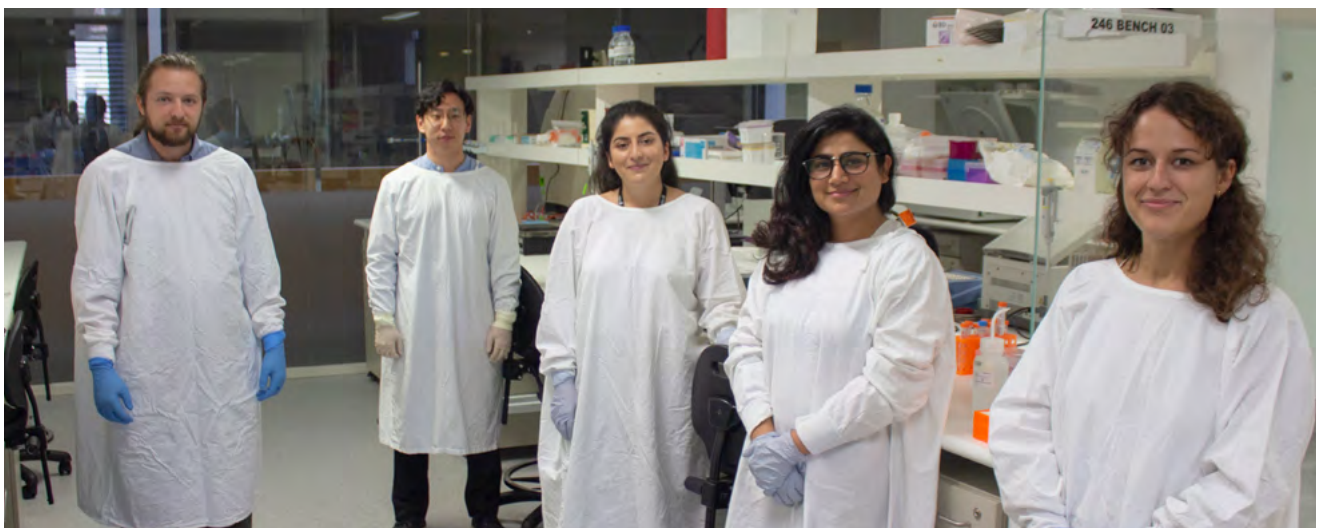
Dr Nady Braidy
Group Leader

Staff

- ◊ Professor Perminder Sachdev
- ◊ Maria Villalva

PhD Students

- ◊ Chul-Kyu Kim
- ◊ Gurjeet Virk
- ◊ Marina Ulanova



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

Funding Success for New Strategy to Promote Healthy Brain Ageing

In September, Leader of the Brain Ageing Research Laboratory, Dr Nady Braidy, was awarded a National Health & Medical Research Council (NHMRC) Investigator Grant to develop a new strategy to improve cognition and quality of life for people living with cognitive impairment and dementia.

The prestigious award will allow Dr Braidy's team to evaluate the prognostic value of the nicotinamide adenine dinucleotide (NAD⁺) metabolome and therapeutic relevance of novel strategies to raise NAD⁺ levels for the treatment of Alzheimer's disease and other dementias, while promoting 'healthy' brain ageing.

CHeBA Co-Director Professor Perminder Sachdev said Dr Braidy was deserving of an Investigator Grant. "Dr Braidy is an international leader in the biology of ageing and has made seminal contributions in the role of NAD⁺, one of the most abundant molecules in the cell and critical for the cell's function."

"His work has the potential to develop strategies for a long and healthy life without dementia. This investigator grant will give him the support needed to move closer to this goal," said Professor Sachdev.

Dr Braidy's research in brain ageing and dementia spans a decade with his influential discovery that the levels of NAD⁺ declines with age in catabolic tissue including the brain in rats and humans.

"This is an exciting time for age-related brain research."

Dr Nady Braidy

"The expectation is that in five years, my laboratory will develop the empirical basis for the use of NAD⁺ to help promote healthy brain ageing and delay, or even reverse dementia," said Dr Braidy.

Using Quantum Dots to Diagnose and Treat Alzheimer's Disease

Brain Ageing Research Laboratory researchers and Dr Vipul Agarwal from the School of Chemical Engineering offered renewed insight into 'Quantum dot' research in 2021, revealing its promising application in Alzheimer's disease diagnosis and therapy.



Lead author of the research, Maria Villalva, said that "Quantum dots are emerging nanomaterials that are making their way into Alzheimer's disease research and have the potential to be used for early diagnosis as well as treatment of Alzheimer's disease."

The review, published in *Nanomedicine*, examined 34 publications to investigate the potential of Quantum dots to target amyloid plaques in the brain, which can be adapted for diagnostic and therapeutic purposes. Quantum dots are able to cross the blood-brain barrier; a tightly regulated system of cells that prevents foreign substances from being transported from the blood to the brain, as well as facilitating the entry of essential nutrients. The blood-brain barrier has been shown to act as a physical limitation for treatment of Alzheimer's disease.

Ms Villalva says the review also looked at the potential toxicity of Quantum dots; a major obstacle in their progression into clinical Alzheimer's disease research. The unique properties of Quantum dots, and their versatility to combine to various biomolecules render them a promising diagnostic and therapeutic tool for Alzheimer's disease.

Leader of the Brain Ageing Research Laboratory and Senior Research Fellow at CHeBA, Dr Nady Braidy, says that further studies are needed to monitor the blood-brain barrier integrity and to establish a gold standard toxicity measure before Quantum dots are used in clinical medicine.

DOI: 10.2217/nnm-2021-0104

Association Between Plasma Lipids and Risk of Alzheimer's Disease

Research published in *Translational Psychiatry* uncovered new insight into the underlying mechanisms of Alzheimer's disease, by examining differences between the plasma lipidome of people with Alzheimer's disease and 'healthy' individuals of the same age from CHeBA's Sydney Memory and Ageing Study.

Senior author and Leader of CHeBA's Brain Ageing Research Laboratory, Dr Nady Braidy, said that the lack of effective treatments and the potential for prevention highlight the importance of identifying early biomarkers for diagnosis, with blood lipids now emerging as promising identifiers of Alzheimer's disease.

"Although there have been numerous studies on the association between lipids and the biological pathology of Alzheimer's disease, few studies have looked at the plasma lipidome. This research looked to determine whether lipid profiles are associated with genetic risk of Alzheimer's disease."

The benefit of lipidomics in biomarker research is that it simultaneously identifies and quantifies hundreds of lipids, acting as a powerful tool for mapping global biochemical changes in disease and treatment. The study also highlighted that genes related to Alzheimer's disease play a role in influencing lipids that are associated with Alzheimer's disease, reinforcing the consequence of physiological factors - such as inflammation - on brain ageing.



Lead author Dr Yue Liu, who recently completed his PhD at CHeBA

Co-Director of CHeBA and co-author Professor Perminder Sachdev said "quantifying these plasma lipids using mass spectrometry provides renewed insight in the underlying mechanisms of Alzheimer's disease and directs us to additional drug targets and benefits in the clinic.

DOI: 10.1038/s41398-021-01362-2



Epidemiology



**Professor Perminder Sachdev &
Professor Henry Brodaty**
Group Leaders

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.

Staff

- | | |
|------------------------------------|---------------------|
| ✧ Emeritus Professor Gavin Andrews | ✧ Dr Suraj Samtani |
| ✧ Dr Nicole Kochan | ✧ Dr Katya Numbers |
| ✧ Dr Karen Mather | ✧ Dr Sophie Xi Chen |
| ✧ Dr John Crawford | ✧ Jess Lo |
| ✧ Dr Anbu Thalamuthu | ✧ Fleur Harrison |
| ✧ Dr Darren Lipnicki | |
| ✧ Dr Yvonne Leung | |
| ✧ Dr Vibeke Catts | |
| ✧ Dr Amanda Selwood | |
| ✧ Dr Teresa Lee | |
| ✧ Dr Ben Lam | |
| ✧ Dr Louise Mewton | |



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

Genomics & 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.



Dr Karen Mather
Group Leader

Staff

- | | |
|----------------------------|-----------------------------|
| ○ Dr Anbupalam Thalamuthu | ○ Dr Naga Mutyala |
| ○ Dr Sumangali Gobhidharan | ○ Sri Chandana Kanchibhotla |

Students

- | | |
|-------------------|----------------------------|
| ○ Dr Adith Mohan | ○ Abdulsalam Toyin Ademola |
| ○ Mary Revelas | ○ Annabel Matison |
| ○ Jessica Lazarus | ○ Russell Chander |
| ○ Irina Freitag | |



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



Western Diet Linked to Increased Depression in Over 45s

A review examining 33 articles published up to December 2020 revealed new insight into the connection between nutrition and depression in adults aged 45 years and older.



Published in *Ageing Research Reviews*, the review indicates a beneficial relationship between higher intakes of vegetables and fruits and lower incidence of depression, with a higher risk of depression for those that consumed a predominantly western diet or foods that increase inflammation in the body.

According to senior author Dr Simone Reppermund and expert in depression and cognitive function, depression is also associated with increased morbidity and suicide.

Lead author and CHeBA student Annabel Matison said that both the Dietary Inflammatory Index and the Western diet were associated with increased depression, whereas higher intake of fruit and vegetables lowered the risk.

DOI: [10.1016/j.arr.2021.101403](https://doi.org/10.1016/j.arr.2021.101403)



“We found that the current evidence suggests Mediterranean diets, ‘healthy’ diets and fish intake were not associated with depression.”

Annabel Matison



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.

Staff

Dr Jiyang Jiang Dr Jing Du

Students

Heidi Foo Chao Dong
Abdullah Alqarni
Dr Jing Du



**Associate Professor
Wei Wen**
Group Leader



New Imaging Measure to Track Brain Ageing

In 2021 the Neuroimaging Group developed an improved neuroimaging measure to monitor age-related cognitive decline in older adults.

The findings, published in *NeuroImage*, indicate that the measure – named ‘Difference in Distribution Function’ will ultimately assist in monitoring the ageing process and brain changes seen in Vascular dementias and Alzheimer’s disease.

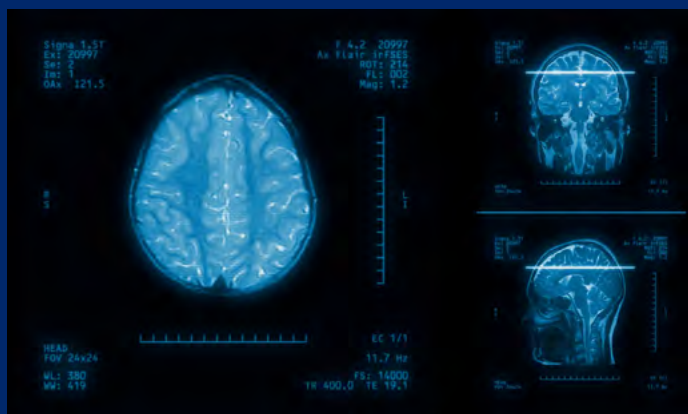
Diffusion Weighted Imaging has been the most widely recognised neuroimaging technique for evaluating the microstructure of white matter in the brain, with white matter integrity critical to normal brain structure and function. Various diffusion weighted imaging measures have been developed to investigate white matter but all have had inherent limitations.

Leader of CHeBA’s Neuroimaging Group Associate Professor Wei Wen said that there was a distinct need for an enhanced neuroimaging measure to be developed to overcome these limitations.

Lead author Dr Jing Du said that white matter is important because it is vulnerable to the effect of vascular risk factors.

“It is possible that ageing brains suffer significant micro-structural changes due to vascular factors before functional changes are obvious, such as cognitive decline and impact on memory.”

Dr Jing Du



Dr Du and colleagues are delighted their work is clinically meaningful and immediately useful to the global neuroimaging community, with the computer program for the improved measure already accessible online: https://bit.ly/CHeBANeuroimaging_DCDF.

DOI: 10.1016/j.neuroimage.2021.118381

Changes to Hippocampus in Alzheimer's Disease

Research led by Dr Heidi Foo has found that specific subregions within the hippocampus may be key in understanding Alzheimer's disease.

The hippocampus is one of the regions in the brain that has been frequently used in the diagnosis of Alzheimer's disease – the most common type of dementia - with hippocampal volume an important biomarker of the disease. Genetic risk of Alzheimer's disease is also indicated by hippocampal atrophy.

The research, published in *Neurobiology of Aging*, examined the factors which influence the subregions of the hippocampus, with findings suggesting that older individuals showed greater vulnerability to higher Alzheimer's disease genetic risk compared to younger individuals.



"The pattern of decline in the subregions in relation to the genetic predisposition in community dwelling healthy individuals may shed light on the pathogenesis of Alzheimer's disease."

Dr Heidi Foo

[DOI: 10.1016/j.neurobiolaging.2020.11.002](https://doi.org/10.1016/j.neurobiolaging.2020.11.002)

Human Longevity is Associated with Brain White Matter Hyperintensities

More research from the Neuroimaging Group revealed new insights into the relationship between human longevity and brain white matter lesions - white matter hyperintensities.



The findings, published in *The Journals of Gerontology Series A: Biomedical Sciences and Medical Sciences*, explored the association between longevity and brain volumes of white matter lesions, a marker of cerebral small vessel disease, from a UK Biobank cohort aged 45-81 years. The researchers also replicated the findings in a combined sample from CHeBA's Sydney Memory and Ageing Study and Older Australian Twins Study, aged 66-93 years.

Lead author, Chao Dong, explained that lower volumes of white matter hyperintensities were associated with longer parental lifespan as well as higher polygenic risk for longevity.

According to Ms Dong this robust association suggests that longevity-related genes may provide some protection against white matter disease. "Long-lived people tend to have lower risk of developing ageing-related diseases, such as cerebral small vessel disease, and my study shows that this is also true for a related neuroimaging abnormality, white matter hyperintensities, which may play an important role in promoting longevity."

[DOI: 10.1093/gerona/glab323](https://doi.org/10.1093/gerona/glab323)

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.

Staff

- Dr Adith Mohan
- Dr Matt Paradise
- Dr Rebecca Koncz



Professor Perminder Sachdev
Group Leader



Funding Success for Functional Neurological Symptom Disorders Clinic

Research Fellow and Senior Lecturer Dr Adith Mohan was awarded a Mindgardens Neuroscience Network Translational Research Grant to establish an intervention clinic for patients with Functional Neurological Symptom Disorders.

The Australian-first clinic will provide multi-disciplinary assessment together with an intervention program for suitable patients.

Dr Mohan, a Consultant Neuropsychiatrist at the Neuropsychiatric Institute, Prince of Wales Hospital, said that the research-ready clinic will see participants referred from their GP or specialist.

"Such a clinic is not currently available in Australia in the public sector and bridges a significant gap in care-provision for a vulnerable group with high rates of physical and mental health morbidity, disability and healthcare needs."

Both Dr Mohan and Professor Perminder Sachdev, fellow research investigator and neuropsychiatrist, have been at the forefront of tertiary care and clinical research in neuropsychiatry for three decades. Having fostered significant collaborative care partnerships across the disciplines of neurology, clinical neuroscience, rehabilitation medicine and neuropsychology, the Neuropsychiatric Institute is an ideal home for a tertiary clinic to operate.

Professor Sachdev, who is Co-Director of CHeBA and Director of the Neuropsychiatric Institute, says the goal is to create and evaluate a model for gold-standard, evidence-based care provision for FND in Australia.



"It will bring together clinical experts from neuropsychiatry, neurology, rehabilitation medicine, physiotherapy, occupational therapy and psychology for the first time."

Dr Adith Mohan

Neuropsychology



Dr Nicole Kochan and Dr Teresa Lee
Group Leaders

The Neuropsychology Group is interested in investigating the cognitive changes occurring in the brain 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. A major project - the CogSCAN Study is evaluating the reliability, validity and usability of computerised neuropsychological assessment for older adults 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 associations between cognition with: brain structure and function, genetics and environmental factors, medical comorbidities, inflammatory markers and falls in the older adult population.

Staff

- Dr John Crawford
- Dr Ben Lam
- Dr Karen Croot
- Dr Adam Bentvelzen
- Matilda Rossie
- Josephine Bigland
- Ashton Trollor

Students

PhD candidates

- Dr Rebecca Koncz
- Annette Spooner
- Zara Page
- Premilla Chinnappa-Quinn

Fourth year medical students (Honours and Independent Learning Project)

- Michael Budiarto
- Christabella Surono



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

International Experts Advise on Standard Assessment for Diagnosing Dementia

Internationally renowned experts in dementia and cognitive assessment, including Dr Nicole Kochan from CHeBA's Neuropsychology Group, provided expert opinion on the development of a standard set of neuropsychological tests for patients presenting to memory clinics, to ensure consistency in diagnosis of Mild Cognitive Impairment and dementia.

The invited experts, which also included CHeBA Co-Directors Professor Henry Brodaty and Professor Perminder Sachdev, acknowledge that a standard assessment for individuals presenting with cognitive difficulty is an international priority.



A critical step in the diagnostic process for people with cognitive complaints referred to a memory clinic is to examine performance on a set of neuropsychological tests. It has been evident that different tests are more sensitive to different disorders which can lead to varied diagnoses for patients.

Dr Nicole Kochan said that the testing process not only differed across regions and countries but also differed among local clinics here in Australia.

“This research recommends a uniform set of tests that a person should receive when attending a memory clinic to receive a comprehensive assessment of their cognition, thinking abilities and problem solving.”

Dr Nicole Kochan

“Standard diagnostic procedures then ensure best practice and consistency across diagnosis of dementia.”

[DOI: 10.1016/j.jalz.2019.06.2875](https://doi.org/10.1016/j.jalz.2019.06.2875)

CogSCAN Webinar Computerised Cognitive Tests: What Participants Told Us

In 2018 to 2020, a large group of adults aged 60 and above in the local community took part in the CogSCAN Study at the Centre for Healthy Brain Ageing.

The study investigated how computerised cognitive tests performed on repeated occasions, how these new tests compared with older-style well-validated pen-and-paper tests, and what people thought and felt about doing the tests.

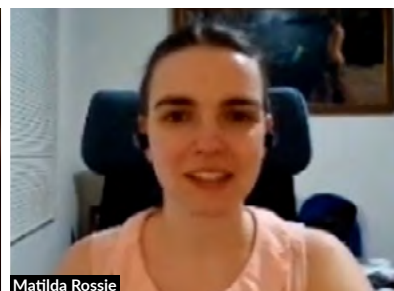
In December 2021 the CogSCAN team, led by Principal Investigator Dr Nicole Kochan, hosted a webinar in which participants were invited to hear the progress of the study and its early findings. They also had the opportunity to pose questions and provide feedback to the team. The 90-minute online session included presentations from Dr Kochan, Neuropsychology Research officer Dr Karen Croot, Research Assistant Matilda Rossie.



Dr Nicole Kochan



Dr Karen Croot



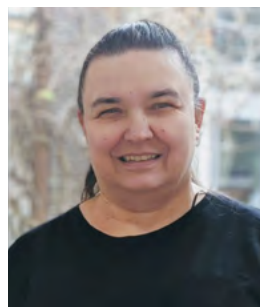
Matilda Rossie

CogSCAN Study of computer-administered neuropsychological tests in seniors

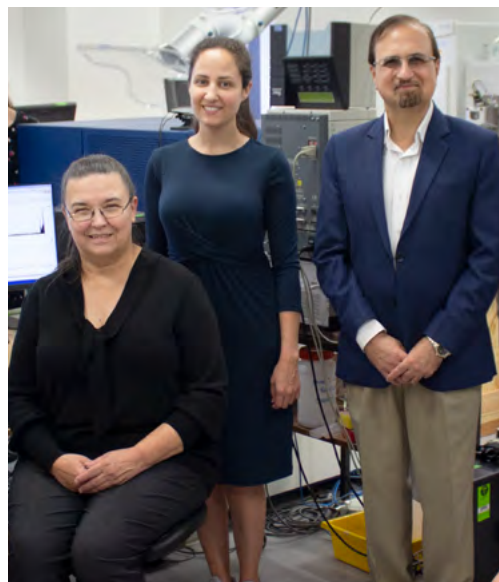
Proteomics

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.



Dr Anne Poljak
Group Leader



**Dr Anne Poljak, Fatemeh Khorshidi,
Professor Perminder Sachdev**

Staff

- Dr Tharusha Jayasena
- Professor Perminder Sachdev
- Maboobeh Hossieni
- Dr Fei Song

PhD Students

- Gurjeet Virk
- Fatemeh Khorshidi
- Rene Jezewski
- Toyin Ademola



Risk Factors

The Risk Factors Group studies risk factors for dementia from a lifespan perspective.

The group uses large-scale population-based studies, neuroimaging data, and epidemiological modelling to understand the risk factors for dementia across the lifespan. One of the main focuses of the Risk Factors Group is alcohol use, and its impact on brain health in foetal development, adolescence, and later life. The group has used longitudinal cohorts from CHEBA (the Sydney Memory and Ageing Study) as well as CHEBA's consortia (COSMIC) to investigate the relationship between alcohol use and dementia in later life. In collaboration with the Global Burden of Disease Study, the Risk Factors Group is also using COSMIC data to better understand the contribution of a range of risk factors to mortality and morbidity associated with dementia globally. The Risk Factors Group also focuses on developing and evaluating novel online behaviour change interventions aimed at reducing risk factors that contribute to the development of dementia in later life.



Dr Louise Mewton
Group Leader

Staff

- ✧ Virginia Winter
- ✧ Sarah Davies
- ✧ Rachel Visontay
- ✧ Nicholas Hoy

Opinion Piece Launched Rethink My Drink

In November the Risk Factors Group launched **Rethink My Drink**, a world-first online study designed to help Australians aged 60-75 years consider their alcohol consumption and be guided to reduce their intake and help prevent dementia.

Low levels of alcohol use, between 1 and 7 standard drinks per week, are associated with small but significant changes in the brains of older adults, with heavy drinkers three times more likely to develop dementia. One large and influential study has even identified heavy drinking as the single most dangerous risk factor for dementia - when compared with other modifiable lifestyle risk factors.

Most recent evidence indicates that one in five Australians over 60 exceeds official guidelines of more than two drinks per day, putting themselves at risk of long term harm - higher than any other age group.

Leader of the Group, Dr Louise Mewton, said it is critical for Australians over 60 to be aware that heavy alcohol use is the strongest modifiable risk factor for dementia in comparison to such things as smoking, obesity, high blood pressure and diabetes.

The world-first study aims to determine whether an online alcohol brief intervention adapted for older adults can slow cognitive decline, while at the same time reduce alcohol consumption in older risky drinkers.



<https://cheba.unsw.edu.au/news/festive-season-opportunity-address-alcohol-concerns>

If you are concerned about your alcohol consumption and would like to participate in this study, register your interest at www.unswalcoholstudy.org.au



**RETHINK
MY DRINK**

CHeBA-led Consortia



“By harnessing international studies into consortia to identify risk and protective factors, we are seeking to develop and validate strategies to delay or even prevent dementia.”

**Professor Perminder Sachdev AM &
Professor Henry Brodaty AO**

This 5-country, 10-university consortium led by CHeBA is driving change to reframe dementia from a “life sentence” to a diagnosis with strategies and support options that will enable people with dementia and their families to come to terms and live better with dementia.

Based on our formative research, we listened to the experience of diagnosis and post-diagnostic support from the perspectives of people with dementia, family carers and health professionals. Results were negative. Diagnosticians reported delivering the diagnosis difficult, feeling they had little to offer patients and families. Patients and families expressed that getting the diagnosis was like “stepping into a void”. They were overwhelmed and unsure of what to do next.

These experiences are troubling. Evidence and clinical experience shows reframing the diagnostic conversation and giving simple information about what to do next gives a sense of hope.

Over 2021, COGNISANCE has sought to address this gap. An intense series of co-design workshops bringing together people living with dementia, carers and a range of health care professionals were held, and a brand for a public campaign and website were developed, called *Forward with Dementia* www.forwardwithdementia.org.au/. *Forward with Dementia* has curated content for our three audiences: people living with dementia, carers and health professionals. The website targets each groups’ specific needs, supplying information, tools, resources, and practical actions. The website is rounded out with personal stories and news items that challenge the status quo of “nothing can be done”. Prior to launch, Australian COGNISANCE team members along with honours student Jacky Zheng, from project partner University of Sydney, undertook comprehensive website user testing, to refine and ensure the experience of the user was a simple and was needed streamlined as possible.

The public campaign, devised by A/Prof Lyn Phillipson, a public health academic from project partner University of Wollongong, was launched on 13 October with a webinar delivered by Chief Investigator and CHeBA co-director Prof Henry Brodaty. He spoke on ‘Rethinking a dementia diagnostic interview’ which was attended by over 200 people, primarily diagnosticians, from Australia, New Zealand Asia and India. A second webinar on 11 November saw Prof Lee-Fay Low, of project partner Sydney University, explore the evidence base of post diagnostic supports and therapies. Social media is used to back the key campaign messages and webinars are posted to our YouTube channel.

While issues and needs are similar across the globe, campaigns vary based on local context. Partners in the UK and Netherlands support specialist dementia nurses to empower their clients.



Dr Meredith Gresham and Nora Wong

Across three provinces in Canada COGNISANCE teams seek to deliver key information to enable people with dementia and carers effectively seek help and support. Partners in Poland are directly challenging the stigma of *otępienie*, the word for dementia which translates as ‘half-conscious, dazed or bewildered’. Their campaign brings messages that dementia is a medical condition that deserves recognition and understanding.

The campaign will continue into 2022.

Staff

UNSW CHeBA

- Professor Henry Brodaty, Chief Investigator
- Dr Meredith Gresham, Project Co-ordinator
- Ms Nora Wong, Research Officer

University of Sydney

- Professor Lee-Fay Low
- Professor Yun-Hee Jeon

University of Wollongong

- Associate Professor Lyn Phillipson

With international project partners from: University College London and Newcastle University UK; Maastricht University, Netherlands; Wroclaw Medical University, Poland; and McGill University, University of Waterloo and New Brunswick University in Canada.

Students

Jointly supervised with University of Sydney

- Mr Jacky Zheng
- Ms Issra Allam

New Program Helps People Find Their Way Forward After a Dementia Diagnosis

An innovative program launched by the COGNISANCE team aims to assist the estimated 60,000 Australians diagnosed with dementia each year to understand the next steps and change outdated perceptions of living with dementia.

Most people feel overwhelmed when first diagnosed with dementia. They despair of their future, lose hope and don't know what to do next.

To address this, COGNISANCE, created *'Forward with Dementia'*; a program designed to improve the diagnostic experience, post diagnosis support and connections for people with dementia and their carers.

The program was jointly planned and developed by leading researchers from UNSW Sydney, the University of Sydney and University of Wollongong in collaboration with colleagues from Canada, the Netherlands, Poland and the United Kingdom.

"People with dementia can live positively for many years. There are treatment strategies and we need to spread the word and assist diagnosticians and other health workers to improve their practice," said Professor Henry Brodaty.

By working together, we can help set people newly diagnosed with dementia on a better path."

Professor Henry Brodaty

Program resources, developed with the help of people living with dementia and their carers, include a website (forwardwithdementia.org/au) to guide people in the first year following diagnosis. The website offers information, advice, and tools, and shares experiences and strategies used by people with dementia and their carers.

'Forward with Dementia' also targets doctors who diagnose dementia.

"We've consulted with diagnosticians throughout Australia, including specialists and support staff in Memory Clinics," Professor Brodaty said. Bill Yeates, who was diagnosed with dementia in 2019, believes the Forward with Dementia Program will be very useful in helping others adjust to life with dementia.

"When I was first diagnosed, I felt lost and so overwhelmed. I didn't know where to turn," said Mr Bill Yeates.

"The Forward with Dementia program is really important as it guides people and their carers on their next steps."

Bill Yeates

"It gives them hope and will also reduce some of the stigma and stereotypes about living a life with dementia," Mr Yeates said.

The Forward with Dementia program was funded by the NHMRC and the European Union (EU) Joint Programme – Neurodegenerative Disease Research (JPND), a global research initiative aimed at tackling the challenge of neurodegenerative diseases.

Key Collaborators: Dementia Australia, Dementia Alliance International, Alzheimer's Disease International, World Health Organisation.



Forward with Dementia Seminars

As part of the launch of Forward With Dementia, researchers hosted two webinars in October and November 2021.

Rethinking Support after Dementia Diagnosis: Unmet Needs and Evidence for Rehabilitation

The webinar covered unmet needs for information, psychosocial support, and treatments to optimise function and wellbeing for Australians living with dementia, and their carers. The webinar also presented practical suggestions on how clinicians can help people with dementia and carers obtain rehabilitation and additional supports after diagnosis.

This webinar was presented by Professor Lee-Fay Low of The University of Sydney, with a live Q&A featuring CHeBA Co-Director Professor Henry Brodaty and chaired by Associate Professor Lyn Phillipson of The University of Wollongong.



Rethinking Dementia Diagnostic Conversation

This webinar helped diagnosticians improve communication of the dementia diagnosis and essential care planning. It highlighted four main themes – communication, compassion, hope and follow-up – and provided details of the 'Forward with Dementia' program.

This webinar was presented by Professor Henry Brodaty and chaired by Professor Lee-Fay Low of Sydney University.



Forward
with dementia





COSMIC is an international consortium to combine data from population-based longitudinal cohort studies to identify common risk factors for dementia and cognitive decline.

By the end of 2021 there were 45 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 2021 include:

1. Signing an MOU with 4 new studies:
 - a. Boston Puerto Rican Health Study;
 - b. Framingham Heart Study;
 - c. The Irish Longitudinal Study on Ageing;
 - d. A study from Uganda.
2. Three new projects were approved, led by either CHeBA researchers or international workgroups:
 - a. The association between diet and depression in older adults;
 - b. Untangling the mechanistic links between heart and brain health in older populations: An Artificial Intelligence (AI) assisted toolkit for assessing dementia risk;
 - c. Trajectories of cognitive decline before and after stroke: an individual participant data meta-analysis from the COSMIC collaboration.
3. One paper was published:
 - a. Hyun J, Hall CB, Katz MJ, Derby CA, Lipnicki DM, Crawford JD, Guaita A, Vaccaro R, Davin A, Kim KW, Han JW, Bae JB, Röhr S, Riedel-Heller S, Ganguli M, Jacobsen E, Hughes TF, Brodaty H, Kochan NA, Trollor J, Lobo A, Santabarbara J, Lopez-Anton R, Sachdev PS, Lipton RB; or Cohort Studies of Memory in an International Consortium (COSMIC). Education, Occupational Complexity, and Incident Dementia: A COSMIC Collaborative Cohort Study. *J Alzheimers Dis.* 2021 Nov 11. doi: 10.3233/JAD-210627. Online ahead of print. PMID: 34776437
4. Presentations at international conferences, including five at AAIC, by project leaders from CHeBA and external to UNSW.
5. International collaborations with:
 - a. The Institute for Health Metrics and Evaluation (IHME) at the University of Washington. We facilitated the provision of data from 16 COSMIC cohorts for the Global Burden of Disease (GBD) study;
 - b. The Davos Alzheimer's Collaborative, who are providing funding and resources to COSMIC cohorts from Malaysia, Singapore, and The Philippines for the collection of new behavioural and genetic data through the use of digital tools and blood assays;

- c. COVID-19 study led by Sarah Baurermeister (University of Oxford), to which around 6 COSMIC cohorts are contributing.

6. Dementias Platform Australia (DPAU).
 - a. The website was launched late in the year;
 - b. Twenty-one COSMIC studies have agreed to upload data to DPAU (another 7 are unable to do so but have agreed to be listed on the site);
 - c. Descriptive summaries have been reviewed and approved for 29 COSMIC studies.

Staff

- | | |
|-------------------------------|--------------------|
| ✧ Professor Perminder Sachdev | ✧ Dr Ben Lam |
| ✧ Professor Henry Brodaty | ✧ Dr Nicole Kochan |
| ✧ Dr Darren Lipnicki | ✧ Dr Louise Mewton |
| ✧ Dr Jiyang Jiang | ✧ Nicholas Hoy |
| ✧ Dr Suraj Samtani | ✧ Jessica Lo |
| ✧ Dr John Crawford | ✧ Rachel Visontay |
| | ✧ Ashley Stevens |
| | ✧ Saly Mahalingam |

Students

- ✧ Dr Matthew Lennon
- ✧ Annabel Matison



Dr Darren Lipnicki
Study Coordinator

Having at Least a High School Degree and a Complex Job Linked to Dementia Prevention

Research from COSMIC found that high occupational complexity is associated with dementia-free survival time, highlighting the importance of maintaining cognitive stimulation throughout life for lowering the risk of dementia.

The collaboration analysed 10,195 older adults across seven international studies from COSMIC.

The study, published in the *Journal of Alzheimer's Disease*, found that having at least completed high school and high occupational complexity were both and independently associated with dementia-free survival time, implying a lower chance of having developed dementia before the study ended.

Study Coordinator of COSMIC, Dr Darren Lipnicki, said that both early life education and mental engagement



at work during adulthood are theorised to help prevent late-life dementia, but little is known about similarities or differences across geographical regions.

The research then examined whether education and occupational complexity were associated with dementia in later life, and whether there were similarities and differences across geographical regions.

[DOI: 10.3233/JAD-210627](https://doi.org/10.3233/JAD-210627)

Support for COSMIC is largely driven by CHeBA's major philanthropic initiative, The Dementia Momentum.



Dementia affects fifty-five million people worldwide. We know that social connections can protect us against cognitive decline and dementia.

However, the type and amount of social connection we need for maintaining good cognitive health remain unknown. To uncover these answers, the NHMRC and European Union Joint Programme - Neurodegenerative Disease Research have funded a project called SHARED (Social Health and Reserve in the Dementia patient journey). 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 the links between social connections, brain health and dementia.



Dr Suraj Samtani
Study Coordinator

In 2021, we published a systematic review on how to preserve and enhance the social connections of older adults with mild cognitive impairment and dementia. We found that music and dance groups helped people with cognitive impairments to stay connected with others. This was true even for those who had severe dementia and had lost their language abilities. Music formed a common thread that linked them to others. Other promising interventions included community social groups, animal-assisted therapy and social robots.

We also looked at how social support impacts mental health in the second half of life.

We analysed social support and depression data from over 19,000 people from eight countries. Our preliminary findings suggest that social support (especially having someone to confide in) is associated with lower depression at 2-year follow-up.

In a joint effort with our international partners, we interviewed people living mild cognitive impairment or dementia, their friends and family, and health

professionals about social connections. We hope to answer the questions, 'How can we measure social well-being for people living with mild cognitive impairment or dementia?' and 'What social factors are important to them?'.

In 2022, we plan to explore what type and amount of social connections are protective against dementia and mortality. We also plan to look at the link between social

connections and brain health using brain scans from large datasets.

Staff

- | | |
|-------------------------------|----------------------|
| ✧ Professor Perminder Sachdev | ✧ Dr Suraj Samtani |
| ✧ Professor Henry Brodaty | ✧ Dr Darren Lipnicki |
| | ✧ Dr Ben Lam |
| | ✧ Saly Mahalingam |

Improving Social Health for People Living with Dementia

In 2021, SHARED researchers pinpointed mechanisms to reduce loneliness and improve social participation and belonging for people with dementia.

The review, published in *Current Opinion in Psychiatry*, used research published in Medline, Medline ePub ahead of print, Embase, PsycINFO, CINAHL, Emcare and Cochrane Library of peer-reviewed journal articles published between January 2019 and June 2020.

"Previous reviews looking at social health interventions focused solely on healthy older adults, excluding people living with dementia," said lead author Dr Suraj Samtani. "Other reviews focused on social connectedness as a protective factor and social isolation as a risk factor for cognitive decline or dementia in healthy older population."

"Also, most interventions for people living with dementia focus on improving cognitive function or physical health, with the social wellbeing of these people often neglected." The review examined recent interventions with social health outcome measures, including interventions across multiple settings from communities to assisted living facilities.

The review revealed that music and/or dance groups significantly improved social participation and belonging for people with dementia and can help to reduce loneliness.

The review also addressed studies involving socially assistive robots and other technology, which produced mixed results but warrants further exploration.

[DOI: 10.1097/YCO.0000000000000683](https://doi.org/10.1097/YCO.0000000000000683)



STROKOG is an international consortium of longitudinal studies of cognitive disorders following stroke, TIA, or small vessel disease. Led by Professor Perminder Sachdev and developed under the auspices of VAS-COG (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 35 international studies participating in STROKOG, which include the following countries: Australia, Bulgaria, China, Finland, France, Germany, Hong Kong, Ireland, South Korea, Nigeria, Poland, Singapore, South Africa, Sweden, The Netherlands, Scotland, Ireland, United Kingdom, and the USA.



Jess Lo
Study Coordinator

In 2021, the following new studies joined STROKOG:

- PROCAS from the Netherlands
- Hallym VCI cohort from South Korea

We published a paper in the *Stroke* journal titled 'Long-Term Cognitive Decline After Stroke: An Individual Participant Data Meta-Analysis'. The project was led by consortium co-ordinator Jess Lo and it included 9 STROKOG studies. We found that patients with stroke experience cognitive decline that is faster than that of stroke-free controls from 1 to 3 years after onset. An increased rate of decline is associated with older age and recurrent stroke.

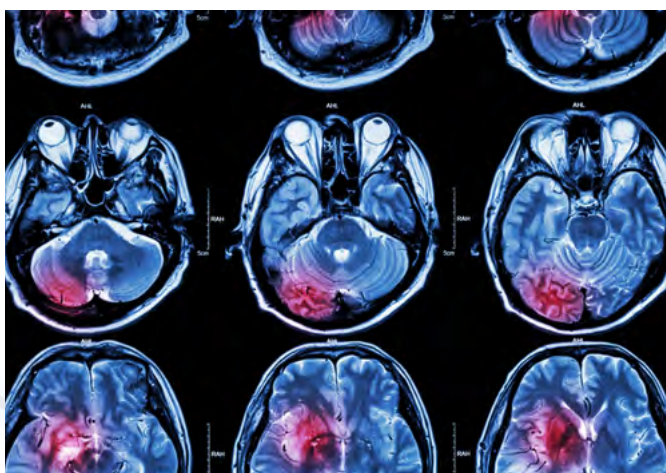
There are 9 on-going STROKOG projects led by CHeBA researchers and external researchers. They include Dr Ben Lam from CHeBA who is finalising a project on post-stroke depression (PSD); Jess completed the key analyses for a new project looking at short-term trajectories of post-stroke cognitive function and which included 9 studies; Dr Nacim Betrouni from the University of Lille, France is making good process with his study using MRI scans to determine patients at risk of post-stroke cognitive impairment; Hanna Laakso from the University of Helsinki in Finland is finalising her paper on domain-specific cognitive impairment and depression as determinants of post-stroke functional disability.

A new project on the comorbidity and interactions of neurobehavioral syndromes is led by Dr Lena Oestreich from the University of Queensland.

Jess was invited to present at the International Stroke Conference 2021 virtual conference held between 17th and 19th March to speak about the STROKOG paper 'Association of Prediabetes and Type 2 Diabetes With Cognitive Function After Stroke' that was selected as a high-impact article of 2020. Perminder was also invited to give a talk about STROKOG at the International Stroke Conference 2021. Ben and Jess presented results from their current STROKOG projects at the bi-annual VASCOG 2021 conference held in August virtually.

The CHeBA communications team set up a private members' section on the STROKOG website this year that allows STROKOG members, which include study PIs and STROKOG researchers to access approved project proposals, updates about progress of the STROKOG projects, and to post on a discussion forum.

A team of researchers led by Professor Sachdev was successful in securing a NHMRC Centre for Research Excellence grant which will partially support STROKOG for the next five years. We also received new ethics approval for STROKOG to continue our research for the next five years beginning October 2021.



Long Term Cognitive Decline Following Stroke

In 2021 STROKOG researchers offered new insights into what happens to cognitive function following a stroke and which risk factors lead to faster cognitive decline.

Although post stroke loss of cognitive ability is common, the trajectory and full extent of brain changes after stroke remains unclear.

Lead author and Study Coordinator of the Stroke and Cognition Consortium (STROKOG), Jess Lo, said the researchers wanted to find out how the cognitive performance of stroke survivors changes over time, specifically whether brain function declines rapidly at a steady state soon after having a stroke.

The researchers also set out to determine the risk factors for cognitive decline after stroke.

The analysis, published in *Stroke*, included 9 studies from STROKOG across 7 countries, including Australia, Asia, Europe and the United States. 1488 stroke patients with ischaemic stroke and a mean age of 66 years were included in the study. The patients were followed up for a median of 3 years.

"We discovered that the cognitive function of stroke survivors improves for a short period soon after a stroke and then decreases – beginning from around one-year poststroke."

Jess Lo

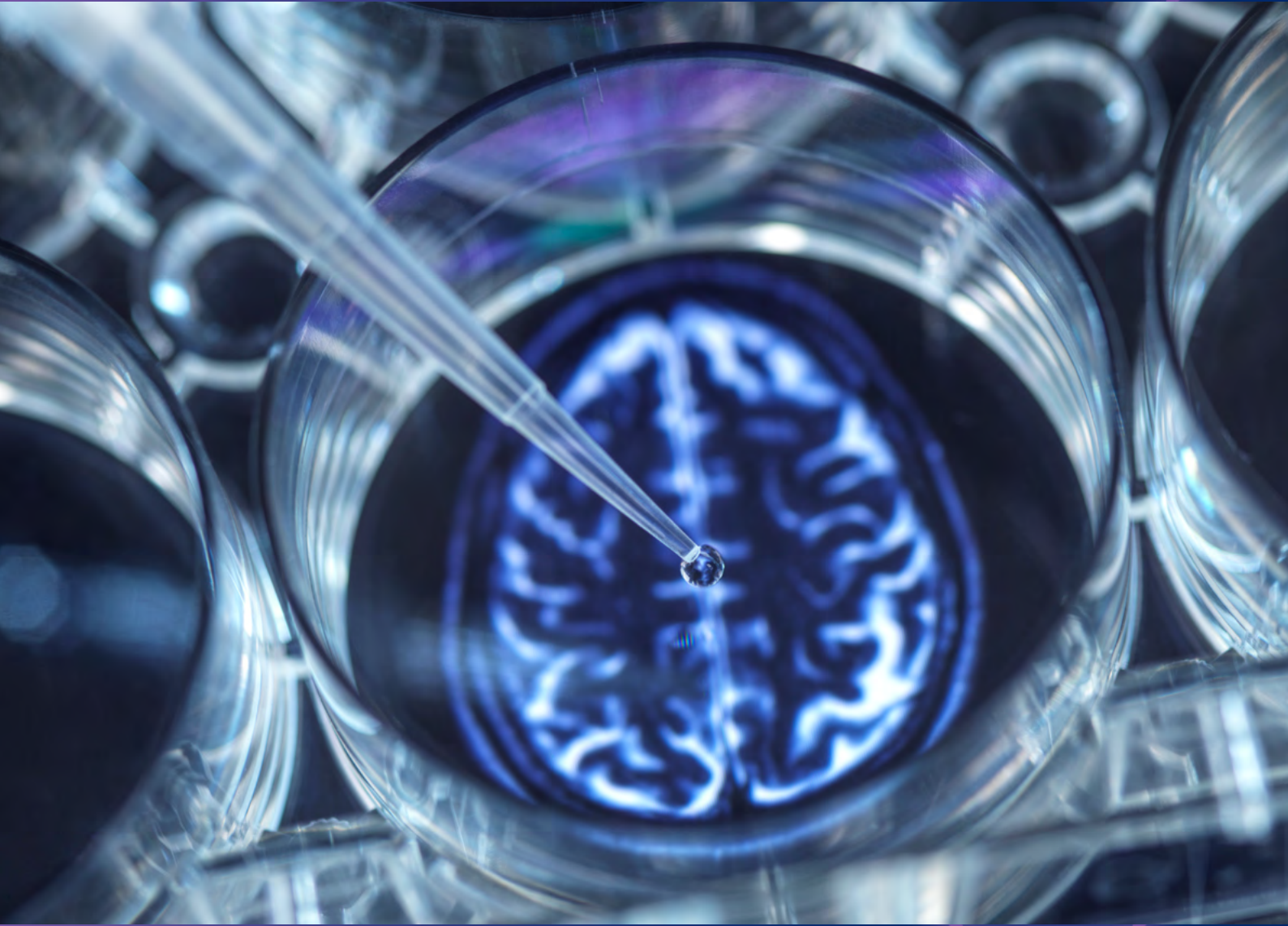
"The decline in stroke patients was small, but faster than that of individuals without stroke, and those with a second stroke during follow up had a much faster rate of cognitive decline."

"We also found that the decline in older stroke patients, compared with younger stroke patients, happened more quickly," said Lo.

According to Lo this research is significant because the results have implications for the design of clinical trials of therapies to prevent or slow poststroke cognitive decline, which should take into consideration the trajectory of initial improvement and subsequent decline in cognition after stroke. Our results could also help clinicians better understand and plan for the long-term needs of patients with stroke.

[DOI: 10.1161/STROKEAHA.121.035796](https://doi.org/10.1161/STROKEAHA.121.035796)

Longitudinal Studies



“Studying people repeatedly over time is the best way to understand ageing and the development of dementia.”

Professor Perminder Sachdev AM

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 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 2021 saw participants complete their final follow-up activities. Approximately 70% of participants have follow-up data and we appreciate the efforts of all participants through the entire trial, particularly during the disruptions of 2020 and 2021. Data collection has ended and we look forward to sharing results in 2022.

Staff

- Professor Henry Brodaty
- Professor Perminder Sachdev
- Tiffany Chau
- Fleur Harrison
- Dr Megan Heffernan (Study Coordinator)
- Juan Carlo San Jose



Dementia Prevention Action Plan Needed Now

Co-Director Professor Henry Brodaty was a contributing author to a Perspective published by *The Medical Journal of Australia*, with a call for dementia prevention to be Australia's next public health area of focus.

The authors are advocating for "substantial, timely, and sustained investment in dementia prevention". Professor Brodaty said that the call for a National Dementia Prevention Plan is timely.

"We now have enough evidence that many lifestyle changes can reduce the risk of dementia by 40% or more."

"This needs a whole-of-government approach and creative ways of helping all of us change our behaviours."

Professor Henry Brodaty AO

"ChEBA is currently trialling an online coaching course – Maintain Your Brain – as one way of achieving these aims," said Professor Brodaty.

The multilayered action plan with eight recommendations can be viewed in *The Medical Journal of Australia*.

[DOI: 10.5694/mja2.50972](https://doi.org/10.5694/mja2.50972)



Older Australian Twins Study

Highlights from 2021

Eleven papers were published in scientific journals, including *Behavior Genetics*, *Nature Genetics*, *The Journal of Gerontology: Series A*, and *Neurobiology of Ageing*. In addition, one conference poster was presented online in June 2021 by Teresa Lee at the 51st Behavior Genetics Association Meeting.

The first wave of data collection on OATS Online was completed in July 2021, with 300 participants completing all activities. A significant minority (45%) of current OATS participants preferred to complete paper questionnaires instead of online assessments. The change to online delivery changed the assessment tools used for neuropsychological testing. The new online neuropsychological tests brought new challenges for participants and the OATS team. Nevertheless, the second wave of OATS Online began in November 2022, incorporating participant feedback.

The OATS Online website was launched in November 2021, with Australia-wide radio, print, and online media coverage. The media coverage brought new participants into OATS Online, with several twin pairs ready to begin participation during the second wave of OATS Online in January 2022.

OATS continued our contribution to several consortia, including IGEMS (Interplay of Genes and Environment across Multiple Studies), a collaboration between 18 twin studies worldwide, incorporating 76,000 twin participants. OATS contributed one IGEMS paper in 2021, authored by OATS team members Vibeke Catts, Teresa Lee, and international collaborators.



Study Participants Barbara Setterfield and Kathleen Byrne

OATS also contributed three papers to the ENIGMA Network, authored by Karen Mather and Perminder Sachdev, and many ENIGMA collaborators.

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.



Dr Vibeke Catts
Study Coordinator

Staff

- | | |
|-------------------------------|---------------------------|
| ✧ Professor Perminder Sachdev | ✧ Dr Amanda Selwood |
| ✧ Professor Henry Brodaty | ✧ Dr Teresa Lee |
| ✧ Professor Julian Trollor | ✧ Dr Karen Mather |
| ✧ Dr Vibeke Catts | ✧ Dr Anbupalam Thalamuthu |
| | ✧ Juan Carlo San Jose |

Students

More than thirty students have used OATS data in their research projects. One of these, Xi (Sophie) Chen, graduated with her PhD in 2021. Ongoing PhD students include:

- | | |
|--------------------|--------------------|
| ✧ Toyin Abdusalam | ✧ Andrea Lammel |
| ✧ Abdullah Alqarni | ✧ Annabel Matison |
| ✧ Chao Dong | ✧ Dr Rebecca Koncz |
| ✧ Annette Spooner | |

In addition, three honours students, Andy Yu, Ewan Barnett, and Shizuka Hayashi, and one ILP student, Christabella Surono, completed their projects using OATS data.

To find out more contact twins@unsw.edu.au

New Direction in Research Comparing Brain Health of Twins

In 2021 OATS took advantage of technology with a move to an online platform, to reach twins residing outside of metropolitan areas.

The launch of OATS Online will not only enable the inclusion of 1/3 of Australian twins living outside major cities but will also facilitate the study of differences in access to specialist health care, health seeking behaviour and other potential contributors to the shortened lifespan of people living in regional and rural areas.

Commencing in 2007 to investigate genetic and environmental differences and how they relate to either healthy brain ageing or age-related neurocognitive disorders, the study takes advantage of the fact that identical twins share 100% of their genetic code, whereas non-identical twins share only approximately 50%. This means that twin studies provide a unique opportunity to identify which specific factors contribute, and which contribute the most, to health outcomes in older age.

Study Coordinator and Research Manager at CHeBA, Dr Vibeke Catts, said that advances in information technology – particularly the refinement of computer administered cognitive tests - now allows researchers to carry out comprehensive and valid neuropsychological assessments with twins in their own home, using an online computer environment. This is something that was not feasible when the study was first launched. Converting to an online platform will also likely lead to policy change and improvements in health care.



Study Participants Shirley Holland and Pearly Hadaway

The online version of the Older Australian Twins Study will retain a longitudinal design – which is a critical component in mapping progression to disorders of older age such as dementia - with planned neuropsychological assessments annually, as well as the collection of detailed lifestyle, mental activity, physical activity and dietary information. It will also continue to examine genetics.

The Older Australian Twins Study Online is targeting recruitment of 1000 twin pairs for the online study with most participants expected to be healthy individuals living in the community.

To find out more contact twins@unsw.edu.au

Sydney Memory and Ageing Study

The Memory and Ageing Study (MAS) began in 2005 and officially concluded at the end of 2020, making it the largest running single cohort study of ageing in Australia.

MAS is renowned for its data nationally and internationally largely because the study has followed the same cohort (e.g., study participants) continuously for almost 15 years. In that time, researchers have gathered a wealth of data around sociodemographic, clinical, neuropsychological, neuroimaging, biochemical, genetics, and proteomics factors associated with brain ageing. Using many data points from the same participants allowed us to look at individual changes over time and better understand what factors predict healthy cognitive ageing versus neurodegenerative diseases like dementia.

MAS began in 2005 with a baseline sample of 1037 older Australians aged 70 – 90, without a dementia diagnosis at the time. Participants underwent extensive face-to-face assessments every two years (called a “Wave”), which included comprehensive neuropsychological testing, a medical examination, detailed medical history, blood

draws, genetic sequencing, and for some participants, brain imaging. Participant and their informants (close friend or family member) were also asked to complete questionnaires about sociodemographic, health, lifestyle, and other factors at each Wave. In December of 2020, when MAS concluded, 258 original participants remained active in the study.

Although MAS is no longer actively testing participants it still contributes valuable data to research projects and student theses. To date, MAS data has contributed to 191 publications in in top-tier scientific journals, with 13 published in the last year alone. In 2021, 15 external research groups requested MAS data for new projects and MAS additionally contributed data to 7 international dementia and ageing consortia. There are currently 25 ILP, Honours, Masters and PhD candidates who are using MAS data as part of their research projects and theses.

Highlights from 2021:

- MAS Investigators and other internationally recognised experts completed and submitted an NHMRC Clinical Trials and Cohorts grant to refresh

the study (outcome pending).

- MAS COVID-19 data was cleaned and shared with studies investigating the impact of the pandemic on older adults around the globe.
- MAS Co-Investigators, PhD and Honours Students have created three novel measures of frailty using MAS data that are now available for release.
- MAS data contributed to 13 new manuscripts and 23 student theses.
- MAS contributed data to 14 global dementia consortia projects in 2021.
- By the end of 2021, all MAS Wave 7 data will be cleaned and released.



Dr Katya Numbers
Study Coordinator

Staff

- | | |
|-------------------------------|--------------------------|
| ○ Professor Henry Brodaty | ○ Professor Brian Draper |
| ○ Professor Perminder Sachdev | ○ Dr Nicole Kochan |
| ○ Associate Professor Wei Wen | ○ Dr Karen Mather |
| ○ Professor Julian Trollor | ○ Dr John Crawford |
| | ○ Dr Ben Lam |
| | ○ Dr Katya Numbers |

Students

- | | |
|----------------------------|----------------------|
| ○ Annabel Matison | ○ Annette Spooner |
| ○ Abdullah Alqarni | ○ Fleur Harrison |
| ○ Russell Chander | ○ Fatemah Khorshidi |
| ○ Sophie Chen | ○ Dr Matthew Lennon |
| ○ Jared Cheung | ○ Nithin Manchery |
| ○ Chao Dong | ○ Zara Page |
| ○ Dr Jing Du | ○ Toyin Abdulsalam |
| ○ Li Li | ○ Dr Mathew Paradise |
| ○ Premilla Chinnappa-Quinn | ○ Mary Revelas |
| | ○ Gurjeet Kaur Virk |

Self-Reported Hearing Loss Linked to Increased Risk of Dementia

A six-year study of older Australians in CHeBA's Sydney Memory and Ageing Study uncovered an Australian-first association between the impact of hearing loss on cognitive abilities and increased risk for dementia.

The research, published in *Aging, Neuropsychology and Cognition*, used data from 1037 Australian men and women aged 70-90 years enrolled in the Sydney Memory & Ageing Study from 2005-2017.

Individuals who reported moderate-to-severe hearing difficulties had poorer cognitive performances overall, particularly in the domains of Attention/Processing Speed and Visuospatial Ability. They also had a 1.5 times greater risk for MCI or dementia at the 6 years' follow up.



Lead author at Macquarie University's Department of Cognitive Science, Dr Paul Strutt, said the findings provide new hope for a means of reducing risk of cognitive decline and dementia in individuals with hearing loss.

"The presence of hearing loss is an important consideration for neuropsychological case formulation in older adults with cognitive impairment."

Dr Paul Strutt

"Hearing loss may increase cognitive load, resulting in observable cognitive impairment on neuropsychological testing."

Co-Director of CHeBA and co-author, Professor Henry Brodaty, said the study was the first of its kind to identify the relationship between hearing loss and risk for mild cognitive impairment or dementia in a large Australian-based study of older adult men and women.

[DOI: 10.1080/13825585.2020.1857328](https://doi.org/10.1080/13825585.2020.1857328)

A Tribute to Lilian Keldoulis

CHeBA's Sydney Memory and Ageing Study is one of the largest continuously running studies of cognitive ageing in Australia with the aims of investigating rates and predictors of healthy cognitive ageing, mild cognitive impairment and dementia in older Australians.

An extraordinary 1,037 older adults have generously committed their time to this research for 15 years. One of these incredible people was Mrs Lilian Keldoulis.

Lilian was born in Sydney in 1931, the second daughter to Greek immigrant parents Betty and Mick Adams.

When Lilian passed away peacefully at home on Christmas Eve 2020, she left behind a multitude of memories across five adoring children (Debbie, Janet, Robert, Richard and John), 10 grandchildren, a great-grandson and a large circle of friends, many of whom donated to research at CHeBA in lieu of flowers.

According to her children, v was fascinated by new research and ideas and was a strong advocate for education. She was always active, being a member at the Australian Golf Club for 50 years and a keen bridge player. These ideals and cognitive interests, coupled with her compassion for a much-loved cousin who suffered from dementia and ended up in a nursing home, are likely what prompted her to become a study participant with CHeBA.

Lead investigators of the Sydney Memory and Ageing Study, Professor Henry Brodaty and Professor Perminder Sachdev, say that without people like Lilian and their families, CHeBA would not be able to conduct long-term research looking at healthy brain ageing.

Study Coordinator Dr Katya Numbers echoes this sentiment.



"The fact that donations to CHeBA were given in lieu of flowers at Lilian's funeral really speaks to her legacy as someone who wanted to give back and make a difference. I am very grateful to these individuals and their families who are invaluable to our research.

"The information learned through people like Lilian will contribute to many new and important findings for years to come."

Dr Katya Numbers



Sydney Centenarian Study

The Sydney Centenarian Study (SCS) was launched in 2007, with 445 Sydney residents aged 95 and above recruited, until the study went on hiatus at the end of 2020. 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 study now has had at least 197 participants who have reached 100 years or older (including one super-centenarian of 110 years of age); and some of our recent participants completed six research assessments over the course of three and a half years.

A wealth of data was collected, which will allow insights into Australia's oldest individuals, including cognition, physical health, psychological health, medical history, medications, functional independence, health behaviours, and falls. Participants also complete a brief physical exam. A knowledgeable person who knows the participant well was interviewed after each assessment to supplement the information provided by the participant as well as comment on their degree of functional independence from an observer's perspective. In addition, optional components of the study provide invaluable information on the biology of centenarians.



Fleur Harrison
Study Coordinator

In total, 64% of participants have provided a blood sample for genetics and proteomics analysis; 12% of participants have undergone structural brain imaging (MRI).

There are currently a number of students and postdoctoral fellows who are using SCS data as part of their research projects, and we anticipate a number of publications to be published in the near future, giving novel insight into longevity, thanks to this unique cohort.

A project to examine the gut microbiome of centenarians is continuing and we are seeking volunteers for this unique study. As a novel project, we are planning to develop a web-based platform to collect data from centenarians around the country as a large national study, and are seeking funds to launch this project.

Happiness of Centenarians a Severely Neglected Area of Research

In 2021, CHeBA researchers led a world first systematic review on the subjective wellbeing of centenarians, and highlighted the need for clearer definitions of 'happiness', 'life satisfaction' and 'positive affect'.

Near centenarians and centenarians remain an underrepresented group in ageing research, despite these populations increasing rapidly – with an expected global rise from 441,000 in 2013 to about 20 million in 2100.

The review, published in *Aging & Mental Health*, identified 18 studies that followed patients from several weeks to 18 years.



Professor Brodaty said that although interest in subjective wellbeing and its relationship with exceptional longevity is increasing, the happiness of centenarians remains a severely neglected area of research which needs to be addressed.

Lead author Adrian Cheng said research into the happiness of centenarians is important because examination of subjective wellbeing in this unique group can reveal factors associated with good psychological health.

"Having a positive view about our own health, or possibly simply having better health, as we age is important as part of the ageing process."

Adrian Cheng

"Future research should be directed towards interventions that promote subjective wellbeing in the oldest old."

[DOI: 10.1080/13607863.2021.1891197](https://doi.org/10.1080/13607863.2021.1891197)

PhD Completions

Dr Sophie Xi Chen

The relationship between dietary patterns and neurocognitive health among older adults

Diet may be a promising strategy to postpone, slow or prevent cognitive decline and reduce the risk of dementia. My thesis investigated the important question as to whether, and how effective, different types of dietary patterns and related food groups are in protecting against neurocognitive decline in older adults.

I am very thankful to have been able to undertake my PhD at CHeBA - where I received incredible academic guidance, constant support, and great encouragement to strive for my best as both researcher and clinician.

Sophie was awarded the UNSW Dean's Award for Outstanding PhD Theses; which is given only to the top 10% of PhD theses.

Dr Sophie Xi Chen was supervised by Professor Henry Brodaty



Dr Heidi Foo

Genetic and environmental influences on the brain functional networks in older adults

More often than not, genetics affects the brain's structure and ability to function. However, not everything can be explained by genetics. Environmental factors such as lifestyle, smoker status, exercise regularity and alcohol consumption also affect brain structure and function, as well as alter internal cognitive processes.

By examining samples of cognitively healthy older people and determining how different factors affect brain health before looking at pathology alone, we can then establish what is normal ageing. I hope that my research can translate to clinical application to enhance the quality of treatment received by people with dementia.

I am grateful to have undertaken my PhD with CHeBA, where my supervisory team has shown me significant support, guidance, and encouragement. Their insights have sharpened my thinking, brought my work to a higher level, and allowed me to grow both academically and personally.

Dr Heidi Foo was supervised by Professor Perminder Sachdev and Associate Professor Wei Wen



Dr Matt Paradise

Neuroimaging of cerebrovascular disease

The importance of vascular disease in dementia and brain health is being increasingly recognised, both as a disease in its own right and as a factor that worsens the risk and expression of Alzheimer's disease. As Cerebrovascular disease research is still relatively in its infancy, increased understanding of the disorders will allow practitioners to make better diagnoses, more accurately differentiate dementia subtypes from one another and better discuss prognosis.

My thesis examined how we can better quantify vascular damage to the brain, using MRI imaging. I assessed the value of several novel markers of damage to the small vessels in the brain and then considered how they could be combined into an index. It is hoped that this research will lead to more accurate dementia diagnoses, ultimately helping both the clinician, the patient and their family.

I am very grateful to have been able to undertake my PhD in CHeBA and DCRC – I have received great support, guidance and encouragement from my supervisors, principally Professor Sachdev as well as the whole CHeBA team.

Dr Matthew Paradise was supervised by Professor Perminder Sachdev and Associate Professor Wei Wen



Dr Lucia Chinnappa-Quinn

The association of acute illness hospitalisation with cognitive trajectory in the Sydney Memory and Ageing Study

Cognitive decline has been documented following certain kinds of hospitalisation, such as surgical hospitalisation and admissions complicated by delirium or requiring intensive care. My project investigated whether these post-hospitalisation cognitive changes were common to all types of acute hospitalisation. My thesis documented the magnitude and direction of these cognitive changes and associated risk factors using CHeBA's Sydney Memory and Ageing Study sample, combined with electronically linked hospitalisation data from the NSW Admitted Patients Data Collection.

I am very appreciative of the research guidance and editorial wisdom of my supervisors and their enormous statistical support. I am also grateful to Professor Henry Brodaty and the MAS Research Team, and the DCRC and the Australian Society of Anaesthetists for funding. It was a tremendous learning experience.

Dr Lucia Premilla Chinnappa-Quinn was supervised by Professor Perminder Sachdev, Dr Nicole Kochan, Dr Ben Lam, Dr John Crawford and Dr Steve Makkar



Dr Heidi Welberry

Using linked health and social care data to monitor dementia incidence and evaluate dementia care in Australia

My thesis explored the use of linked administrative data for detecting and monitoring dementia in Australia and used these data to understand the care pathways followed by people with dementia, and to address policy-focused questions aimed at improving dementia care. This work included evaluating the impact of home care programs on reducing time spent in residential care and the impact of changing general practitioner on psychotropic prescribing in residential care. I hope the findings from these studies can help to drive future improvements to aged care programs in Australia to better support people living with dementia.

I feel so lucky to have had the privilege to work with my incredibly knowledgeable and wise supervisors including Professor Louisa Jorm from the Centre for Big Data Research in Health and Professor Henry Brodaty from CHeBA. I have learnt so much about dementia from Henry, and I continue to be inspired by how hard he works to improve the lives of people living with dementia.

Dr Heidi Welberry was supervised by Professor Henry Brodaty

Dr Heidi Welberry has been well cited from her 2020 and 2021 papers, including:

Welberry HJ; Brodaty H; Hsu B; Barbieri S; Jorm LR, 2020, 'Impact of Prior Home Care on Length of Stay in Residential Care for Australians With Dementia', *Journal of the American Medical Directors Association*, vol. 21, pp. 843 - 850.e5, <http://dx.doi.org/10.1016/j.jamda.2019.11.023>

Welberry H; Brodaty H; Hsu B; Barbieri S; Jorm L, 2020, 'Measuring dementia incidence within a cohort of 267,153 older Australians using routinely collected linked administrative data', *Scientific Reports*, vol. 10, pp. 1 - 14, <http://dx.doi.org/10.1038/s41598-020-65273-w>



Congratulations to PhD Student Annette Spooner,

who received the Faculty of Engineering Outstanding Higher Degree Research Student Award for her thesis Predicting Dementia using Machine Learning, as well as the Norman Foo Memorial Best Research Paper Prize.

Annette's thesis involves developing advanced machine learning techniques that are capable of analysing high-dimensional, heterogeneous, clinical data. Such data presents challenges to both statistics and machine learning, but machine learning can give more accurate results than traditional statistical methods when modelling this type of data.

Annette is supervised by Professor Arcot Sowmya (CSE), Associate Professor Gelareh Mohammadi (CSE) and Professor Perminder Sachdev



Other Student Achievements



Dr Alice Powell was successful in receiving an NHMRC Postgraduate Scholarship to fund her PhD examining exceptional cognition in older people or 'super-ageing.' It will focus on how super-ageing is defined, prevalence and predictors, trajectories of cognitive maintenance or decline in these individuals and associations with other aspects of ageing well. The project draws data from all three of CHeBA's longitudinal studies: the Sydney Centenarian Study, Sydney Memory and Ageing Study and the Older Australian Twins Study.



Zara Page won a UNSW Ageing Futures Institute Award for coming second in the Celebrating Students in Ageing Research Competition with her talk on "Towards achieving culture-fair neuropsychological assessment for MCI and dementia in CALD older Australians". Zara was also successful with a \$500 UNSW Development and Research Training Grant and was awarded \$100 school funds (via CogSCAN) to attend a professional course.

CHeBA Publication Awards



Dr Katya Numbers won the 2021 Publication Award in the Early Career Category for her paper published in *Nature Reviews Neurology*: The effects of the COVID-19 pandemic on people with dementia.



Annabel Matison was awarded the Publication Award in the student category, for her paper: Associations between nutrition and the incidence of depression in middle-aged and older adults: A systematic review and meta-analysis of prospective observational population-based studies.



Our Community



"I continue to hope that research will uncover the complex layers of this disease and find a way to earlier intervention, effective treatments, and possibly even a cure."

**Richard Grellman AM
Spokesman, The Dementia Momentum**

The Dementia Momentum

Spokesman's Report

As CHeBA will mark its tenth anniversary next year, it feels appropriate to reflect on the evolution of The Dementia Momentum and give recognition to the extraordinary number of partners, donors, fundraisers and supporters that have chosen to support it.

When I accepted the request to be Spokesman for The Dementia Momentum, there were almost 150,000 fewer people living with dementia. My hope was to bring a like-minded community together to change the future of Alzheimer's disease and other dementias for the generations to follow, through significant research funding and a willingness to increase the conversation to help reduce stigma and improve awareness.

I am pleased to see that this hope was not in vain and the objectives are increasingly being met.

In 2021, The Dementia Momentum saw tremendous involvement across both the corporate and community sectors.

KPMG Sydney announced its continuing support of the initiative as major in-kind partner, and we were extremely fortunate to be able to hold our annual luncheon hosted by KPMG at their Barangaroo offices, in June; an event that had been thwarted the previous year by the global pandemic. I am enormously grateful to KPMG for their ongoing involvement, and particularly to Senior Partner Eileen Hoggett for the steadfast commitment she has shown to the cause.

Through this year, 317 individuals, Foundations and corporate organisations have donated or pledged a total of \$571,868 to The Dementia Momentum initiative, taking the total raised so far to over \$8.8 Million. 64 senior corporate executives have committed themselves to the March 2022 Wipeout Dementia event.

On World Alzheimer's Day, we launched the Change Makers – Next Gen Philanthropy initiative with Ambassadors PJ Lane, Ed Caser and Keri Kitay – and received national media coverage. With a vision of empowering emerging leaders aged 18-40, this initiative was launched in partnership with KPMG Australia and promotes the importance of modifiable lifestyle factors to reduce the risk of Alzheimer's disease and other dementias.

I extend my gratitude to the initiative's major donors: the Vincent Fairfax Family Foundation, the John Holden Family Foundation, Roger Layton AM, the Mostyn Family Foundation, Phil Cave and Judy Harris, the Sachdev Foundation, Peter and Yvonne Halas, Morgans Foundation and Idle Acres Foundation.



Dr Richard Grellman
Spokesman,
The Dementia Momentum

To the individuals who supported The Dementia Momentum by running the 2021 Blackmores Virtual Sydney Running Festival, coordinated matching gifts through employers, arranged donations in lieu of flowers after the passing of a loved one, or secured a sponsorship for a CHeBA event, I applaud you.

I extend my deepest personal thanks to every other donor that has given their dollars to this cause – because the reality is that every single dollar does count.

I continue to hope that research will uncover the complex layers of this disease and find a way to earlier intervention, effective treatments, and possibly even a cure – so that people in the future do not endure what I and my wife Suellen have endured, and what my children and grandchildren have missed out on.

A handwritten signature in black ink, appearing to read 'Richard Grellman'.

Dr Richard Grellman AM

Richard's wife Suellen has advanced young-onset Alzheimer's disease and has been in high-level care since 2016.



KPMG Sydney Commits to Ongoing Support for The Dementia Momentum

The Dementia Momentum celebrated its anniversary with KPMG Sydney hosting an exclusive lunch for major donors and corporate partners of the initiative at their Barangaroo offices on Wednesday, 2 June 2021, with KPMG announcing its commitment to continued partnership of the initiative KPMG Sydney has been In-kind partner of The Dementia Momentum since 2015.

The event, sponsored by private markets finance and investment house Wingate featured speeches by Dr Richard Grellman AM, Professor Henry Brodaty AO, Professor Perminder Sachdev AM and Mr Edward Caser. Guests included senior executives involved in the Wipeout Dementia corporate surf fundraiser, which raises money for The Dementia Momentum initiative.

Senior Partner at KPMG Eileen Hoggett, opened the anniversary event with a dire warning.

"Globally and in Australia, the population is ageing. Currently about 15% of the Australian population are over 65 years of age and this is projected to increase to 25% by the middle of the century.

Spokesman for the initiative Dr Richard Grellman AM – who spent 32 years working at KPMG and whose wife Suellen has very advanced young onset Alzheimer's disease - addressed the global pandemic and reminded all guests that although it feels Australia may be getting on top of COVID-19 that the dementia curve remains unabated.

"Our only hope is research to unlock the cause, treatment and thereby prevent or cure this disease."

Dr Richard Grellman AM

Guest speaker Edward Caser, boutique investment platform co-founder whose mother was diagnosed with Alzheimer's disease in 2016, called upon the corporate sector to further support The Dementia Momentum.

"From my experience in trying to find information, work out who is actively doing something about this disease, my feeling is the group at CHeBA truly are leaders in dementia research not just in Australia, but globally," he said.

Ms Hoggett paid special tribute to key donors for their significant contribution to The Dementia Momentum, and extended collective condolences to the family of John Holden, who passed away last week. The J Holden Family Foundation was a major donor of The Dementia Momentum.



Eileen Hoggett



Dr Richard Grellman AM



Edward Caser

Change Makers – Next Gen Philanthropy

This year in line with World Alzheimer's Day on 21 September and in partnership with KPMG Sydney, CHeBA launched Change Makers – Next Gen Philanthropy.

With a vision of empowering emerging leaders aged 18-40 to elevate philanthropic support of dementia research, the new initiative will promote the importance of modifiable lifestyle factors to reduce the risk of Alzheimer's disease and other dementias.

KPMG's Eileen Hoggett said the initiative aligned with KPMG's core values.

"As an organisation we are extremely proud of our people and the importance they place on social responsibility," said Ms Hoggett. "I encourage our next generation leaders to get involved."

We welcomed Ambassadors for the new initiative, PJ Lane, Edward Caser and Keri Kitay, who have all witnessed the devastating impact of Alzheimer's disease.

PJ Lane, who gave up his burgeoning basketball career in the United States to return to Australia and help look after his father, entertainer Don Lane, says the next generation should already be thinking about their brain health in late life.



PJ Lane, Ambassador

"By the time those currently aged 18-40 are in their 50s, 60s and 70s, it is expected that the number of people with dementia will have more than tripled," said PJ.

"Change Makers will support research that will inevitably impact their own future."

PJ Lane

Dr Richard Grellman AM said that given three in 10 Australians over 85 have dementia, there is a critical need for increased investment in research toward prevention of Alzheimer's disease and other dementias.

"At the same time, the goal is to advance knowledge across all generations to maintain physical activity from a young age throughout life so as to reduce risk of dementia in late life," said Dr Grellman.

"For that to occur, we need the next generation's support of research and awareness raising."



Ruby Pradhan and Lily Calderbank, Change Makers founding philanthropists

Dr Grellman acknowledged the efforts of the initiative's Ambassadors and congratulated the founding philanthropists, Ruby Pradhan and Lily Calderbank.

"Philanthropy isn't just for people who have extraordinary wealth. Through regular giving I am proud to be part of something that improves the world in which we live," said Ruby.



Keri Kitay and Edward Caser, Ambassadors

The Change Makers – Next Gen Philanthropy program provides the next generation of Australians with the opportunity to make an enormous difference, by combining monthly or three-monthly regular giving donations to amount to larger, more impactful research contributions. Change Makers will have access to tours in the CHeBA laboratory and educational workshops covering healthy brain ageing – geared specifically to 18-40 year olds. To become a Change Maker: <https://alumni.unsw.edu.au/giving/Med/Changemakers>.

Sachdev Foundation

Since 2014, the Sachdev Foundation has supported CHeBA, providing significant funding for projects undertaken across multiple research groups, including identifying genetic factors linked to exceptional longevity, examining biomarkers of neurodegeneration in centenarians and near-centenarians with dementia, and identifying retinal biomarkers for dementia.

In 2021, the Sachdev Foundation generously donated \$45,000 to fund nanotechnology research to diagnose Alzheimer's disease and vascular dementia, and a further \$50,000 to fund critical research looking at blood biomarkers for dementia and mild cognitive impairment.

Nanomedicine uses revolutionary technology that deals with nanoscale materials that can interact directly with diseased or damaged cells. The research funded by the Sachdev Foundation exploits recent advances in nanotechnology, magnetic resonance imaging (MRI) and a new, emerging imaging technique - magnetic particle imaging (MPI) - to develop novel magnetic nanoparticles and adapt existing ones to act as contrast agents for the diagnosis of dementia.

The development of these agents will enable MRI, and in the future MPI, to assist with dementia diagnosis, bringing accurate diagnosis of disorders such as Alzheimer's disease and vascular dementia within the reach of all Australians. Thanks to the research funded by the Sachdev Foundation, these diagnostic techniques could potentially replace expensive positron emission tomography (PET) based investigations, making the diagnostic imaging process more readily available.

The Sachdev Foundation is also funding research into blood biomarkers, making it possible for researchers to tap into a wealth of information in blood which aims to distinguish profiles of normal ageing from disease trajectories, identify biochemical targets for lifestyle intervention and to identify potential causative or protective factors for disease onset.

Through the enduring support of the Sachdev Foundation, CHeBA has been able to conduct significant research into diagnosis and treatment of age-related brain diseases.

Mostyn Family Foundation

Founded in 2011 by Bob Mostyn, the Mostyn Family Foundation has been significant supporters of CHeBA since 2019, funding a pilot project on the role of the gut microbiome in ageing successfully and living to 100, research into the blood brain barrier and integrity in the ageing brain, and most recently into lipid profiling of vascular dementia.

This latest contribution from the Mostyn Family Foundation studies the association between dietary patterns, plasma lipid profiles and inflammatory potential in people with vascular dementia, to provide insights into the pathobiology of this disease.

CHeBA's researchers compared lifestyle indicators such as smoking, alcohol drinking, physical activity, diet and plasma lipid profiles, among 150 participants aged between 68 and 106 years old.

Findings showed that vascular dementia participants tend to have higher lipid profiles, do less exercise, and engage less frequently in social interaction and educational or reading activity.

This research concluded that a higher empirical dietary inflammatory index was significantly associated with an increased risk of developing vascular dementia.

This important study funded by the Mostyn Family Foundation underscores the importance of a healthy lifestyle for the prevention of vascular dementia.



Giving in Memory

Melbourne-based donor, Francesca Wood, became a significant supporter of CHeBA's research in 2021 following her Mother's passing from vascular dementia.

Initially, Francesca's generous support came as a personal donation, followed by matching gift support through her employer bp, and donations in lieu of flowers at her mother's memorial service.

Her mother, Mrs Helen Reading, was diagnosed with dementia in 2017 and passed away during the COVID-19 restrictions in Melbourne, on 25 May 2020, causing significant angst for the family who were then unable to hold an appropriate memorial service until almost a year later.

"To endure the devastation of dementia in conjunction with a global pandemic that placed enormous restrictions on our visits to Mum before she passed was truly heartbreaking."

Francesca, a successful Reward Manager with bp, became aware of the research being conducted at CHeBA while attending a Chief Executive Women's Leadership program in 2019.

"It felt extremely fortunate timing to meet Heidi Douglass at the CEW course.



Helen Reading and Francesca Wood

Her passionate delivery of the research being undertaken at CHeBA resonated with me and stayed with me during Mum's last year."

For Francesca, making a personal donation to CHeBA, arranging donations in lieu of flowers and her employer bp matching her donation through their charitable matching-funds program, has felt rewarding and an appropriate tribute to her Mum.

Francesca continued her incredible support of CHeBA's research by participating in the Blackmores Virtual Sydney Running Festival with her husband and two children, together raising an additional \$3,238.

Francesca's ongoing support will have a significant impact on research into vascular dementia at CHeBA.

Professor Roger Layton AM

Emeritus Professor Roger Layton AM, dedicated member of CHeBA's Advisory Committee since 2012 and the father of modern marketing in our region, passed away on 5 June 2021, leaving behind a legacy that will live on in the hearts of his three daughters and those closest to him, and in the minds of future generations of marketing students.

Roger became an advocate for CHeBA and in 2016 made his first donation to The Dementia Momentum initiative of \$25,000, in honour of wife Dr Marilyn Layton who passed away from Alzheimer's disease in 2012. This was the first of many donations he made including a final significant show of support in his Will.

Roger's view was that CHeBA's research was critical to improving future dementia care in Australia and reducing suffering in families like his own.

Roger was the first Professor of Marketing at UNSW, pioneering the first degrees in marketing and establishing the first School of Marketing and its highly successful PhD program.

His principles, philosophies and achievements made an enormous contribution to the field of marketing and



Emeritus Professor Roger Layton AM

research, but it was his enthusiasm for thought-provoking discussion and investigation of ideas that may remain strongest for those that knew him.

"Roger's professional and personal experience and sage advice were invaluable to CHeBA and to me - his support for our Centre extremely generous. We miss him and extend our best wishes to his daughters."

Professor Henry Brodaty AO

The Brain Dialogues

CHeBA's blog continued to have a strong readership throughout 2021. The Brain Dialogues covers a range of topics surrounding brain health, research, sociocultural issues, and donor impact.

Here is an excerpt from one of 2021's most popular articles by Professor Perminder Sachdev; No Place for Ageism in our Society.

There is some evidence that ageism is now more prevalent than sexism or racism.

Nowhere is ageism as pervasive and a contributor to injustice and inequality as in the workplace. Even as many governments are working toward extending work lives and have removed mandatory age-based retirement, older workers face discrimination when seeking new work or maintaining employment in times of economic distress.

Ageing stereotypes not only poison our behaviour towards others, such stereotypes are often internalised by the old persons themselves, affecting their attitudes, aspirations and behaviour.

It does not have to be this way. There are many positive aspects of ageing that are highlighted only infrequently. Not all cognitive abilities decline with age, and some such as vocabulary in fact improve.

Read the full article at <https://cheba.unsw.edu.au/blog/no-place-ageism-our-society>.



Blackmores Virtual Running Festival

Between 19 September and 17 October, a team of dedicated CHeBA runners across three different states took part in the Blackmores Virtual Running Festival.

Walkers and runners took to the streets of Brisbane, Melbourne and Sydney and clocked over 40km, raising close to \$7,000 towards CHeBA's research into Alzheimer's disease and other dementias.

Edward Caser ran for better brain health for all Australians. Having cared for his mother after her Alzheimer's disease diagnosis in 2016, Edward believes that research is critical to altering the course of this insidious disease.



Edward Caser

"I'm proud to support The Dementia Momentum led by CHeBA, which has been a lighthouse for me personally," said Edward.

Fellow runner Francesca Wood ran with her husband and daughters in honour of their mother, mother-in-law and Grandma Helen, who sadly passed away from vascular dementia during the COVID-19 restrictions in 2020.



Francesca Wood and family

"We know she would have wanted to support research to stop this disease so that other people in the future do not go through what she did," said Francesca.

Co-Directors Professor Henry Brodaty and Perminder Sachdev are humbled by the fundraising efforts of all of the walkers and runners as CHeBA strives to change the future of dementia.

In 2022, the Blackmores Sydney Running Festival will be a feature event for CHeBA. To find out more contact janelle.burns@unsw.edu.au.



Jodette Gibson and PJ Lane, CHeBA runners

#WithYou

On October 10, World Mental Health Day and one day before Greater Sydney lifted its lockdown restrictions, we acknowledged the efforts of the World Health Organization (WHO) to scale up mental health services across the globe by launching our #WithYou campaign. CHeBA staff shared messages of support to individuals, families and businesses who suffered during lockdown and calling for Sydney to stay united during such a challenging time.



"To everyone separated from their families during COVID-19, we're #WithYou." *Dr Anne-Nicole Casey*



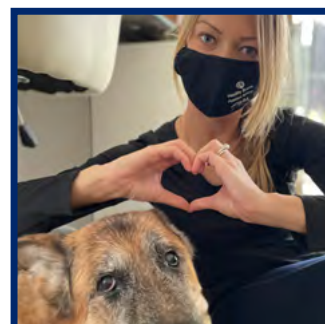
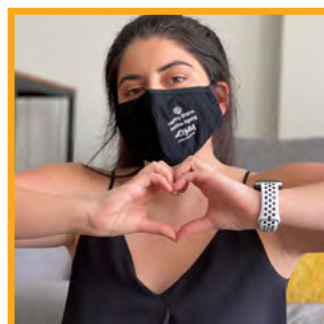
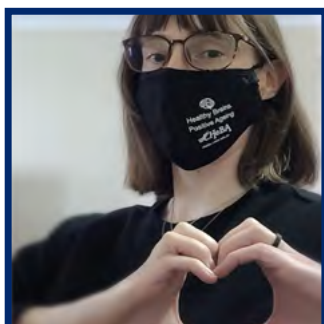
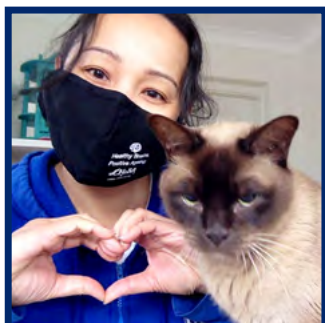
"For carers of those living with dementia, sending you a message of hope and resilience. We're #WithYou." *Nora Wong*



"To the international students who have not been able to see their families, we're #WithYou." *Dr Jing Du*



"To residents and staff of aged care homes, we're #WithYou." *Professor Henry Brodaty*



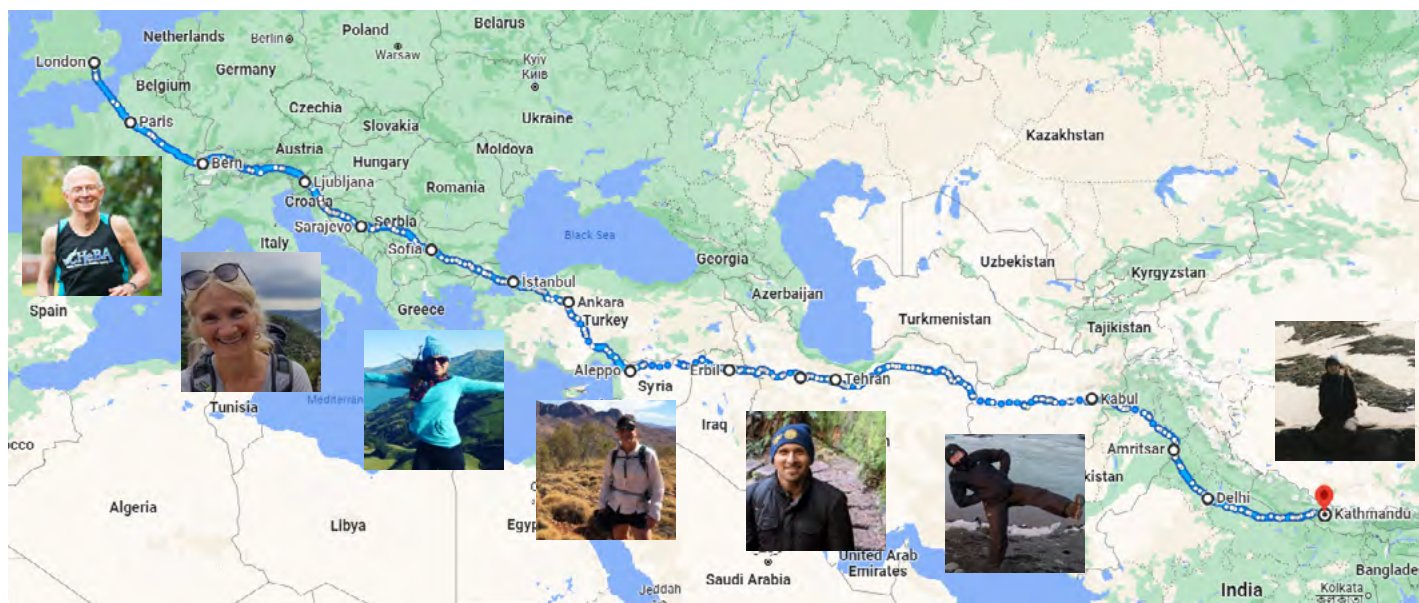
CHeBA Lockdown Challenge

During September – World Alzheimer's Month - CHeBA staff and students united virtually to clock more than 10,000 kilometres from London to the Himalayas to promote the significance of social connectedness and physical health during Sydney's lockdown.

The ambitious distance was a tribute to CHeBA's leaders, Professor Henry Brodaty AO and Professor Perminder Sachdev AM. As a young 26-year old, Co-Director Henry Brodaty chose to study in London for his specialist

training in psychiatry and as such, his first job as a psychiatry trainee was in the Academic Department of Psychiatry, Middlesex Hospital. Co-Director Perminder Sachdev completed his schooling at St Luke's School in Solan, just 1,000kms away from Kathmandu where the Lockdown Challenge concluded.

The CHeBA Lockdown Challenge raised close to \$7,500 to support research not only into early diagnosis, treatment and care for those with dementia, but also its prevention, and the promotion of positive ageing for the future.



CHeBA in the Media

2021 was a prominent year for CHeBA, with a number of high-profile media stories featuring our research.

More than 400 articles were printed online, with more than 30 radio interviews covering CHeBA's research. Significant highlights included coverage of the Older Australian Twins Study coordinated by Dr Vibeke Catts and the Rethink My Drink Study led by Dr Louise Mewton, both in print and on television nationally. Dr Katya Numbers and Professor Henry Brodaty's opinion, Effect of COVID-19 Greatest on People Living With Dementia, published in *Nature Reviews Neurology*, was publicised nationally in many reputable media outlets.

In a year where the importance of social connectedness was consistently recognised, Channel 7 interviewed our resident expert, Dr Suraj Samtani - Leader of CHeBA's SHARED project.

The launch of Change Makers – Next Gen Philanthropy also attracted national attention, with Channel 7 highlighting the innovative program in a dementia feature during peak-time news coverage.

In addition to specific study outcomes and research project launches, CHeBA's researchers were sought regularly for expert comments on radio, in print and on television.



Dr Vibeke Catts



Dr Louise Mewton

Super Agers

The following is an excerpt from the SMH's interview with Professor Perminder Sachdev and Sydney Memory and Ageing Study participant, Nina Malanos, on the concept of super agers.

Study participant Nina Malanos is a 'super ager'; a term describing older adults who perform at the standard of someone at least 20 years younger.

Nina is what's known as a "super ager", says Professor Perminder Sachdev.

He says the term refers to people in their "70s, 80s and beyond" whose ability – whether it be their memory, way of thinking, or even aerobic fitness – is of the standard of someone "at least 20 years younger".

Naturally, the question on everyone's lips is: how does one become a super ager? Sachdev says there are a few common themes among super agers.

First, they tend to live active lifestyles and remain active "even well into their 80s and 90s". They also continue to challenge themselves with new tasks, such as learning a new language or going back to university.

After retiring, they continue to challenge themselves. They also seem to share a similar sunny attitude. "They're not deterred easily and have a sense of optimism."

Genetics also plays a part, Sachdev says. While you



can't control your genes, he says if you do develop a disease such as diabetes or high blood pressure, the key is to "manage it competently".

When it comes to lifestyle factors, Nina ticks all the above boxes. She's never smoked, enjoys an occasional tippie with dinner, has maintained a fairly healthy weight her whole life and eats a healthy diet – with room for dessert. Nina has also stayed physically and socially active her whole life.

She believes her active lifestyle has contributed to her ageing well. Not that she considers herself a "super ager" – she brushes off the notion with a laugh, saying she's "very ordinary".

This article appeared in Sunday Life magazine within the Sun-Herald and the Sunday Age.

Australians are living longer but what does it take to reach 100 years old?

The following is an excerpt from ABC News' interview with 96 year old CHeBA Sydney Centenarian Study participant Patricia Segal.

At age 96, Patricia Segal lives alone in an airy Sydney apartment with views of the sea. Time spent with her feels uplifting, invigorating, and when you ask for her secret Segal doesn't hesitate: her positive and curious attitude is the key to her longevity, she says.

Researchers say Australians are entering an era in which remaining vital well into your 90s will be not just possible, but common. And your 80s may well deliver some of the best years of your life.

The average lifespan of an Australian woman is now about 85, packing on 25 additional years in a century, meaning one in two women will reach this age or beyond.

But researchers like Co-Directors of the Centre for Healthy Brain Ageing Professor Perminder Sachdev, and Professor Henry Brodaty who collaborates with him on the Sydney Centenarian Study, note growing evidence that successful ageing includes less tangible and more mysterious influences.

"We found people who are 100-plus and they are still volunteering in committees and other areas, engaged socially and with their great grandchildren."

Professor Perminder Sachdev AM

"It is this kind of physical and mental activity we tend to see repeated in different [ageing] studies around the world," Sachdev says.

Quality education in childhood, and lifelong learning, is also key. Precisely how it impacts longevity and brain health is not fully understood.



CHeBA Visiting Lecture Series

Throughout 2021, CHeBA continued to host some of the world's leading brain and ageing researchers in a series of interactive webinars open to the public, which are available for viewing on the CHeBA website.

A significant highlight of our 2021 Visiting Lecture Series was from Professor Roddy Roediger of Washington University in St. Louis and former clinician to President Ronald Reagan, whose talk on super ageing and super-duper ageing attracted a significant online audience.

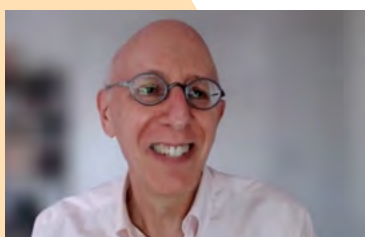
The following talks can all be viewed on the CHeBA site at: <https://cheba.unsw.edu.au/visiting-lecture-series/previous-presentations>.



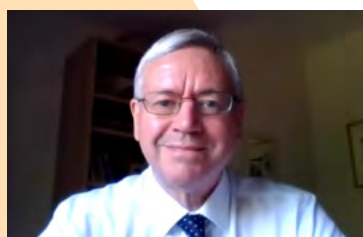
Professor Roddy Roediger
Washington University in St. Louis
Super Ageing and Super-duper Ageing



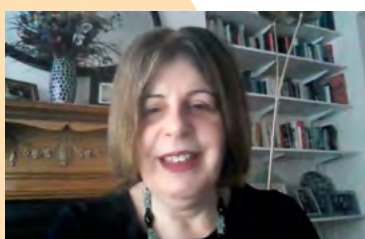
Professor Carol Brayne
University of Cambridge
Population Studies and our Ageing Brains Today



Professor Yaakov Stern
Columbia University
Update on Cognitive Reserve



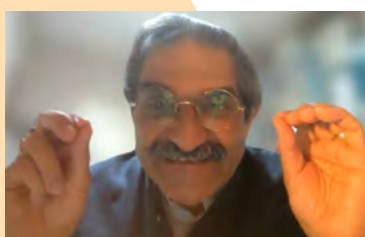
Professor John O'Brien
University of Cambridge
Improving the Diagnosis and Management of Lewy Body Dementia



Professor Gill Livingston
University College London
Preventing Dementia: What Should We Do?



Professor Dilip Jeste
University of California San Diego
Wisdom, Ageing, and the Pandemics



Professor Rajesh Kalaria
Newcastle University
Post-Stroke Dementia

Public Forums

More than 400 people from around the globe joined together online for the October Eastern Suburbs Older Persons' Mental Health Service's healthy ageing forum, ***Keeping Connected: Social Health and Ageing***.

The free event, supported by CHeBA, sought to promote finding ways to remain socially connected and implement strategies to combat adversity, with special guest – social researcher and author of *The Kindness Revolution* Hugh Mackay AO telling the audience that as humans we are members of a social species and therefore built to connect: "We are hopeless in social isolation".

Mr Mackay said the sort of global social trends that have been reshaping us - such as shrinking households, busyness, and our enthusiastic embrace of social media - have all been contributing to social fragmentation and increasing the risk of social isolation.

"This distracts us from the idea that, as members of a co-operative species, we all need to engage with the task of building social harmony."

Other speakers included Postdoctoral Fellow from CHeBA, Dr Suraj Samtani, who discussed the importance of social connections for mental health, Geriatrician and CHeBA Research Fellow Dr Stephanie Ward, who showed a heart-warming highlight from the intergenerational project she was involved with: ABC's *Old People's Home for 4 Year Olds*, and Professor Henry Brodaty, CHeBA Co-Director, who recapped the various stressors we all experienced during the wake of the COVID-19 Ruby Princess outbreak.

Professor Brodaty explained the stress response in relation to the COVID-19 pandemic and touched on how resilience can moderate the response.

"Resilience is managing stress. Resilient people use more active coping styles to manage adversity." - Professor Henry Brodaty AO

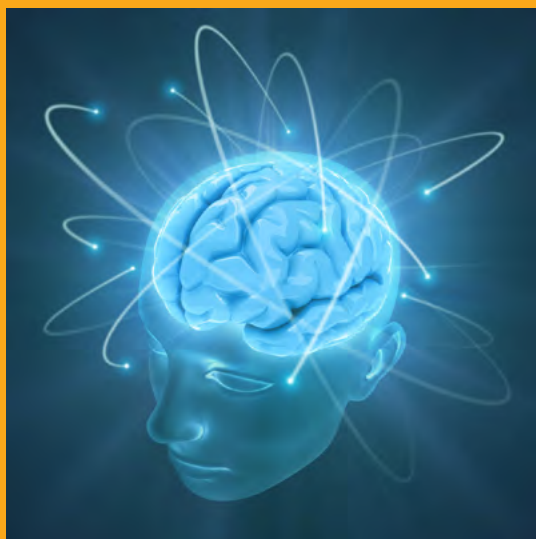
Interestingly, during the pandemic older adults have demonstrated less anxiety and depression than younger adults possibly on the average they are more resilient and more capable of regulating emotions than younger adults. This is due to the fact that older adults have a reservoir of knowledge and skills to help them adjust – and according to Professor Brodaty this is a learned process.

"Coping strategies are essential for our wellbeing," said Professor Brodaty, who then listed four core components to building resilience: social connections, fostering wellness, embracing healthy thoughts and finding purpose.



Demystifying Brain Research Webinar

CHeBA Postdoctoral Fellow Dr Suraj Samtani was the key speaker at Youth Neuro Australia's 2021 webinar event as part of Brain Awareness Week in March. Dr Samtani led an engaged student audience with his presentation: *Demystifying Brain Research through the lens of an international dementia research collaboration*, followed by a live Q&A.



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Sachdev Foundation

Roger & Merrilyn Layton

J Holden Family Foundation

Dr Denise Sporr

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Donors

In 2021, 309 donations were made in support of our community and staff fundraisers who participated in the Blackmores Virtual Running Festival, the CHeBA Lockdown Challenge and Wipeout Dementia.

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CHeBA Collaborators

INDUSTRY

Aman-Aged Care Limited
BaptistCare NSW/ACT
Montefiore
The Lebanese Muslim Association

SOCIETIES/ PROFESSIONAL ASSOCIATIONS/ NON- PROFIT ORGANISATIONS

Alzheimer's Disease International (ADI)
Australian Society for Medical Research (ASMR)
Australasian Association of Gerontology (AAG)
Australasian Society for Psychiatric Research (ASPR)
Behavior Genetics Association (BGA)

Dementia Alliance International
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International Neuropsychiatric Association (INA)
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Tasmania

University of Tasmania, Hobart

New South Wales

NSW Health (Older People's Mental Health OPMH)
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
Ageing Futures Institute, UNSW Sydney
Australasian Research Institute, Sydney Adventist Hospital
Bankstown-Lidcombe Hospital
Bioanalytical Mass Spectrometry Facility, Mark Wainwright Analytical Centre, UNSW Sydney
Black Dog Institute
Centre of Excellence in Population Ageing Research (CEPAR), UNSW Sydney
Clinical Research Unit for Anxiety and Depression (CRUfAD), UNSW Sydney
Garvan Institute of Medical Research
Geriatric Medicine, Prince of Wales Hospital
Macquarie University
National Drug & Alcohol Research Centre (NDARC), UNSW Sydney
Neuropsychiatric Institute (NPI), Prince of Wales Hospital
Neuroscience Research Australia (NeuRA)
School of Biotechnology and Biomolecular Sciences (BABS), UNSW Sydney
School of Medical Sciences (SOMS), UNSW Sydney

School of Psychology, UNSW Sydney
St George Clinical School (The Microbiome Research Centre), UNSW Sydney
St Vincent's Centre for Applied Medical Research
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 Cognitive Function & Ageing Studies, England

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 Leeds-Beckett University, 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



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

**Professor Henry Brodaty AO &
Professor Perminder Sachdev AM**

Current Projects

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).

Aim: 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 centres. 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: Dr Betrouni found that texture features from T1 MRI scans are early markers of post-stroke cognitive decline. Summary results were shared with CHeBA staff in early October 2021. Dr Betrouni is working on a first draft to be circulated with co-authors in 2022.

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 (Curtin University) (CHeBA Hon. Research Fellow), Dr Rick Tankard (Postdoctoral Fellow), BRIDGET Consortium members.

Aims:

- Identify rare and common genetic variants and DNA methylation loci 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, including white matter hyperintensities, 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).

CogSCAN – Study of computer-administered neuropsychological tests in older adults

CHeBA staff: Nicole Kochan, Perminder Sachdev, Henry Brodaty, Karen Croot, Matilda Rossie, Josephine Bigland, John Crawford, Ben Lam, Teresa Lee, Brian Draper.

Other investigators: Julie Henry (University of Queensland), Jacqueline Close (NeuRA), David Bunce (Leeds University), Peter Gonski (UNSW).

Aim: To systematically evaluate and compare four prominent computerised neuropsychological batteries in cognitively healthy older adults, and individuals living with Mild Cognitive Impairment and mild dementia.

Findings: An older adult cohort rated their user-experience of undergoing traditional face-to-face assessment more favourably than computerised neuropsychological assessments (CNAs). Nonetheless, CNAs received more positive than negative ratings, and generally did not elicit more negative experiences than face-to-face assessments suggesting that CNAs be an acceptable alternative. Recent mood, cognitive level, computer attitudes and computer experience influenced emotions during CNA testing and test acceptability [DOI: 10.1002/alz.044730].

Medicine Honours student, Michael Budiarto, working on the CogSCAN at Home Study, found that 23 older adult participants who self-administered computerized tests from 2 CNAs, in their homes, rated them as generally acceptable and gave high ratings of usability. They were satisfied with the help they received via telephone support by research assistants and favoured performing the tests at home over in-person CNA testing at the research centre.

Funding: NHMRC Boosting Dementia Research grant, UNSW Medicine Interlude Grant.

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.

Aim: This study will expand upon an earlier COSMIC project to use a Reliable Change Index to quantify cognitive decline separately for verbal memory and visual memory. The risk of AD for individuals with amnesic 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.

Determining the genetic factors linked to odour identification

CHeBA Staff: Karen Mather, Anbupalam Thalamuthu, Siddharth Raj (Medicine ILP student).

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

Aim: To identify genetic variants associated with olfactory identification.

Findings: Using data from the Sydney Memory and Ageing Study and the Older Australian Twins Study, suggestive evidence was found for genetic associations with 8 individual odours. This work has now been published (Raj et al., 2021, *Genes*, 12: 669). This research is being extended by collaborating with other Australian and international studies to undertake a larger genetic study.

Funding: NHMRC.

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).

Aim: 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.

Aim: 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 Cohort 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).

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

Findings: A systematic review was undertaken examining longitudinal studies investigating diet and depression incidence in adults aged 45 and over. Meta-analyses found higher intake of fruit and vegetables was associated with reduced risk of incident depression. This research has now been published in the journal, Ageing Research Reviews (Matison et al., 2021, 70:101403).

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: Manuscript under review.

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).

Aim: 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.

Dose-response relationship between late-life physical activity and incident dementia: a pooled analysis of 10 cohort studies of memory in an international consortium

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

Other investigators: Ding Ding (Fudan University, China) and contributing COSMIC study leaders and associates from 10 COSMIC cohorts.

Aim: To examine the dose-response relationship between late-life physical activity and incident dementia among older adults.

Findings: This cross-national analysis suggests that performing 3.1-6.0 hours of physical activity and expending 9.1-18.0/MET-hours of energy per week may reduce dementia risk. A manuscript revised after initial review has been submitted.

Funding: NIH.

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 (Curtin University, CHeBA Hon. Research Fellow), EADB Consortium members.

Aim: To identify common and rare novel genetic variants

for Alzheimer's disease. The Consortium will facilitate this work by collecting a very large data set of individuals from around the world 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. In 2021, the consortium published a study with over 400,000 participants and found six new genetic variants (de Rojas et al., 2021, Nat Commun, 12(1):3417).

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: The project proposal was approved by the research scientific committee at the end of 2019 and 13 studies/PIs have agreed to join the workgroup. A protocol for processing MRI using CHeBA's pipeline has been established. For the second aim, imaging researchers from three international studies worked with CHeBA staff and contributed data. We found that the pipeline for processing WMH, originally developed for healthy ageing participants, tended to segment both WMH and stroke infarcts which overestimate WMH volumes. A progress summary report was sent out to the workgroup in early 2021. While we had proposed to update our pipeline using DWI, further discussion with other imaging experts led to a change in direction for this project. In 2022, as part of the new NHMRC CRE grant, we will propose a new MRI project which will be conducted by a new PhD student.

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, Janine Grossman.

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) type, frequency and severity of physical aggression in PLWD; and 6) use of physical and chemical restraint in PLWD.

Methodology: 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: Mixed methods were used to obtain the following data: • 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 - recorded aggression incidents in residents; chemical and physical restraint use with residents.

Findings: Primary outcomes: Staff confidence in caring for persons with dementia. There was no improvement in the total self-report SCIDS mean score ($p=0.194$), however, there was a statistically significant improvement ($p=0.030$) in the 'Building Relationships' sub-score. This finding indicates that staff had improved confidence in relationship-building, which is one of the key elements in attaining confidence in caring for persons with dementia. Staff skill in caring for persons with dementia. In each of the four care units, between 10-18 residents and between 2 and 5 staff were observed with the QUIS at any one time in public areas, resulting in approximately 2-3 observations recorded each minute. A total of 2745 interactions in a total duration of 4115 minutes of observation (68.6 hours) occurred. Positive care (PC) was the most frequently observed interaction code (50%), followed by Positive Social (PS) (43.2%) and a relatively small number of Neutral interactions (N) (5.6%), Negative Protective (NP) (1.1%) and Negative Restrictive (NR) interactions (0.1%). Negative staff-resident interactions occurred between one or two staff members and one or two residents at any one time. Staff-instigated NP and NR interactions were seen to trigger anger/irritation and in some cases verbal and/or physical aggression in the

affected resident.

Secondary outcomes: Staff attitudes towards persons with dementia. Non-significant improvements occurred in the total ADQ mean score ($p=0.062$), and the Hope sub-score ($p=0.076$). The improved Hope score indicates that staff had a better understanding of the resident's individual nature and improved appreciation of the resident's remaining strengths, which are indicators of a positive attitude towards persons with dementia. Maybo training evaluation. There was a statistically significant improvement in self-report ($p=0.024$) on training acquired, indicating that staff considered that Maybo training increased their knowledge and skills in recognising risks, preventing and managing physical aggression through improved communication approaches. Aggression incidents. Resident-to-resident aggression incidents occurred in eight ($n=8$) of a total of 72 residents, and resident-to-staff aggression occurred on six ($n=6$) occasions. Aggression incidents were confined to only three ($n=3$) of 72 residents. Staff responses toward 'resident-to-resident' and 'resident-to-staff' anger and aggression indicated that most staff had acquired knowledge and skills in diffusing anger through inquiring what was troubling the individuals involved, taking time to listen to their feelings, providing explanations, apologising to the resident where warranted, and using calming verbal approaches. Staff also used effective distraction techniques, such as taking the disaffected resident to their bedroom and staying with them until they felt calmer, providing individual activity programs in separate areas of the loungeroom, providing snacks and warm drinks. Physical handling of angry residents was done carefully and respectfully and was guided by the person's response to being touched.

Funding: Montefiore Homes.

Publications: Project methods and findings presented at the Association of Gerontology Conference October 2021. Journal publication in progress.

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 (Curtin 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.

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.

Other investigators: N/A.

Aim: 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 (Adjunct Senior 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 $\epsilon 4$ 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:

- The heritability of global amyloid burden was moderate (0.41-0.52).

- APOE ϵ 4 explained a significant proportion of the variance of amyloid burden, globally and in specific brain regions.
- Vascular risk factors were not significantly associated with β -amyloid load. There were no significant genetic correlations between global amyloid burden and imaging markers of cerebral small vessel disease.
- These findings have now been published: Koncz R, et al The heritability of amyloid burden in older adults: the Older Australian Twins Study, *Journal of Neurology, Neurosurgery & Psychiatry* Published Online First: 17 December 2021. doi: 10.1136/jnnp-2021-326677
- We have commenced investigation into the shared genetic basis of amyloid burden with cognition (Aim 4), planned for completion in early 2022.

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).

Aim: 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 bundle has not been investigated. We aim to explore these characteristics of white matter fibre bundles 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 bundle and further extract the main features of the bundle 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).

Other investigators: A/Professor Nicola Armstrong (Curtin 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).

Aim: 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). Current research is being undertaken to assess 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 and other studies from around the world.

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 (Curtin 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.

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

Findings:

- WMH are regions of hyperintensity in the white matter, which are observed on neuroimaging scans. High burden of WMH is associated with negative health outcomes, including dementia and disability. WMH can be sub-classified into two categories based on their location in the brain, deep and periventricular WMHs. 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, such as short tandem repeats, 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 (Curtin 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).

Aim: 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 a recent publication, copy number variants on the long arm of chromosome 1 were associated with brain structure and cognitive performance (Sonderby et al., 2021, *Transl Psy*, 11:182).

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 (Curtin 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).

Aim: Identify genetic variants including single nucleotide polymorphisms (SNPs) and copy number variants and differentially methylated sites associated with cognitive performance and other measures, such as brain imaging traits.

Findings: CHeBA studies (Sydney Memory and Ageing Study, Older Australian Twins Study) have contributed to a number of projects on a variety of phenotypes using not only genetic data but also epigenetic data (DNA methylation). In a recent publication using over 50,000 participants, novel genetic loci for circulating serum levels of the cytokine, interleukin-6, were identified (Ahluwalia et al., 2021, *Human Mol Genet*, 30:393-409).

Funding: NHMRC, Thomas Foundation.

Identifying expression quantitative trait loci (eQTLs) and pQTLs in older adults

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

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

Aim: Identify genetic variants associated with blood gene expression and protein levels.

Findings: SNPs controlling the expression level of genes (eQTLs) have been identified in the Sydney Memory and Ageing Study cohort. This analysis has been extended to the Older Australian Twins cohort, which is being used as a replication cohort for the Sydney Memory and Ageing Study results. In silico replication using data from the Consortium for Architecture of Gene Expression is also being performed. The eQTL analysis will help determine the function of SNPs that are associated with age-related phenotypes. This work is being written up for publication. Work seeking to identify SNPs associated with protein levels (pQTLs) has begun.

Funding: NHMRC.

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

CHeBA staff: Anne Poljak (Adjunct), Karen Mather, Vibeke Catts, Sumangali Gobbidharan, Tharusha Jayasena, Henry Brodaty, Perminder Sachdev.

Aims:

- Inventory and aliquot samples for ready distribution to researchers.
- Improve the long-term secure storage and utility of samples by aliquoting and transferring samples into -80oC freezers and vapour phase nitrogen storage.

Findings: Biobanking is an ongoing project for stored CHeBA blood samples from existing studies and for any new projects. A biobanking subcommittee has been setup and ethics approval obtained. Further funding is being sought to continue this important work to preserve our biospecimen collections for future studies.

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:

- Zara Page, PhD student had her first paper published – Comparison of computerised and pencil-and-paper neuropsychological assessments in older culturally and linguistically diverse Australians – in the Journal of the International Neuropsychological Society. doi:10.1017/S1355617721001314 In this paper, Zara's study found that test performances of culturally and linguistically diverse (CALD) individuals and people of English-speaking background differed more on traditional pencil-and-paper tests than computerised tests. However, caution is needed in concluding that computerised tests are more culturally-appropriate for assessing cognitive decline in older CALD groups as a number of linguistic and acculturation characteristics evidently influenced their performance on these computerised tests. Improving culture-fairness of cognitive testing is the focus of Zara's PhD and she is working on a number of projects.
- 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: NHMRC/DCRC PhD Scholarship, UNSW.

Improving health outcomes, well-being and care of people living with dementia in the hospital setting

CHeBA Staff: Lynn Chenoweth, Henry Brodaty, Claire Burley, Fleur Harrison, Mayouri Sukhapure.

Other investigators: Associate Professor Anna Williams (UNDA), Dr Zhixin Liu (Stats Central, UNSW), Dr Patricia Reyes (SESLHD, UNSW), Ms Jane McGuire (SESLHD), Ms Genevieve Maiden (SESLHD), Ms Jacqueline Cook (PhD applicant UNSW).

Aims: To identify 1) the impact that the person-centred approach has for persons living with dementia during a sub-acute hospital stay (neuropsychiatric symptoms, delirium and other iatrogenic harms, psychotropic prescription, length of stay, discharge destination, hospital readmission within 30 days, satisfaction with service), 2) identify how the person-centred approach impacts on services operations and quality, 3) determine the cost and cost-benefit of implementation, and 4) understand the organisational requirements to implement and maintain the person-centred care approach in routine services.

Methodology: This evidence-translation project employs a pre/post/follow-up evaluation of the person-centred approach to sub-acute hospital services on outcomes for prospective patients with a diagnosis of dementia (n=80), compared with a comparison group (n=80) (6-months de-identified, aggregated retrospective in-patient data). Evaluation of staff's person-centred care knowledge, skills, participation and satisfaction is obtained via direct observation, chart audit, survey and interviews with family/carers (n=80), patients (n=80) and clinical staff (medical, nursing, allied health) (n=60).

PhD Study: Ms Jacqueline Cook is undertaking an embedded PhD study, which focuses on developing, implementing, and evaluating the staff's on-line person-centred service education program.

Results: The main project has received all ethics approvals and is in progress. Retrospective patient data is being entered in REDCap, staff recruitment and pre-intervention survey has occurred, staff training in person-centred approach commences end of February, patient and family/carer recruitment will commence April/May. The PhD study has received all ethics approvals and is in progress. The staff Champion training program has been developed and is manualised, the 12-module staff on-line education program is almost complete and learning modules are being loaded to the study's on-line learning platform hosted by Uniting War Memorial Hospital. Hospital staff have been recruited, consented and pre-intervention surveys have been completed.

Funding: NHMRC / Dementia Collaborative Research Centre (DCRC).

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, H.M., 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 analysed and a manuscript is in preparation.

Funding: NIH.

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.

Aim: 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).

Aim: 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: Three STROKOG studies will be included in this project. Thibaut has begun data processing and harmonisation in 2021. A PhD student Florine Ruthmann from the University of Lille has joined the team of researchers for this project in late 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).

Aim: 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: Eight studies have been provided data. Initial data harmonisation began in 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).

Aim: 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.

Aim: 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.

Aim: 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.

Rethink my drink trial: reducing alcohol consumption and preventing cognitive decline in older Australians

CHeBA staff: Louise Mewton, Virginia Winter, Sarah Davies, Nicolas Hoy, Rachel Visontay, Nicole Kochan, Perminder Sachdev.

Other Investigators: Maree Teesson, Andrew Baillie, Nicola Newton, Cath Chapman, Matthew Sunderland (The Matilda Centre for Mental Health and Substance Use, Sydney University).

Aims:

- To determine whether an online alcohol intervention (Rethink My Drink) is effective in reducing alcohol use in older Australians (aged 60-75 years; $n=850$)
- To determine whether an online alcohol intervention is effective in reducing cognitive decline in older Australians
- To determine whether an online alcohol intervention is effective in reducing alcohol-related harms and improving quality of life in older Australians.

Findings: The online intervention has been fully developed and recruitment is underway. Hoy, N., Newton, N., Kochan, N., Sunderland, M., Baillie, A., Chapman, C., Winter, V., Sachdev, P., Teesson, M., Mewton, L. (2021). Rethink My Drink: study protocol for a 12-month randomised controlled trial comparing a brief internet-delivered intervention to an online patient information booklet in reducing risky alcohol consumption among older adults in Australia, *Addiction*, doi: 10.1111/add.15672.

Funding: Dementia Centre for Research Collaboration (DCRC) World Class Research Grant.

Revealing the genomic, epigenomic and transcriptomic landscape of metabolic syndrome

CHeBA Staff: Anbupalam Thalamuthu, Karen Mather.

Other investigators: A/Professor Nicola Armstrong (Curtin University) (CHeBA Hon. Research Fellow), A/Professor John Kwok (University of Sydney; UNSW), Professor Peter Schofield (NeuRA; UNSW), Professor Margaret J. Wright (Queensland Brain Institute, University of Queensland), Professor David Ames (National Ageing Research Institute, Royal Melbourne Hospital), Professor Bernhard Baune (University of Münster), Dr Liliana Ciobanu (University of Adelaide).

Aim: To identify genomic, epigenomic and transcriptomic factors associated with metabolic syndrome.

Findings: Analyses are underway using different datasets from the UK Biobank, the Sydney Memory and Ageing Study, the Older Australian Twins Study and the Sydney Centenarian Study. Multi-omic analyses will also be undertaken.

Funding: NHMRC.

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. Lena Oestreich has included three additional STROKOG studies and conducted new analyses in 2021. A manuscript draft 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: Sensitivity analyses are being finalised and manuscript is in preparation.

Funding: NIH.

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

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

Aim: 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 study in this research theme appeared in *Neurobiology of Aging* (2021: <https://doi.org/10.1016/j.neurobiolaging.2020.11.001>). Results showed that the burden of WMH was significantly higher in women compared to men, especially in the deep WMH (DWMH). In the generalized linear model that included the interaction between sex and body mass index (BMI), there was a differential association of BMI with DWMH in men and women in the exploratory sample, that is, the Sydney Memory and Ageing Study, $n = 432$, aged between 70 and 90. The finding of a higher BMI associated with a higher DWMH in men compared to women was replicated in the Older Australian Twins Study sample, $n = 179$, aged between 65 and 90. The risk factors of WMH pathology are suggested to have a different impact on the aging brains of men and women.

For the next study, we will try to examine: 1) whether hormones are the underlying mechanisms for the observed sex differences, and 2) whether genetic risk factors for WMH also showed differences between men and women.

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: Results are being finalised.

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

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 a 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.

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.
- Efficient and low-cytotoxicity inhibitors, graphene quantum dots (GQDs) can inhibit the aggregation of A β peptides.
- GQDs can be functionalized with amyloid targeting ligands to detect amyloid plaques using fluorescent imaging.

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 A β 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, Mehdi-pour 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.
- Villalva MD, Agarwal V, Ulanova M, Sachdev PS, Braidy N. Quantum dots as a theranostic approach in Alzheimer's disease: a systematic review. *Nanomedicine (Lond)*. 2021 Aug;16(18):1595-1611. doi: 10.2217/nnm-2021-0104. Epub 2021 Jun 28. PMID: 34180261. <https://pubmed.ncbi.nlm.nih.gov/34180261/>

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 analyse 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), phospholipids 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 ϵ 4 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. A higher empirical dietary inflammatory index (EDII) was significantly associated with increased risk of developing VaD. Diet may influence the development of VaD via modulation of several lipid and inflammatory pathways. Our findings underscore the importance of a healthy lifestyle for the prevention of vascular cognitive impairment that is recommended by the American Heart and Stroke Associations.

There are three 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.
- Chen R.F., Braidy N., Xu Y.H., et al. (2021). Macrophage- and Microglia-Related Chemokines Are Associated with Small Vessel (White Matter) Vascular Dementia: A Case-Control Study. *Dement Geriatr Cogn Disord* (DOI:10.1159/000519885)

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 has been provided by COSMIC studies.

Funding: NIH.

The association between diet and depression in older adults

CHeBA staff: Annabel Matison, Karen Mather, Simone Reppermund, Darren Lipnicki, Perminder Sachdev.

Other investigators: Vicki Flood (Sydney University) and investigators from contributing COSMIC studies.

Aims: To assess the longitudinal relationship between baseline diet and incident depression and/or change in depressive symptoms over time after adjusting for relevant confounders.

Findings: Project approved.

Funding: NIH.

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 obtained and analyses are currently underway.

Funding: NIH.

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 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: (1) 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

(2) What are the most common predictors of poor mobility across countries?

Findings: Feedback on some preliminary results requires some new statistical approaches to be undertaken.

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.

Aim: 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, DCRC 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 Genomics and Epigenomics 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 modelling 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 ̵4 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, Brodaty 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; ID1093083).

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 Münster), Dr Liliana Ciobanu (University of Adelaide), A/Professor Nicola Armstrong (Curtin University) (CHeBA Hon. Research Fellow), A/Professor John Kwok (University of Sydney; UNSW), Professor Peter Schofield (NeuRA; UNSW).

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

Findings: This work is ongoing with analyses using data from both the Sydney Memory and Ageing Study and the Older Australian Twins Study, examining a variety of phenotypes. Heritability of gene expression in older adults using participants from the Older Australian Twins Study has been undertaken and compared with two prior studies. Genes related to the immune response were amongst the top heritable genes. This work is being written up for publication.

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

Trajectories of cognitive decline before and after stroke: an individual participant data meta-analysis from the COSMIC collaboration

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

Other investigators: Investigators from contributing COSMIC studies.

Aims: (1) To map the trajectory of cognitive function pre- and post-stroke, compared with the trajectories of stroke-free individuals and stratify the trajectories by patient characteristics, and (2) examine cross-ethno-regional differences.

Findings: Project approved.

Funding: NIH.

Untangling the mechanistic links between heart and brain health in older populations: An AI assisted toolkit for assessing dementia risk

CHeBA staff: Darren Lipnicki, Perminder Sachdev.

Other investigators: Blossom Stephan, Graziela Figueredo, Jacob Brian (University of Nottingham), Stephen Kaptoge (Cambridge University), investigators from contributing COSMIC studies.

Aims: To develop novel models for predicting risk of incident dementia in the context of cardiovascular disease using artificial Intelligence (AI) methods synthesising clinical/biological, lifestyle, health, and socio-demographic data.

Findings: Project approved.

Funding: NIH, also being sought from the UKRI: Artificial intelligence for better biomedical and health research call.

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: We have received data from Gothenburg H70, KLOSCAD (Korean Longitudinal Study on Cognitive Aging and Dementia), and Sydney MAS (Memory and Ageing Study). Data from PATH (The Personality and Total Health Through Life project) and SLAS (The Singapore Longitudinal Ageing Studies) are being uploaded. A preliminary analysis in Gothenburg H70, KLOSCAD and Sydney MAS showed that hypertension, diabetes, history of cardiovascular diseases, stroke, inadequate physical exercises, and higher BMI were associated with greater white matter lesion burdens. These associations didn't differ between Caucasians and Asians. In the future, we will include the PATH and SLAS data in the analyses, and examine cognitive outcomes, in addition to vascular risk factors.

Funding: NIH, Vincent Fairfax Family Foundation, John Holden Family Foundation.

Completed 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 conferred 10 June 2021)

CHeBA staff: L N Premilla Chinnappa-Quinn, 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 ϵ 4 allele (APOE ϵ 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 A β 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.

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.

Aim: 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).

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: <https://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.

Aim: 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.

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.

Publication: Jang S, Numbers K, Pan Lam BC, Sachdev PS, Brodaty H, Reppermund S (2021). Performance-Based vs Informant-Reported Instrumental Activities of Daily

Living in Predicting Dementia. Journal of the American Medical Directors Association, in press

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.

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, Braid 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, Braid 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, Braid 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.
- Braid 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 β 40 oligomers in human astrocytes. *Front Aging Neurosci.* 2019; 11: 177.
- Chen Z, Jiang R, Chen M, Zheng J, Chen M, Braid 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, Braid 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., Braid, 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., Braid, 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 Braid.

The effects of intravenous NAD⁺ on Ageing and Metabolic Syndrome

CHeBA staff: Nady Braid.

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 F₂ α (8-iso-PGF₂ α), 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- κ B 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:

- Braid 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, Braid 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, Braid 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.

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.

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).

Aim: 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 modelling 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.

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.

Aim: 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 through 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 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.

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.

Appendices



“The message is that while ageing is inevitable, losing our mental capacity is not.”

Professor Perminder Sachdev AM

Appendix A: Staff List

Leadership

Henry Brodaty

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

Perminder Sachdev

Scientia Professor, Co-Director CHeBA, Leader Epidemiology Group, Leader Neuropsychiatry Group

Angela (Angie) Russell

Centre Manager

Academic Staff

Adam Bentvelzen

Research Fellow / Senior Neuropsychologist, ADNet Project (ADNet-MC Initiative)

Nady Braidy

Research Fellow / Leader Brain Ageing Research Laboratory

Claire Burley

Postdoctoral Fellow / Patient Centre Care (PCC) in Sub-acute care study

Lynn Chenoweth

Professor of Nursing / Lead, NHMRC-DCRC World Class Project – Improving health outcomes, well-being and care of people living with dementia in the hospital setting (PCC in Sub-acute care study)

Meredith Gresham

Research Fellow / COGNISANCE Project Co-ordinator

Megan Heffernan

Postdoctoral Fellow / Maintain Your Brain Trial Coordinator

Tharusha Jayasena

Postdoctoral Fellow / Brain Ageing Research Laboratory

Jiyang Jiang

Postdoctoral Fellow / Neuroimaging Group

Nicole (Nicky) Kochan

Research Fellow / Leader, CogSCAN Study; Co-Leader Neuropsychology Group

Mari Kondo

Vice Chancellor's Postdoctoral Fellow / Genomics & Epigenomics Group (until 22 October 2021)

Chun Pan (Ben) Lam

Postdoctoral Fellow / Consortia

Darren Lipnicki

Postdoctoral Fellow / COSMIC Consortium Co-ordinator

Jessica (Jess) Lo

Research Associate / STROKOG Consortium Co-ordinator

Karen Mather

Senior Research Fellow / Leader Genomics & Epigenomics Group

Louise Mewton

Senior Research Fellow / UNSW Scientia Program of Research / Lead, NHMRC-DCRC World Class Project – Healthier drinking choices and cognitive decline in older risky drinkers

Adith Mohan

Senior Lecturer / PhD Candidate

Katya Numbers

Postdoctoral Fellow / Memory & Ageing Study (MAS)
Co-ordinator

Matt Paradise

Senior Research Fellow / Medical Fellow, ADNet Project (ADNet-MC Initiative)

Suraj Samtani

Postdoctoral Fellow / SHARED Project Co-ordinator

Anbupalam (Anbu) Thalamuthu

Postdoctoral Research Fellow / CHeBA Longitudinal Studies

Stephanie Ward

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

Heidi Welberry

Research Fellow / Health Data Linkage Specialist, Maintain Your Brain Trial

Wei Wen

Associate Professor / Leader Neuroimaging Group, Director Neuroimaging Laboratory

Professional & Technical Staff – Research

Karen Allison

Research Officer / CogSCAN Project (until 3 June 2021)

Valerie Arsenova

Research Officer / ADNet Project (ADNet-MC & ADNet-CQR Initiatives)

Suzanne (Suzi) Artiss

Data Manager (until 30 June 2021)

Josephine (Josie) Bigland

Research Assistant / CogSCAN Study (until 31 December 2021) / Research Assistant (Casual), CHeBA Longitudinal Studies

Kim Burns

Research Associate / Update to dementia behaviour management app - 4-G3D95QC Project

Anne-Nicole Casey

Research Officer / Update of Behavioural & Psychological Symptoms of Dementia (BPSD) Handbook Project

Vibeke Catts

Research Manager / Older Australian Twins Study (OATS)
Co-ordinator

Russell Chander

Research Assistant (Casual) / CHeBA Longitudinal Studies (until 24 November 2021)

Tiffany Chau

Research Assistant / Maintain Your Brain Trial

Xinyue (Rory) Chen

Senior Project Officer / Dementia Platforms Australia (DPAU) Project

Rhiagh Cleary

Research Assistant / Social Cognitive Change in Late Adulthood (SocCog) Study Co-ordinator (until 4 June 2021)

John Crawford

Senior Statistician / CHeBA Longitudinal Studies

Karen Croot

Research Officer / CogSCAN Study

Sarah Davies*Research Assistant / Rethink My Drink Project***Jing Du***Student Assistant (Casual) / Neuroimaging Group***Sumangali (Sumi) Gobhidharan***Research Officer / Genomics & Epigenomics Group***Danika Hall***Research Assistant (Casual) / COGNISANCE Project***Fleur Harrison***Research Assistant / Sydney Centenarian Study (SCS); HOAM Study; Patient Centre Care (PCC) in Sub-acute care study***Shizuka Hayashi***Student Assistant / CHeBA Longitudinal Studies (until 31 December 2021)***Nicholas (Nick) Hoy***Research Assistant / COSMIC Alcohol Study***Sri Chandana Kanchibotla***Research Assistant / Genomics & Epigenomics Group***Gowsaly (Saly) Mahalingam***Research Assistant / SHARED Project***Niki McDonagh***Research Officer / Social Cognition Intervention Project***Inga Mehrani***Project Manager / The Australian Dementia Network (ADNet) Project***Nanmaran Anbupalam***Student Assistant (Casual) / CHeBA Longitudinal Studies***Zara Page***Student Assistant / CHeBA Longitudinal Studies***Matilda Rossie***Research Assistant / CogSCAN Study (until 31 December 2021)***Juan Carlo San Jose***Health Informatics Specialist***Amanda Selwood***Research Assistant / Older Australian Twins Study (OATS)***Ashley Stevens***Research Assistant / SHARED Project (until 6 August 2021)***Mayouri Sukhpure***Research Assistant / Patient Centre Care (PCC) in Sub-acute care study***Ashton Trollor***Student Assistant (Casual) / CogSCAN Study; CHeBA Longitudinal Studies***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 Officer / Rethink My Drink Project***Nora Wong***Research Officer / COGNISANCE Project***Professional & Technical Staff – Support****Sophia Dean***Administrative Officer / CHeBA Operations Team***Janelle Burns***Engagement & Projects Officer / CHeBA Operations Team***Heidi Douglass***Marketing, Communications & Projects Officer / CHeBA Operations Team***Helena Hudson***Project Administrator / CHeBA Operations Team***Laurie Mock***Digital Communications Officer / CHeBA Operations Team***UNSW Adjunct & Conjoint Staff****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***Premilla Chinnappa-Quinn***Honorary Lecturer***Kristan Kang***Honorary Senior Lecturer***Mari Kondo***Honorary Associate Lecturer (until 31 December 2021)***Kuldip Sidhu***Honorary Associate Professor, Co-Leader Molecular Biology & Stem Cells Group***Michael Valenzuela***Honorary Professor***UNSW Visiting Fellows****Jessica (Jess) Baker***Visiting Fellow***Helen Lapsley***Visiting Professorial 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
- 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)
- WHO Mental Health Gap (mhGAP) Depression Guidelines Development Group
- 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)
- Chair, Dementia Expert Advisory Group, Australian Institute for Health and Welfare (2022-2025)
- 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), Alzheimer's and Dementia: Journal of the Alzheimer's Association (2005-present), Australian and New Zealand Journal of Psychiatry (1981-present), CNS Drugs (1999-present), Dementia and Geriatric Cognitive Disorders (2010-present), International Psychogeriatrics (1996-2017), Neurodegenerative Disease Management (2010-present), The Australian Journal of Dementia Care (2012-present)
- Deputy Editor, International Psychogeriatrics (2017-2021)

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 (2006-2021)
- Acting Head of School of Psychiatry, UNSW Sydney (2017-2018)
- Head (and Founder), Memory Disorders Clinic, Prince of Wales Hospital (1985 -2020)
- Senior Clinician, Older Persons' Mental Health Service, 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)
- Research Coordinator, Susan Wakil School of Nursing and Midwifery, Faculty of Medicine and Health, University of Sydney, Evaluation study of the Meeting

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 (2019-) and Australian Society for Medical Research (2006-)

Professor Lynn Chenoweth

- Adjunct Professor, the University of Notre Dame Australia (2018-)
- Research Grant Review panel member: NHMRC Health Services Research, Health Promotion & Ageing discipline Project Grants (2019-2022); Dementia Australia Research Grants (2018-)
- Editorial Board member (2018-): Journal of Older People Nursing, Older People Nursing Journal, Austin Journal of Nursing and Health Care, Open Nursing Research Journal, Worldviews on Evidence-based Nursing, Annals of Alzheimer's and Parkinson's Disease, Future Medicine – Neurodegenerative Disease Management, Healthcare Journal, Geriatrics Journal

Dr Nicole Kochan

- Member ADNeT-Memory Clinics Steering Committee (2020-)
- Honorary Associate, Department of Psychology, Macquarie University (2007-)
- Member Steering Committee, UNSW Psychiatry Forums for General Practitioners and for Psychiatrists (2018-2019)
- Renji UNSW CHeBA Neurocognitive Centre (RUCNC) – Clinical Reviews Panel – collaboration with Renji Hospital, Jiao Tong University, Shanghai China (2018-)

Dr Rebecca Koncz

- Senior Lecturer, Concord Clinical School, Sydney Medical Program, University of Sydney (2018-)
- Clinical academic neuropsychiatrist, Sydney Local Health District (2017-)
- Adjunct Senior Lecturer, School of Psychiatry, UNSW Sydney (Aug 2020-)
- Fellow, Royal Australian and New Zealand College of Psychiatrists (RANZCP) (2017-)
- Member, "Motivation" taskforce, The Human Affectome Project (2017-)
- Member, Physical Health in Mental

Health expert group, NSW Ministry of Health (2019-2021)

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

Dr Teresa Lee

- Senior Clinical Neuropsychologist and Clinical Psychologist, Neuropsychiatric Institute, Prince of Wales Hospital (until July 2021)
- 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 Ben Lam

- Honorary Research Fellow, School of Psychology, University of Queensland (2018-)
- Editorial Board Member, Asian Journal of Social Psychology (2021-)

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 Alzheimer's Disease

Dr Darren Lipnicki

- Review Editor in Frontiers in Epidemiology (Section: Neurological and Mental Health Epidemiology)

Dr Karen Mather

- NeuRA Senior Research Scientist, Conjoint Appointment
- Member of Australian Association of Gerontology, ISTAART, American Society for Human Genetics

Dr Louise Mewton

- University of Sydney Honorary Senior Lecturer (2019-)
- Member, Research Society on Alcoholism (2019-)
- Editorial Board Mental Health and Prevention (2019-)

Dr Adith Mohan

- Senior Staff Specialist, Neuropsychiatry, SESLHD
- Site Chair for ECT, Prince of Wales Hospital, Eastern Suburbs Mental Health Service, SESLHD
- Chair, Mental Health Medical Staff Council, SESLHD
- NSW Jurisdictional Representative, Section of Neuropsychiatry, RANZCP

Dr Katya Numbers

- Associate Investigator, Ageing Futures Institute (AFI) (2019-)
- Member, Alzheimer's Association International Society to Advance Alzheimer's Research and Treatment (ISTAART) (2019-)

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 (NSWBNN)
- Member, Scientific Advisory Committee, Rebecca L. Cooper Medical Research Foundation
- Member, Cochrane Community
- Reviewer, Alzheimer's Association International Conference (biomarkers, non-neuroimaging)

Dr Simone Reppermund

- International Psychogeriatric Association membership committee (2021-)
- Associate Editor Frontiers in Aging Neuroscience (2021-)
- Associate Editor Neurodegenerative Diseases (2021-)

Professor Perminder Sachdev

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

2018)

- Visiting Professor, Jiao Tong University, Shanghai (2018-)
- 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-)
- 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-)
- Chair, Medical Advisory Committee of the Tourette Syndrome Association of Australia (1996-)
- Fellow of the Australian Academy of Health & Medical Sciences (2015-)
- Fellow of the NHMRC Academy 2011 (2011-)
- Member of the NHMRC Assigner's Academy (2012-)
- Invited Member, Task Force of the International League Against Epilepsy (ILAE) Neuropsychobiology Commission (2011-)
- 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

Dr Suraj Samtani

- Member of Australian Psychological Society, Australian Clinical Psychology Association
- Sessional Lecturer (NYU Sydney) January-May 2021

Appendix C: Postgraduate Students

Current

Toyin Abdulsalam Ademola

Scientia PhD student

Bioinformatics using multi-omics data integration strategies to predict age-related phenotypes and longevity

Discipline of Psychiatry and Mental Health, School of Clinical Medicine, UNSW Medicine and Health

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's and cerebrovascular disease brain pathology

Discipline of Psychiatry and Mental Health, School of Clinical Medicine, UNSW Medicine and Health

Supervisors: Prof Perminder Sachdev, Prof Glenda Halliday (USyd)

Abdullah Alqarni

PhD student

Sex differences in risk factors for white matter hyperintensities in non-demented older individuals

Discipline of Psychiatry and Mental Health, School of Clinical Medicine, UNSW Medicine and Health

Supervisors: A/Prof Wei Wen, Dr Jiyang Jiang, Prof Perminder Sachdev

Russell Chander

Scientia PhD student

Social cognition in the older adult lifespan

Discipline of Psychiatry and Mental Health, School of Clinical Medicine, UNSW Medicine and Health

Supervisors: Prof Perminder Sachdev, Prof Julie Henry (UQ)

Chao Dong

Scientia PhD student

Genetic and environmental influences on human brain changes in ageing

Discipline of Psychiatry and Mental Health, School of Clinical Medicine, UNSW Medicine and Health

Supervisors: A/Prof Wei Wen, Dr Jiyang Jiang, Dr Karen Mather, Dr Anbu Thalamuthu, Prof Perminder Sachdev

Jing Du

PhD student

Investigation of cerebrovascular burden using neuroimaging techniques in ageing brains

Discipline of Psychiatry and Mental Health, School of Clinical Medicine, UNSW Medicine and Health

Supervisors: A/Prof Wei Wen, Dr Jiyang Jiang

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

Discipline of Psychiatry and Mental Health, School of Clinical Medicine, UNSW Medicine and Health

Supervisors: Prof Henry Brodaty, Dr Liesbeth Aerts,

Dr Katrin Seeher, Prof Adam Guastella, Prof Julian Trollor, Prof Andrew Lloyd

Nicholas Hoy

PhD student

Investigating transdiagnostic models of mental illness across the lifespan, as well as the genetic and neural structures that influence transdiagnostic risk of mental illness

Discipline of Psychiatry and Mental Health, School of Clinical Medicine, UNSW Medicine and Health

Supervisor: Dr Louise Mewton

Fatemeh Khorshidi

PhD student

Pharmacological promotion of NAD+ anabolism to reduce AD pathology and delay cognitive decline

Discipline of Psychiatry and Mental Health, School of Clinical Medicine, UNSW Medicine and Health

Supervisors: Prof Perminder Sachdev, Dr Anne Poljak

Chulkyu Kim

PhD student

Nutrigenomic activators: A target for neurocognitive disorders and healthy brain ageing

Discipline of Psychiatry and Mental Health, School of Clinical Medicine, UNSW Medicine and Health

Supervisors: Dr Nady Braidy, Prof Perminder Sachdev

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

Discipline of Psychiatry and Mental Health, School of Clinical Medicine, UNSW Medicine and Health

Supervisors: Prof Perminder Sachdev, Prof Christopher Rowe (Austin Health, Melbourne), A/Prof Wei Wen, Dr Anbu Thalamuthu

Matthew Lennon

PhD student

Risk and preventive factors in Dementia – An international harmonization of longitudinal studies

Discipline of Psychiatry and Mental Health, School of Clinical Medicine, UNSW Medicine and Health, and St Vincents Clinical School, 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

Discipline of Psychiatry and Mental Health, School of Clinical Medicine, UNSW Medicine and Health, and St Vincents Clinical School, UNSW

Supervisors: Dr Karen Mather, Dr Simon Reppermund

Janet Mitchell

PhD student

Meaningful relationships with care – The Social Orientation of Care in Aged Living (SOCIAL)

Discipline of Psychiatry and Mental Health, School of Clinical Medicine, UNSW Medicine and Health

Supervisors: Prof Henry Brodaty, Professor Lynn Chenoweth, Prof Jeffrey Braithwaite (Macquarie University)

Adith Mohan

PhD student

Human brain transcriptome changes during ageing - a post-mortem brain tissue study – A large multi-site RNA sequencing study investigating age-related change in the human brain transcriptome

Discipline of Psychiatry and Mental Health, School of Clinical Medicine, UNSW Medicine and Health

Supervisors: Prof Perminder Sachdev, Dr Karen Mather, Dr Anbu Thalamuthu

Zara Page

PhD student

Towards achieving culture-fair neuropsychological assessment for Mild Cognitive Impairment and dementia in culturally and linguistically diverse (CALD)

Discipline of Psychiatry and Mental Health, School of Clinical Medicine, UNSW Medicine and Health

Supervisors: Dr Nicky Kochan, Prof Henry Brodaty, Dr Karen Croot

Alice Powell

PhD student

Exceptional cognition in old age and interactions with other aspects of successful ageing

Discipline of Psychiatry and Mental Health, School of Clinical Medicine, UNSW Medicine and Health

Supervisors: Prof Henry Brodaty, Prof Perminder Sachdev, Dr Nicky Kochan

Mary Revelas

PhD student

The genetics of exceptional longevity and successful ageing

Discipline of Psychiatry and Mental Health, School of Clinical Medicine, UNSW Medicine and Health

Supervisors: Dr Karen Mather, Dr Anbu Thalamuthu, Prof Perminder Sachdev

Annette Spooner

PhD student

Predicting Dementia using Machine Learning School of Computer Science and Engineering (CSE)

Faculty of Engineering, UNSW

Supervisors: Prof Arcot Sowmya (CSE), A/Prof Gelareh Mohammadi (CSE), Prof Perminder Sachdev

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, UNSW Medicine and Health
Supervisor: Dr Nady Braidy

Gurjeet Kaur Virk

Scientia PhD student

Development of blood biomarkers for early onset Alzheimer's disease using discovery proteomics

Discipline of Psychiatry and Mental Health, School of Clinical Medicine, UNSW Medicine and Health

Supervisors: Dr Anne Poljak, Prof Perminder Sachdev

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

Discipline of Psychiatry and Mental Health, School of Clinical Medicine, UNSW Medicine and Health

Supervisors: Prof Henry Brodaty, Prof Brian Draper

Completed

Lucia Premilla Chinnappa-Quinn, PhD

The association of acute illness hospitalisation with cognitive trajectory in the Sydney Memory and Ageing Study

School of Psychiatry, UNSW Medicine and Health

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)

Degree conferred: June 2021

Sophie Xi Chen, PhD

The relationship between dietary patterns and cognitive health among older adults

School of Psychiatry, UNSW Medicine and Health

Supervisors: Prof Henry Brodaty, Dr Fiona O'Leary (USyd)

Degree conferred: 2021

Heidi Foo, PhD

Genetic and environmental influences on the brain functional networks in older adults

Discipline of Psychiatry and Mental Health, School of Clinical Medicine, UNSW Medicine and Health

Supervisors: Prof Perminder Sachdev, A/Prof Wei Wen

Degree conferred: 15 Dec 2021

Matthew Paradise, PhD

Neuroimaging of cerebrovascular disease

Discipline of Psychiatry and Mental Health, School of Clinical Medicine, UNSW Medicine and Health

Supervisors: Prof Perminder Sachdev, A/Prof Wei Wen

Degree conferred: 30 Jan 2022

Heidi Welberry, PhD

Using big data to understand health related trajectories for older Australians at risk of dementia

Discipline of Psychiatry and Mental Health, School of Clinical Medicine, UNSW Medicine and Health

Supervisor: Prof Henry Brodaty

Degree conferred: 2021

Honours and ILP Students 2021

Michael Budiarto

Honours student

User experience of computerised neuropsychological assessments in older adults at home: A mixed methods study

Supervisors: Dr Nicole Kochan, Dr Karen Croot

Jared Duc-Lok Cheung

Honours Student

Intrinsic Capacity: An Alternative Predictor of Frailty in Older Adults?

Supervisors: Prof Henry Brodaty, Dr Katya Numbers, Dr Suraj Samtani

Shizuka Hayashi

Honours Student, First Class

Explore human brain measures computed from longitudinal and cross-sectional pipelines of FreeSurfer

Supervisors: A/Prof Wei Wen, Dr Jiyang Jiang, Dr Yang Song (School of Computer Sciences and Engineering)

Keshuo Lin

Honours Student

Automated rating of perivascular spaces in ageing brains using UK Biobank data

Supervisors: Dr Jiyang Jiang, A/Prof Dadong Wang (CSIRO; School of Computer Science and Engineering, UNSW), A/Prof Wei Wen

Christabella Nicole Surono

ILP Student

The Influence of Genetic and Environmental Factors on The Relationship between Mood and Cognition

Supervisors: Dr Vibeke Catts, Dr Teresa Lee, Prof Perminder Sachdev

Andy Yu

Honours Student

Examining the Heritability of the Spatial Distribution of Brain White Matter Fibre Tracts Using Diffusion Tensor Imaging Scans of OATS by employing Data Curves' Depths

Supervisors: Prof Pierre Lafaye de Micheaux, A/Prof Wei Wen, Dr Pavlo Mozharovskyi

Appendix D: Awards and Promotions

Dr Vibeke Catts

Appointed as the CHeBA Research Manager in 2021

Dr Sophie Xi Chen

2021 Winner for Best PhD, UNSW Medicine and Health

Professor Lynn Chenoweth

Australian Association of Gerontology Research Trust (\$30,000) Consumer and clinician led priority setting for the NNIDR MEDicines and DEMentia (MEDDEM) National Research Action Plan (Reeve E, ..., Chenoweth L, et al.)

Health@Business and UNSW Collaboration Seed Fund Grant (\$18,000) The structure and predictive value of intrinsic capacity in a longitudinal study of ageing (Hanewald K, Chenoweth L, et al.)

Health@Business and UNSW Collaboration Seed Fund Grant (\$15,000) Exploring Adoption and Functional Outcomes of Technology in Persons 60 years and above (Land L, Chenoweth L)

Montefiore at Residential Funding. Evaluating Maybo training to improve staff response to aggression in people living with dementia (Chenoweth L, et al.)

NSW Government Technology (\$40,000) Developing a Competency for Aged and Dementia Healthcare Leaders (Traynor V, ..., Chenoweth L, et al.)

UNDA seed research grant (\$25,000) and St. Vincent's Heath Network (\$20,000 in-kind) Person centred care Intervention for People with dementia in hospital settings: a feasibility pilot study (The PiP Study) (Chenoweth L, et al.)

Dementia Australia World Class Dementia Grant (\$536,000) Improving health outcomes, well-being and care for people living with dementia in the hospital setting (Chenoweth L, Brodaty H, et al.)

NHMRC targeted palliative care grant scheme (\$3,000,000) CELPI: A randomised trial of a Carer End of Life Planning Intervention in people with dementia (Arends G, Chenoweth L, et al.)

UNSW ARC Centre of Excellence in Population Ageing Research (CEPAR) (\$24,311) Age-Period-Cohort Patterns

in Intrinsic Capacity (Hanewald K, Chenoweth L, et al.)

Dr Nicole Kochan

UNSW Interlude Grant (RG210805) (\$100,000) Cross-comparison, validation and performance of computerised neuropsychological assessment devices in the evaluation of mild cognitive impairment and dementia.

UNSW Medicine and Health Research Stopgap Scheme (RG163145) (\$12,468). CogSCAN: Cross-comparison, validation and performance of computerised neuropsychological assessment devices in the evaluation of mild cognitive impairment and dementia

Dr Ben Lam

Dementia Centre for Research Collaboration (DCRC) Conference Scholarship 2021

Dr Adith Mohan

Grant Funding as Chief Investigator (\$149,913). The Mindgardens Functional Neurological Symptom Disorders (FND) Clinic – Evaluation of feasibility and effectiveness of a multidisciplinary tertiary FND clinic with a nested brief psycho-behavioural intervention study

Dr Alice Powell

NHMRC Postgraduate Scholarship (2021/GNT2014262) (\$123793.50) Exceptional cognition in old age and interactions with other aspects of successful ageing

Dr Simone Reppermund

UNSW Scientia fellowship renewal 2021

Dr Suraj Samtani

DCRC-DARF 2021 Pilot Study Grant (\$75,000). A novel social cognition intervention for older adults with cognitive impairment: co-design and pilot study

Dr Annette Spooner

The Norman Foo Memorial Best Research Paper Prize (for the best PhD research paper). Awarded by the UNSW Faculty of Engineering, 24 Mar 2021

UNSW Faculty of Engineering "Outstanding HDR Student Award", 6 Dec 2021

Zara Page

UNSW Ageing Futures Institute Award

2021 PhD Pitch. Celebrating Students in Ageing Research Competition "Towards achieving culture-fair neuropsychological assessment for MCI and dementia in CALD older Australians". Submitted recorded 90-sec pitch presentation, awarded 2nd place prize (\$500)

UNSW Development and Research Training Grant (DRTG) Scheme 2021 (\$500)

Awarded \$100 school funds (via CogSCAN) to attend R Course

Appendix E: Research Grants & Funding

Grants

Developing robust biomarkers for vascular cognitive impairment and dementia: adding V to the ATN research framework

Funding Source: NHMRC
Project ID: RG193540 / RG193540-A
Investigator/s: Prof Perminder Sachdev
Duration: 5 years: 2021-2025
Total Funds: \$3,289,215

Improving health outcomes, well-being and care of people living with dementia in the hospital setting

Funding Source: NHMRC / Dementia Collaborative Research Centre (DCRC)
Project ID: RG180842-E
Investigator/s: Prof Lynn Chenoweth, Prof Henry Brodaty
Duration: 2 years: May 2021-May 2023
Total Funds: \$536,000

Infrastructure support for CHeBA

Funding Source: Black Dog Institute / NSW Health Medical Research Support Program
Project ID: RG211967
Investigator/s: Prof Perminder Sachdev, Prof Henry Brodaty
Duration: 2 years: Jan 2021-Jul 2022
Total Funds: \$423,596

The Mindgardens Functional Neurological Systems Disorders (FND) Clinic

Funding Source: Mindgardens Neuroscience Network / MNN Commonwealth Funded Research Projects
Project ID: RG200893-O
Investigator/s: Dr Adith Mohan
Duration: 2 years: 2021-2022
Total Funds: \$150,000

Update to dementia behaviour management app – 4-G3D95QC

Funding Source: Department of Health / Dementia and Aged Care Services (DACS)
Project ID: RG211792
Investigator/s: Prof Henry Brodaty
Duration: 2 years: 2021-2022
Total Funds: \$366,000

Update of Behavioural and Psychological Symptoms of Dementia (BFSD) Handbook

Funding Source: NSW Ministry of Health / State Government

Project ID: RG212282
Investigator/s: Prof Henry Brodaty
Duration: 2 years: 2021-2022
Total Funds: \$90,907.28

Strengthening professional collaboration in dementia care giver education and research via the provision and evaluation of the iSupport program in Australia and Greater China

Funding Source: Department of Health / Dementia and Aged Care Services (DACS)
Project ID: RG203295
Investigator/s: Prof Henry Brodaty
Duration: 1 years: 2021
Total Funds: \$13,200

W.H.O. Dementia Research Blueprint

Funding Source: World Health Organisation
Project ID: RG213500
Investigator/s: Prof Perminder Sachdev
Duration: 1 year: 2021
Total Funds: \$20,134.23

A novel social cognition intervention for older adults with cognitive impairment: co-design and pilot study

Funding Source: NHMRC / DCRC & Dementia Australia Research Foundation (DARF)
Project ID: RG181322-A (NHMRC / DCRC) & RG203202-A (DARF)

Investigator/s: Dr Suraj Samtani
Duration: 1 years: 2021*
Total Funds: \$75,000

*Extended to 1 August 2022

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: RG192990

Investigator/s: Dr Karen Mather

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: 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: 2019/20-2022/23

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 December 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

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 2022

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: 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 October 2022

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 2022

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 2022

Total Funds: USD40,534.34

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 Lautenschlager, 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)

*Extended to 31 December 2022

The long-term effectiveness of a combined prevention model for anxiety, depression and substance use in adolescents

Funding Source: Australian Rotary Health Research Fund (ARHRF)

Project ID: RG180380

Investigator/s: Dr Louise Metwon

Duration: 3 years: 2018-June 2020*

Total Funds: \$209,830

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 2017-31 August 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 2022

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

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

*Blood biomarkers for dementia and pre-dementia syndromes in MA

**APOe4 - Maintain Your Brain

***FUS Equipment

Funding Source: Anonymous

Project ID: PS63712_PS64010

Awardee/s: *Prof Perminder Sachdev / Prof Henry Brodaty
**Prof Henry Brodaty / Dr Katya Numbers
***Dr Nady Braidy

Total Funds: \$250,000

New dietary interventions to promote healthy ageing

Funding Source: Rhyolite Innovation

Project ID: PS62564_PS62584

Investigator/s: Dr Nady Braidy

Total Funds: \$200,000

Lipid profiling of VaD research

Funding Source: The Mostyn Family Foundation

Project ID: PS62091_PS62138

Awardee/s: Dr Nady Braidy

Total Funds: \$250,000 (\$50,000/yr x 5 years 2021-2025)

The application of nanotechnology to the diagnosis of AD and VD

Funding Source: Anonymous

Project ID: PS63654_PS63673

Awardee/s: Dr Nady Braidy

Total Funds: \$250,000 (5 years)

Nanotechnology to the diagnosis of AD

Funding Source: Sachdev Foundation

Project ID: PS63669_PS65012

Awardee/s: Dr Nady Braidy

Total Funds: \$45,000

Blood biomarkers for dementia and mild cognitive impairment (MCI) in MAS

Funding Source: Sachdev Foundation

Project ID: PS63671_PS65013

Awardee/s: Prof Perminder Sachdev

Total Funds: \$50,200

Retinal biomarkers in dementia

Funding Source: Sachdev Foundation

Project ID: PS61547_PS61604

Awardee/s: Prof Perminder Sachdev

Total Funds: \$52,534 (*\$30,860)

*As at 31 December 2021

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 (*\$12,147)

*As at 31 December 2021

The blood brain barrier (BBB) 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: \$30,031*

*As at 31 December 2021

Magnetic particle imaging in Alzheimer's disease

Funding Source: John Holden Family Foundation

Project ID: PS59199_PS59205

Awardee/s: Prof Perminder Sachdev

Total Funds: \$300,000 (*\$252,442)

*As at 31 December 2021

New therapeutic strategies for the treatment of Alzheimer's disease

Funding Source: Biospecialties Australia Pty Ltd
Project ID: PS44672_PS44710
Awardee/s: Dr Naidy Braidy
Total Funds: \$25,000 (*\$1604)

*As at 31 December 2021

Mapping Neuropathology in Centenarians with Dementia

Funding Source: Sachdev Foundation
Project ID: PS55062_PS55172
Awardee/s: Prof Perminder Sachdev
Total Funds: \$46224*

*As at 31 December 2021

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
Total Funds: \$529,183 (*\$130,177)

*As at 31 December 2021

The CHeBA Cerebral Small Vessel Disease (SVD) Fund

Funding Source: John Holden Family Foundation
Project ID: PS41604_PS41625
Awardee/s: Prof Perminder Sachdev
Total Funds: \$600,000 (*\$15,228)

*As at 31 December 2021

The Thomas Foundation Grant

Funding Source: The Thomas Foundation
Project ID: PS34586_PS34589
Awardee/s: Prof Henry Brodaty Prof Perminder Sachdev
Total Funds: \$1,000,000 (\$22,587*)

*As at 31 December 2021

The Dementia Momentum Grants (excluding miscellaneous donations & Wipeout Dementia Campaign)

Funding Source: Miscellaneous
Project ID: PS38235_PS38252
Awardee/s: Prof Perminder Sachdev, Prof Henry Brodaty
Total Funds: \$500,000

*Acquitted March 2021

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: \$363,983*

*As at 31 December 2021

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: \$1,303*

*As at 31 December 2021

The Kwan & Yuet Ying Fung Health Brain Ageing Research Award

Funding Source: Kwan & Yuet Ying Fung Estate
Project ID: PS36983_PS37138
Awardee/s: Prof Perminder Sachdev
Prof Henry Brodaty

Duration: Ongoing

Total Funds: \$108,745*

*As at 31 December 2021

The Josh Woolfson Memorial Scholarship Fund

Funding Source: Woolfson Family
Project ID: PS42978_PS42948
Awardee/s: Prof Perminder Sachdev, Prof Henry Brodaty

Duration: Ongoing

Total Funds: \$104,760*

*As at 31 December 2020

Appendix F: Statement of Financial Performance

Statement of Financial Performance for the year ended 31 December 2020

	Notes	2021	2020
Funds			
Research Revenue		3,577,019	4,588,028
Donations		1,249,395	549,129
Fees		-	-
Faculty Funds	3	-	-
UNSW Contribution - Competitive	1	149,876	92,336
UNSW Contribution - Strategic	2	-	-
Sundry Other Revenue		15,070	(4,703)
Total Funds		4,991,360	5,224,790
Costs			
People Costs		5,005,890	4,985,618
Scholarship Stipends		102,352	58,886
Contract & Consulting Services		387,366	129,982
Repairs and Maintenance		-	423
Consumables		50,836	94,053
Travel		3,737	8,839
Equipment		5,288	75,940
Entertainment		-	-
Marketing		5,787	9,784
Overheads		6,087	2,403
Other Expenses		321,121	374,311
Interest Expense		-	-
Other Expenses		332,995	386,498
Internal Expense		166,320	178,179
Total Costs		6,054,783	5,918,418
Operating result		(1,063,423)	(693,628)
Opening Balance		2,569,306	3,262,934
Closing Balance		1,505,883	2,569,306

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, Lapkin S. 2021. Considering the older person. Adapting nursing: Life stages and transitions. *Potter & Perry's Fundamentals of Nursing* 6th edition. Eds. Crisp, J., Douglas, C., Rebeiro, G., Waters, D. Part 5, Ch.32, pp. 1252-1290.
2. Chenoweth, L. & Williams, A. 2021, Working in the aged care sector. Adapting Nursing: Contexts of Care. *Potter & Perry's Fundamentals of Nursing* 6th edition. Eds. Crisp, J., Douglas, C., Rebeiro, G., Waters, D. Part 5, Ch.37, pp.1379-1412.
3. Sachdev P, Mohan A. Neurocognitive disorders (Chapter 13). In: Ramalingam J (Ed) *Atlas of Psychiatry*. 2021.

Journal Articles

1. Ahluwalia TS, Prins BP, Abdollahi M, Armstrong NJ, Aslibekyan S, Bain L, ..., Thalamuthu A, ..., Trollor J, ..., Baune BT, ..., Sachdev PS, et al. Genome-Wide Association Study of Circulating Interleukin 6 Levels Identifies Novel Loci. *Hum Mol Genet*. 2021 Apr 27; 30(5):393-409. DOI: 10.1093/hmg/ddab023. PMID: 33517400 / PMCID: PMC8098112.
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*. 2021 Feb; 98:197-204. DOI: 10.1016/j.neurobiolaging.2020.11.001. PMID: 33307330.
3. Almendral Rangel C, Noble Y, Radd-Vagenas S, Mavros Y, Flood VM, O'Leary F, Brodaty H, Sachdev PS, Heffernan M, Valenzuela M, Anstey KJ, Daniel K, Ginige JA, San Jose JC, Chau T, Garnés Rancurello S, Fiatarone Singh MA. Nutrition Module Design in Maintain Your Brain: An internet-based randomized controlled trial to prevent cognitive decline and dementia. *Br J Nutr*. 2021 Jun 3:1-28. DOI: 10.1017/S0007114521001859. PMID: 34078487.
4. Batouli SAH, Sisakhti M, Haghsheenas S, Dehghani H, Sachdev P, Ekhtiari H, Kochan N, Wen W, Leemans AI, Kohanpour M, Oghabian MA. Iranian Brain Imaging Database: A Neuropsychiatric Database of Healthy Brain. *Basic and Clinical Neuroscience*. 2021 Jan-Feb; 12(1):115-132. DOI: 10.32598/bcn.12.1.1774.2. PMID: 33995934.
5. Braidy N, Alicajic H, Pow D, Smith J, Jugder BE, Brew BJ, Nicolazzo JA, Guillemain GJ. Potential Mechanism of Cellular Uptake of the Excitotoxin Quinolinic Acid in Primary Human Neurons. *Mol Neurobiol*. 2021 Jan; 58(1):34-54. DOI: 10.1007/s12035-020-02046-6. PMID: 32894500.
6. Boccardi M, Monsch AU, Ferrari C, Altomare D, Berres M, Bos I, Buchmann A, Cerami C, Didic M, Festari C, Nicolosi V, Sacco L, Aerts L, Albanese E, Annoni JM, Ballhausen N, Chicherio C, Démonet JF, Descloux V, Diener S, Ferreira D, Georges J, Gietl A, Girtler N, Kilimann I, Klöppel S, Kustyniuk N, Mecocci P, Mella N, Pigliautile M, Seeher K, Shirk SD, Toraldo A, Brioschi-Guevara A, Chan KCG, Crane PK, Dodich A, Grazia A, Kochan NA, de Oliveira FF, Nobili F, Kukull W, Peters O, Ramakers I, Sachdev PS, Teipel S, Visser PJ, Wagner M, Weintraub S, Westman E, Froelich L, Brodaty H, Dubois B, Cappa SF, Salmon D, Winblad B, Frisoni GB, Kliegel M; Consortium for the Harmonization of Neuropsychological Assessment for Neurocognitive Disorders. Harmonizing neuropsychological assessment for mild neurocognitive disorders in Europe. *Alzheimers Dement*. 2021 May 13. DOI: 10.1002/alz.12365. PMID: 33984176.
7. Burley CV, Casey AN, Chenoweth L, Brodaty H. Reconceptualising Behavioral and Psychological Symptoms of Dementia: Views of People Living With Dementia and Families/Care Partners. *Front Psychiatry*. 2021; 12:710703. DOI: 10.3389/fpsy.2021.710703. PMID: 34484001 [Epub 2021 Sep 7].
8. Camaya I, Mok TY, Lund M, To J, Braidy N, Robinson MW, Santos J, O'Brien B, Donnelly S. The parasite-derived peptide FhHDM-1 activates the PI3K/Akt pathway to prevent cytokine-induced apoptosis of β -cells. *J Mol Med (Berl)*. 2021 Nov; 99(11):1605-21. DOI: 10.1007/s00109-021-02122-x. PMID: 34374810.
9. Cao X, Liu T, Jiang J, Liu H, Zhang J, Kochan NA, Niu H, Brodaty H, Sachdev PS, Wen W. Alteration in Effective Connectivity With Cognitive Aging: A Longitudinal Study of Elderly Populations. *Front Aging Neurosci*. 2021; 13:755931. DOI: 10.3389/fnagi.2021.755931. PMID: 34867282.
10. Cations M, Lang CE, Ward SA, Caughey GE, Crotty M, Whitehead C, Ahern S, Maddison J, Inacio MC. Using data linkage for national surveillance of clinical quality indicators for dementia care among Australian aged care users. *Sci Rep*. 2021 May 21; 11(1):10674. DOI: 10.1038/s41598-021-89646-x. PMID: 34021203.
11. Cations M, Lang CE, Ward SA, Crotty M, Whitehead C, Maddison J, Inacio M. Cohort profile: Dementia in the Registry of Senior Australians. *BMJ Open*. 2021 Feb 1; 11(2):e039907. DOI: 10.1136/bmjopen-2020-039907. PMID: 33526495.
12. Chen SX, Lam BCP, Liu JH, Choi HS, Kashima E, Bernardo ABI. Effects of containment and closure policies on controlling the COVID-19 pandemic in East Asia. *Asian J Soc Psychol*. 2021 Mar; 24(1):42-7. DOI: 10.1111/ajsp.12459. PMID: 33821141.
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15. Chen X, Liu Z, Sachdev PS, Kochan NA, Brodaty H, O'Leary F. Association of adherence to the Australian Dietary Guidelines with cognitive performance and cognitive decline in the Sydney Memory and Ageing Study: a longitudinal analysis. *J Nutr Sci*. 2021; 10:e86. DOI: 10.1017/jns.2021.44. PMID: 34733498.
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17. Cheng J, Liu Z, Guan H, Wu Z, Zhu H, Jiang J, Wen W, Tao D, Liu T. Brain Age Estimation From MRI Using Cascade Networks With Ranking Loss. *IEEE Trans Med Imaging*. 2021 Dec; 40(12):3400-12. DOI: 10.1109/tmi.2021.3085948. PMID: 34086565
18. Chenoweth L, Cook J, Williams A. Perceptions of Care Quality during an Acute Hospital Stay for Persons with Dementia and Family/Carers. *Healthcare*. 2021 Sep 7; 9(9):1176. DOI: 10.3390/healthcare9091176. PMID: 34574951.
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community. *Arch Osteoporos*. 2021 Aug 17; 16(1):120. DOI: 10.1007/s11657-021-00966-x. PMID: 34405278.

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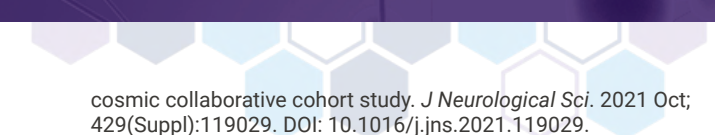
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Appendix H: Conference Presentations

Conferences

1. Brodaty H [Invited Plenary Speaker]. Pseudodementia, pseudo-pseudodementia and pseudodepression. *19th Annual Mild Cognitive Impairment Symposium*. 28 Feb 2021; Miami USA and virtual.
2. Brodaty H [Invited Speaker]. *Virtual workshop: WHO's Dementia Research Blueprint*. 19-20 May 2021; online.
3. Brodaty H [Invited Keynote Speaker]. Preventing cognitive decline online: The Maintain Your Brain randomised controlled trial. *3rd Krems Dementia Virtual Conference Virtual*; 30 Oct 2021; Austria and online.
4. Brodaty H [Plenary Speaker]. The DCRC over 15 years. *Australian Dementia Forum*. 31 May 2021 – 1 June 2021; virtual conference.
5. Brodaty H [Invited Speaker]. Can dementia be prevented? Seminar at the *George Institute*. 16 June 2021; virtual presentation.
6. Brodaty H [Invited Speaker]. Public Forum on COVID. 7 Oct 2021; online.
7. Brodaty H [Invited Plenary Speaker]. BPSD and research – What have we learned and do we need new trials? *Dementia Trials Australia (DTAus) – Alzheimer's beyond COVID-19*. 8 Oct 2021; online.
8. Brodaty H [Invited Panel Discussion] The patient journey. *Dementia Trials Australia (DTAus) – Alzheimer's beyond COVID-19*. 12 Oct 2021; online.
9. Brodaty H [Invited Speaker]. Influencing policy through dementia research. *ADNeT Early-Mid Career Researchers Accelerator Group, hosted by the Australian Dementia Network*. 20 Oct 2021; online.
10. Brodaty H [Invited Plenary Speaker]. Forward with Dementia: a guide to post-diagnostic care. *RANZCP Faculty of Psychiatry of Old Age 2021 Conference*. 4 Nov 2021; online.
11. Brodaty H [Invited Plenary Speaker]. Post-diagnostic care for dementia. *National Dementia & Aged Care Reform Conference*. 24 Nov 2021; Melbourne and online.
12. Gresham MD [Invited Speaker]. All the questions you were afraid to ask. *Western Sydney Virtual Dementia Conference*. 21 & 23 Sept 2021.
13. Gresham MD, Low L-F, Jeon Y-H, Swaffer K, Brodaty H. Facing the void: The experience of Australian care partners and people living with dementia following diagnosis [Poster Presentation]. *Alzheimer's Association International Conference*; 26-30 July 2021; Denver, CO, USA and online.
14. Gresham MD, Low L-F, Phillipson L, Jeon Y-H, Swaffer K, Brodaty H. Delivering a diagnosis of dementia is hard, but what comes next is critical. *Australian Dementia Forum*. 31 May-1 June 2021; virtual.
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16. Hanewald K, Beard J, Ye S, Liu Z, Chenoweth L. Intrinsic Capacity: Validation of a New Who Concept for Healthy Ageing. *2021 World Congress on Health Economics*. March 2021; virtual.
17. Hanewald K, Beard J, Ye S, Liu Z, Chenoweth L. Identifying Intrinsic Capacity factors in persons 65 and over. *Population Aging Conference 2021. Challenges and resilience related to population ageing*. University of Indonesia, Faculty of Public Health. 7-8 April 2021; virtual.
18. Kochan N [Invited Speaker]. Reliability, validity and usability of computerised neuropsychological instruments to detect cognitive impairment in older adults. *International Conference of the Korean Dementia Association*. 1-2 Oct 2021. Seoul, South Korea; virtual.
19. Kochan N [Invited Speaker]. Computerised cognitive testing in older adults. The 3rd Renji Hospital China-Australia Neurocognition Forum. 20 Nov 2021; Shanghai, China and virtual.
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21. Lam BCP, Lo JW, Reppermund S, Oestreich L, O'Sullivan M, Crawford J, Brodaty H, Sachdev PS and the Stroke and Cognition (STROKOG) Collaboration. Risk factors for onset of post-stroke depression in diverse ethno-regional groups. *11th International Conference of the VasCog Society*. 8-9 Sep 2021; Newcastle University, UK and virtual.
22. Lam B, Crawford JD, Lipnicki DM, Mewton L, Sachdev PS, and the Cohort Studies of Memory in an International Consortium (COSMIC). Longitudinal examination and validation of the latent dementia phenotype factor in 10 harmonized cohort studies. *Alzheimer's Association International Conference*. 28 July 2021; virtual.
23. Lo J [invited speaker]. Association of Prediabetes and Type 2 Diabetes With Cognitive Function After Stroke. *International Stroke Conference 2021*. 17-19 March 2021; virtual.
24. Lo J. Short-term trajectories of post-stroke cognitive function: a STROKOG Collaboration Study. *VasCog 2021: 11th International Conference of the VasCog Society*. 8-9 Sep 2021; Newcastle University, UK and virtual.
25. Mather K. Discovering putative protein biomarkers for successful ageing using polygenic risk scores & the exceptional longevity model. *Gene Mappers 15th Annual Conference*. 23-25 June 2021; Brisbane, Australia and virtual.
26. Matisson A, Reppermund S, Flood V, Mather K. Meta-analysis reveals higher intake of fruit and vegetables is protective against depression in older adults. *Australian Dieticians 2021 Conference*. 11-13 July 2021; virtual.
27. Page ZA, Croot K, Sachdev PS, Crawford JD, Lam BCP, Brodaty H, Miller-Amberber A, Numbers K, Kochan NA. Comparing cognitive performance on computerised and paper-and-pencil neuropsychological assessments in older culturally and linguistically diverse Australians [Virtual Poster Presentation]. *Alzheimer's Association Addressing Health Disparities Conference*. 14-16 June 2021; virtual with accompanying 3 min audio/video recording.
28. Page ZA, Perales JP [Invited Talk Webinar]. Diversity and Disparities PIA: Innovative Approaches to Improving Accessibility and Quality of Dementia Diagnostic, Care, and Caregiver Support Services: Updates From Equity-driven Projects in the US and Australia. *International Society to Advance Alzheimer's Research and Treatment (ISTAART) Webinar: Diversity & Disparities PIA*. 25 June 2021; virtual.
29. Reppermund S, Jang S, Numbers K. Prediction of dementia: Differences between performance-based versus informant-reported measures of functional impairment. *Australian Association of Gerontology*. 9-12 Nov 2021; virtual.
30. Reppermund S [invited speaker]. Late-life depression and dementia –health profiles, health services use and transition to dementia. *Dementia Collaborative Research Centre: Anxiety and Depression in Dementia Research Network International Symposium*. 17 Sep 2021; Sydney, Australia and virtual.
31. Revelas M. Exceptionally long-lived individuals are metabolically healthy: Analysis of polygenic risk for MetS & the presence of metabolic syndrome. *International Centenarian Consortium (ICC 2021)*. 29 June 2021; virtual.
32. Revelas M. High polygenic risk score for exceptional longevity is associated with a healthy metabolic profile. *GeneMappers Conference*. 23-25 June 2021; virtual.
33. Rossie M, Croot K, Allison K, Brodaty H, Crawford JD, Lam BCP, Lee T, Henry JD, Draper B, Close J, Ong MY, Sachdev PS, Kochan NA. Evaluating user-experience of Computerised Neuropsychological Assessment in an older Australian sample: Findings from the CogSCAN Study. *Australian Dementia Forum 2021*. 31 May – 1 June 2021; virtual.
34. Sachdev P [Invited Speaker]. Dementia. *ICC 2021 Annual Meeting*. 29 June 2021; Sydney and online.
35. Sachdev P [Invited Chair]. Biomarkers I -SVD Pathophysiology. *11th International Conference of the VasCog Society*. 8-9 Sep 2021; Newcastle University, UK and online.
36. Sachdev P [Invited Speaker]. Happiness of Centenarians. *Regional Meeting of the International Psychogeriatric Association (IPA) with the collaboration with the Japanese Psychogeriatric Society (JPS)*. 16-18 Sep 2021; Kyoto, Japan and online.
37. Sachdev P [Invited Speaker]. Management of movement disorders including tardive dyskinesia. *21st World Congress of Psychiatry 'New World, New Challenges for Psychiatry & Mental Health'*. 18-21 Oct 2021; virtual.

38. [Samtani S](#), Stevens A, Lipnicki DM, Sachdev PS, Brodaty H, SHARED Consortium. Social Health And Reserve in the Dementia patient journey (SHARED): Social factors linked to distinct cognitive trajectories in the clinical phase of dementia. *Australian Dementia Forum*. 30 April 2021; virtual.
39. [Samtani S](#), Stevens A, Lipnicki DM, Sachdev PS, Brodaty H, SHARED Consortium. Social Health and Reserve in the Dementia patient journey (SHARED): The role of social interactions in the clinical phase of dementia (poster). *Alzheimer's Association International Conference*. 27 July 2021; virtual.
40. [Samtani S](#), Stevens A, Lipnicki DM, Castro Costa E, Guerchet M, Preux P-M, Skoog I, Scarmeas N, Kim K-W, Ganguli M, Crowe M, Ng TP, Numbers K, Sachdev PS, Brodaty H and the SHARED consortium for the Cohort Studies of Memory in an International Consortium (COSMIC). Social Health And Reserve in the Dementia patient journey (SHARED): Females, older adults, and people living with dementia are vulnerable to social isolation, in "Social health: A pathway to inclusion and cognitive health" by Prof Myrra Vernooij-Dassen, Rabih Chattat, Suraj Samtani and Isabella van der Velpen. *International Psychogeriatrics Association, on-demand symposium*. 10 Oct 2021 – 31 May 2022; virtual.
41. [Thalumuthu A](#) [Invited Speaker]. An overview of statistical methods in genomics of Longevity. *Virtual National Conference on Theoretical and Applied Statistics*. Department of Statistics, Kristu Jayanti College, Bengaluru, India. 9-10 Feb 2021; virtual.
42. Wesson J, Brodaty H, [Chenoweth L](#). Responding to aggression in people living with dementia through the Maybo approach. *Australian Association of Gerontology National Conference*. 12 Nov 2021; virtual.
17. [Samtani S](#) [invited lecture]. Dementia and Alzheimer's Disease. *UTS Master of Pharmacology Program*. 17 Mar 2021; virtual.
18. [Samtani S](#) [invited speaker]. Social connectedness for mental health. *Older Person's Mental Health Forum*. 27 Oct 2021; virtual.
19. [Thalumuthu A](#) [Invited Speaker]. Genetics of Age-related phenotypes. *American Society for Microbiology (ASM), Student Chapter series 2019-2021 Webinar Series*. Organised by the School of Biotechnology, Madurai Kamaraj University, Madurai, Tamil Nadu, India. 8 Dec 2021; virtual.
20. [Thalumuthu A](#) [Invited Speaker]. Monte Carlo Simulation, Permutation and Bootstrap for Statistical Inference. *Workshop at the Department of Statistics, Bharathiayar University*. Coimbatore, Tamil Nadu, India. March 2021; virtual.
21. [Wen W](#), [Du J](#), [Dong C](#). Neuroimaging Applications. *CHeBA Seminar Series*. 19 July 2021; virtual.

Seminars/Lectures

1. [Brodaty H](#) [Invited Speaker]. *Inaugural MCI Masterclass*. Online webinar; 1 Sep 2021.
2. [Brodaty H](#) [Invited Speaker]. Q&A Session for New restrictive practice legislation: What prescribers need to know. *CESPHN Update*. Online webinar; 1 Sep 2021.
3. [Brodaty H](#) [Invited Speaker]. Australian dementia care policies & practices. *National Foundation for Australia-China Relations*. Hosted by Flinders University, [online Webinar](#); 13 Sep 2021.
4. [Brodaty H](#), [Hanewald K](#), [Cheung J](#). *Intrinsic Capacity: Operationalisation and Validation of a New WHO Concept for Healthy Ageing*. *CHeBA Seminar Series*. 20 Sep 2021; virtual.
5. [Catts V](#), [Lipnicki D](#), [Chen R](#). How Data Sharing is Changing the Way we Study Dementia. *CHeBA Seminar Series*. 15 Nov 2021; virtual.
6. [Kochan N](#) [Invited Speaker]. Healthy Brain ageing and brain fitness. *U3A Kingston Public Forum*. 12 July 2021. Melbourne, Australia; virtual.
7. [Kochan N](#), [Croot K](#), [Rossie M](#). Computerised tests: What you told us. *CogSCAN Research Webinar (Community Forum)*. 8 Dec 2021; virtual.
8. [Mather K](#). Healthy Ageing: Studying centenarians to reveal the secrets of healthy ageing. *War Memorial Hospital Health Promotion Group Seminar*. 1 Nov 2021; virtual.
9. [Mather K](#). Increasing our understanding of healthy ageing by studying exceptional longevity. *St. George and Sutherland Clinical School Research in Progress Meeting*. 25 Aug 2021; virtual.
10. [Mather K](#). Dare to Care Presenter. *UNSW Medical Science Society: Dementia Advocacy Event*. 2 Nov 2021; virtual.
11. [Mewton L](#), [Winter V](#). Alcohol-related brain impairment: Epidemiology and avenues for prevention. *CHeBA Seminar Series*. 21 June 2021; virtual.
12. [Mohan A](#). Lecturer on the Postgraduate Psychiatry teaching program. Brain and Mind Research Institute, University of Sydney, Australia.
13. [Numbers K](#), [Reppermund S](#), [Jang S](#). The Association Between Independence in Instrumental Activities of Daily Living and Incident Dementia? *CHeBA Seminar Series*. 16 Aug 2021; virtual.
14. [Reppermund S](#) [invited speaker]. To tweet or not to tweet? Using Twitter to promote research. *Australasian Society for Intellectual Disability Webinar*. 10 June 2021; virtual.
15. [Sachdev P](#), [Numbers K](#), [Ginnivan N](#). #NeverTooOld: Challenging Everyday Ageism. *CHeBA Seminar Series*. 22 Feb 2020; virtual.
16. [Samtani S](#), [Stevens A](#). Social Health and Reserve in the Dementia patient journey (SHARED): The relationship between social health

