UNSW SYDNEY

Centre for Healthy Brain Ageing (CHeBA)

Annual Report 2022

Positive Ageing

Prevention

Big Data

Research

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Contents

Co-Directors' Report

2022 was a big year for us as we celebrated our 10 year anniversary. We continued to commit ourselves to a vision of healthier brain ageing, while striving toward having greater impact on the future of dementia in Australia and globally.

Conducting innovative research remained a strong focus in our tenth year, particularly in the areas of vascular dementia, neuroimaging and genetic markers of vascular cognitive disorders, mild cognitive impairment, and better clinical care for those in need. After a decade, it continues to be our belief that the multidisciplinary approach taken by CHeBA is helping us achieve our aspiration to be a world-leader in brain ageing research.

We embraced change under the new Vice Chancellor of UNSW Sydney and celebrated numerous scientific achievements. Our research discoveries continued to be published in prestigious journals which is indicative of CHeBA's success and critical for allowing our outcomes to be disseminated across the global research community.

Our unique work in the development of consortia to research the epidemiology of dementia continues to have a transformational impact – specifically in relation to risk and protective factors for dementia.

We are proud to have been awarded significant accolades this year from the Ryman Foundation and the Academy of the Social Sciences in Australia, in recognition of our dedication to this field of research but also in acknowledgment of our calibre, high quality research output and our influence on research internationally. We also had the honour of the World Health Organisation asking CHeBA to lead the development of a Dementia Research Blueprint to help make dementia research an international priority.

We were encouraged by a $3.3 million NHMRC grant to understand how generational changes in health and lifestyle challenges influence the risk for dementia and the prevalence of cognitive decline with ageing.

This year also saw many other noteworthy mentions, including continued support from Aria Restaurant Sydney and KPMG Sydney to drive our philanthropic and corporate donor engagement. We welcomed iPartners as a new corporate sponsor to our events and witnessed nine corporations sign up for the Sydney Running Festival in support of CHeBA.

We are grateful for the generosity of so many that provide us with the means to bring our community together, none more than Dr Richard Grellman AM, whose staunch support in the year of his wife Suellen's passing from young onset Alzheimer's disease demonstrated his bravery, resilience, and dedication to the cause. The positive effect of Richard's involvement with CHeBA is indisputable, with Wipeout Dementia once again reaching its highest fundraising to date with over $350,000 in contributions. We extend our enormous thanks to all the Captains in the property industry Wipeout Dementia campaign for their support and devotion to the event – Peter Clemesha, Craig Rodgers, Philip Vivian, Steve Watson, Darren Beasley, Anthony Scotts and Joel Ducey.

Throughout this year our talented and fervent team of researchers continued in their pursuit of academic excellence and scientific discovery toward a collective goal of healthier brain ageing for all individuals. We thank them for their dedication and enthusiasm. We would also like to thank our exceptional Centre Manager, Angie Russell, and the CHeBA research support team for their hard work through the year.

We hope that the success of 2022 will continue into 2023 and beyond, and that CHeBA will continue to bring hope to older people with brain disorders around the world.

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 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 and 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.
- Determine the prevalence of age-related neurodegenerative and cerebrovascular disorders and develop biomarkers for their early diagnosis.
- 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 in diverse populations with neurocognitive disorders.

Our Vision

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

Our Mission

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

Our 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 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.

> Increase the number of post graduate 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.

2022 Centre Highlights

"One of the major strengths of CHeBA is its multidisciplinary approach to age-related brain disorders."

Perminder Sachdev AM & Professor Henry Brodaty AO

Professor Perminder Sachdev Awarded the 2022 Ryman Prize

Professor Perminder Sachdev was awarded the 2022 Ryman Prize by the Rt Hon Jacinda Ardern, former Prime Minister of New Zealand, in recognition of research that has substantially enhanced the life of older people around the world.

The Ryman Prize is the world's richest prize of its type and was established to create the equivalent of a Nobel Prize for people working in the field of the health of older people.

The nomination was made by the former UNSW Sydney Vice Chancellor, Professor Ian Jacobs, who said he holds Professor Sachdev in the highest esteem and "as someone who has rendered conspicuous service to medical and health science, and the community at large, in the fields of brain ageing and dementia."

"It is a great honour to be so recognised by one's peers. I share this recognition with the many colleagues and students who have borne much of the burden of the research, and my wife and family who have provided unconditional support throughout my career. I also pay tribute to my patients and research participants who volunteered their time and effort so that future generations may benefit. They have all shared my vision of achieving healthier brain ageing and better clinical care for all," said Professor Sachdev.

Over his 35-year career, Professor Sachdev's research and academic contributions have been influential and vast. His work in the development of consortia to research the epidemiology of dementia has had a transformational international impact. These consortia are unique in their global reach and are leading a re-evaluation of risk and protective factors for dementia.

His work has also informed three prevention trials with lifestyle factors, as well as a repurposed drug being assessed for dementia prevention. The influence of his work is such that in 2022 the World Health Organisation invited Professor Sachdev to lead the development of a Dementia Research Blueprint to help make dementia research an international priority.

Professor Jacobs said that he was "delighted and excited by this well-deserved recognition for Professor Sachdev" and emphasised that in the nomination Professor Sachdev it had "championed the inclusion of diversity in dementia research."

Rt Hon Jacinda Ardern and Professor Perminder Sachdev AM

Professor Henry Brodaty Honoured by ASSA

Professor Henry Brodaty AO

"I am honoured and excited to join the Academy of Social Sciences Australia and to have the opportunity to collaborate with like-minded scientists"

Each year, the Academy of the Social Sciences in Australia elects the most distinguished scientists in Australia as Fellows. This year, the Academy recognised Professor Henry Brodaty for his excellence and input in the field of social sciences, with his work having had major impacts on policy, services, research, and community advocacy for older people. As regards policy, he is an advisor and serves on committees for the World Health Organisation, Australian and NSW governments, the Australian Institute for Health and Welfare and the Australian Commission for Quality and Safety in Health Care on dementia, ageing and mental health services.

"Being awarded the Fellowship is important to me because the social determinants of health are now well-recognised. Social health, itself, is a core component of health and wellbeing."

"I am interested in the links between social, psychological and physical health, and particularly the link between social and cognitive health."

Professor Brodaty has been a leader in the development of psychiatry for the elderly as a specialty in Australia and internationally, especially when previously serving as President of the International Psychogeriatric Association. His research into service improvements include better diagnosis and care in general practice, better post-diagnostic care and better care in residential aged care with a focus on person-centred care.

His widely emulated program to assist family carers of people with dementia reduced carer distress and maintained people living in the community for longer. More recently, the program combined with respite care confirmed delay in nursing home admission, huge potential cost savings which led to a federal budget allocation of $32 million to roll this out nationally.

His studies of population cohorts have advanced the understanding of social and environmental contributions to dementia and demonstrated the importance of social health to maintaining cognitive health. He has a focus on preventing cognitive ageing through modifying lifestyle risk factors and led the world's largest randomised trial of lifestyle online interventions that demonstrated the benefits of preventing cognitive decline.

For over 40 years, Professor Brodaty has been an advocate against the stigma of ageing and dementia through his involvement with Dementia Australia, Alzheimer's Disease International, mainstream media, and regular public talks.

"I am honoured and excited to join the Academy of Social Sciences Australia to have the opportunity to collaborate with like-minded scientists to explore these issues and to be stimulated to think in novel ways."

Study of Centenarians Looks at Prevalence of Dementia

This year CHeBA led the world's largest research project bringing together studies of centenarians and near-centenarians (95+) to look at the global prevalence of dementia in the exceptionally old.

This world-first study obtained and harmonised data of 4,427 people from 18 studies that are part of the CHeBA-led International Centenarian Consortium-Dementia, spanning 11 different countries.

The population of people aged 100 – set to reach 2.2 million people within 30 years – has increased dramatically over the last few decades. Policy makers have concerns about the potential impact of this exceptionally ageing population, particularly around increased rates of disease and disability burden upon health and social systems.

According to Dr Yvonne Leung, lead author on the research, an important concern is the increasing risk of dementia with age, with some questioning whether dementia is inevitable for those that live to an extreme old age.

"Our primary aim was to obtain a better estimate of dementia prevalence in the very old population from around the world and explore risk and protective factors for dementia that are robust across ethno-regional groups," said Dr Leung.

The findings, published in *Alzheimers & Dementia* indicated that among the exceptionally old, dementia prevalence was 53.2% in women and 45.5% in men, and remains higher in the older participants.

Co-Director and senior author on the paper, Professor Perminder Sachdev, said "prevalence of dementia, cognitive and functional impairments increased with age without any indication of levelling off after the age of 100".

"However, unlike the findings from the younger old, dementia was not associated with diabetes, vision and hearing impairments, smoking and body-mass index. We believe that this ethno-regional diverse dataset and its initial findings will facilitate future projects on understanding exceptional longevity and offer important insights into successful ageing."

Living with Others and Community Engagement are Keys to Reduced Dementia Risk

Research led by Dr Suraj Samtani and published in *The Lancet Healthy Longevity* provides evidence to support that living with others, community group engagement and never feeling lonely are associated with slower cognitive decline.

While it is widely recognised that poor social connections such as small networks, infrequent interactions, and loneliness are modifiable risk factors for cognitive decline, research had not examined data beyond North America and Europe until now. Existing research has also combined variables indicating good social connections (such as living with others and being married) instead of looking at each one separately. This means that we couldn't say what exact type or number of social connections we need for healthy brain ageing.

This research looked at approximately 40,000 people across 13 international studies and investigated a range of measures of social connectedness to discover which had the most robust findings in relation to risk reduction of cognitive decline and dementia.

"Our goal was to investigate the association between various social connection markers and the rate of annual change in cognition.

According to co-author Professor Henry Brodaty, the findings have socio-economic significance.

"We found that sharing a home with one or more persons and weekly community group engagement had the most robust results across studies, indicating these factors are fundamental components in the link with less cognitive decline".

"We also identified an association between never feeling lonely and a slower rate of cognitive decline."

Through research such as this we are able to develop and implement societal shifts to reduce risk of memory decline and dementia.

Funding: EU Joint Programme–Neurodegenerative Disease Research grant, funded by the National Health and Medical Research Council Australia, and the National Institute on Aging of the US National Institutes of Health.

DOI: 10.1002/alz.12828

$3.3 Million to Understand Generational Health Challenges

"This study will ultimately enable insight into how to live longer without cognitive decline by targeting dementia prevention strategies."

This year Professor Henry Brodaty was awarded a highly competitive NHMRC grant to understand how generational health challenges influence the prevalence of dementia.

The $3.3 million grant will allow his expert team of researchers to ascertain what changes have occurred in Sydney's next generation of 70 to 90-year-olds in terms of physical, psychological, social and brain health.

Age-related conditions and disabilities are major drivers of care needs and cost associated with ageing, and the top three diseases causing burden in people over the age of 70 are coronary heart disease, dementia, and stroke.

According to Professor Brodaty, the time to prioritise dementia prevention is now, but in order to maximise return on investment there is a need to understand changes at a population level in people's exposure to risk factors, and their uptake of evidence-based strategies for healthy living.

"Ultimately, we want to be able to help inform planning for services and health policy – and better target preventative strategies against Alzheimer's disease and other dementias."

The study will address questions of health challenges by repeating one of Australia's largest population-based longitudinal studies of ageing – CHeBA's Sydney Memory and Ageing Study – one generation later. The highly successful study, which has a strong track record with over 180 peer-reviewed published papers, recruited 1037 dementia-free individuals aged 70-90 and followed them for 14 years.

Professor Brodaty will lead an exceptional research team of experts in epidemiology, cohort studies, big data, physical health, psychological health, social health, cognitive ageing, health economics, diabetes and proteomics and metabolomics, genetics, neuroimaging, neuropsychology, and cognitive testing.

"Research is ***the key*** to the health gains the world has made."

Our Groups

"For dementia research to have an impact, we must understand both risk and protective factors for cognitive decline associated with ageing."

Professor Perminder Sachdev AM

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 post mortem 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 disease and neurodevelopmental diseases. It also focuses 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 collaborates with CKC Technologies (founded by Adjunct Associate Professor Kuldip Sidhu) 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

Recently Dr Nady Braidy was awarded $1.6 million to further develop the NAD+ metabolome as new prognostic biomarkers that could predict disease severity and the progression rate of decline in brain function. The identification of distinct NAD+ metabolome profiles can be used to distinguish between dementia or its preclinical stages. Promoting healthy brain ageing and increasing healthspan is of considerable importance since there have been significant increases in life expectancy due to improved standards of living and access to better healthcare in the developed world. "Unhealthy" ageing has a considerable negative impact on employee performance, workforce engagement, and other societal interactions leading to reduced productivity and placing an immense burden on social welfare. Therefore, renewed understanding of the molecular mechanisms that underlie healthy brain ageing will enable the development of novel strategies to promote healthy brain ageing. Direct health and residential care costs of the aged population currently exceed $10 billion per annum, while the indirect costs in foregone earnings, carer time and expenses are many times of this. Understanding the role of NAD+ metabolism in healthy brain ageing may have translational outcomes of major national benefit in terms of prevention strategies, such as nutritional and life-style interventions.

Group Leader: Dr Nady Braidy

Staff: Professor Perminder Sachdev, Dr Tessa Helman, Dr Marina Ulanova

Current PhD Students: Chul-Kyu Kim

Completed PhD Students: Dr Marina Ulanova, Dr Gurjeet Kaur Virk

Epidemiology

The Epidemiology Group is 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 those led by CHeBA – COSMIC, STROKOG and International Centenarian Consortium for Dementia (ICC-Dementia). An important aspect of this work is genetic epidemiology, which uses various approaches including genome-wide association studies and Mendelian randomisation methods to examine risk factors for dementia and other neurocognitive disorders.

Group Leaders: Professor Perminder Sachdev, Professor Henry Brodaty

Staff: Dr Nicole Kochan, Dr Karen Mather, Dr John Crawford, Dr Anbupalam Thalamuthu, Dr Darren Lipnicki, Dr Yvonne Leung, Dr Vibeke Catts, Amanda Selwood, Dr Teresa Lee, Dr Ben Lam, Dr Louise Mewton, Dr Suraj Samtani, Dr Katya Numbers, Jessica Lo, Fleur Harrison, Dr Sophie Xi Chen

Professor Perminder Sachdev AM & Professor Henry Brodaty AO
Group Leaders

Genomics & Epigenomics

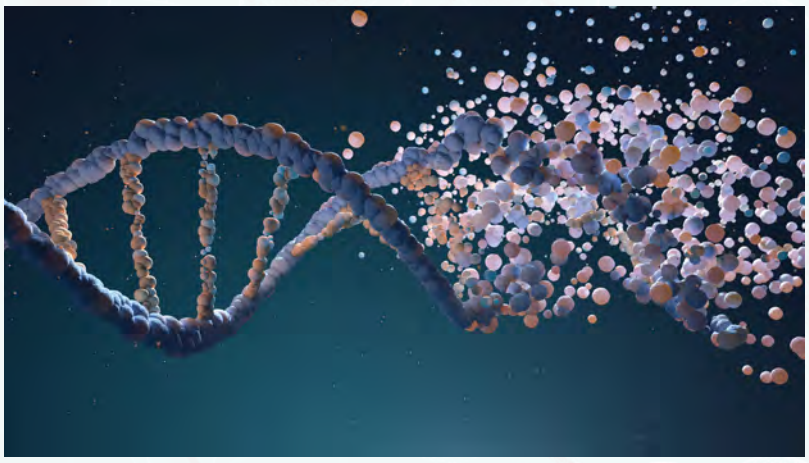
Dr Karen Mather
Group Leader

The overall aim of this group is to identify the genomic, epigenomic and transcriptomic factors associated with healthy ageing and longevity, with a focus on the brain and dementia. To this end, we investigate these questions using data from CHeBA studies: the Sydney Memory and Ageing Study, the Older Australian Twins Study, and the Sydney Centenarian Study. We have collected whole genome sequencing, 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 or transcriptomic factors that contribute to complex traits and disease. We use data from biobanks, such as the UK Biobank and publicly accessible data. The findings of this work have facilitated the identification of novel genes and pathways that contribute to a wide range of traits, including brain structure and cognitive performance, leading to new insights into the underlying biology. Ultimately, we aim to translate these findings into diagnostic, preventative and/or treatment strategies to promote healthy ageing.

Group Leader: Dr Karen Mather
Staff: Dr Anbupalam Thalamuthu, Dr Sumangali Gobhidharan, Ms Sri Chandana Kanchibhotla

Students: Mary Revelas, Dr Adith Mohan, Jessica Lazarus, Abdulsalam Toyin Ademola, Annabel Matison, Fatemeh Amjadimoheb, Anthony Liao

Visiting Student: Emilie Kjeldsen (University of Copenhagen)



Molecular Biomarkers Group

The Molecular Biomarkers Group has a focus on identifying blood biomarkers and understanding mechanisms of dementia using blood samples, diverse clinical cohorts and state-of-the art mass spectrometry techniques and software.

The Group uses the diverse clinical data and blood samples available from CHeBA studies to identify biomarkers of age-related neurodegenerative diseases, particularly vascular dementia, vascular cognitive impairment, stroke, Alzheimer's disease, and mild cognitive impairment.

Group members include clinicians, biochemists, and laboratory scientists. Close collaborations are fostered with many groups within UNSW and beyond, including the UNSW Mark Wainwright Analytical Centre, The University of Melbourne, Washington University School of Medicine, The University of Newcastle (Hunter Medical Research Institute), Garvan Institute of Medical Research, Victor Chang Cardiac Research Institute Limited, Florey Institute of Neuroscience and Mental Health. Such collaborations encourage data sharing and provide group members with access to a variety of research tools, supporting exploration of diverse research angles and methodological innovation.

Group Leader: Dr Anne Poljak

Staff: Dr Tharusha Jayasena, Dr Satoshi Hosoki, Dr Vibeke Catts, Dr Gurjeet Kaur Virk, Dr Fatemeh Khorshidi

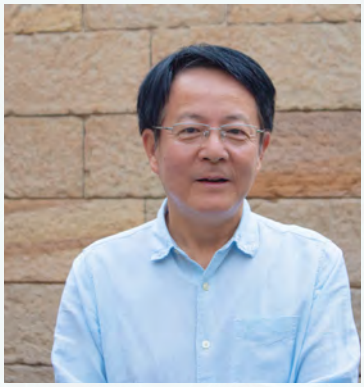
Students: Gurpreet Hansra

Dr Anne Poljak
Group Leader

Molecular Biomarkers Group Projects

- Determining biomarkers of Vascular Dementia, particularly in blood samples, exosomes, etc
- Managing the CHeBA BioBank, samples storage, aliquoting, addressing samples requests, assisting with transition to management by UNSW Biorepository
- Determining blood biomarkers of Alzheimer's disease
- Other projects: (a) develop a blood assay for oxytocin; (b) understanding the hormesis response of cells with exposure to natural products

Neuroimaging



Associate Professor Wei Wen
Group Leader

The Neuroimaging Group is dedicated to researching the ageing of the human brain. By using neuroimaging, we aim to improve our understanding of brain ageing pathways, which in turn will lead to clinical advances in prediction, diagnosis, and treatment. We are interested in computational neuroanatomy, structural, functional, and physiological imaging of the ageing brain using MRI. Our neuroimaging studies address normal ageing, mild cognitive impairment (MCI) and dementia with a special research interest in cerebrovascular burden.

Group Leader: Associate Professor Wei Wen

Staff: Dr Jiyang Jiang, Shizuka Hayashi, Keshuo Lin

Students: Abdullah Alqarni, Chao Dong, Shizuka Hayashi, Mohammed Alghamdi, Keshuo Lin

Neuropsychiatry

Professor Perminder Sachdev AM
Group Leader

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 for treatment. In 2022, a new clinic to assess and treat Functional Neurological Disorders (FND) was started under the auspices of the Mindgardens Neurosciences Network. The group also provides important education services for clinicians and trainees.

Group Leader: Professor Perminder Sachdev

Staff: Dr Adith Mohan, Dr Rebecca Koncz, Dr Matt Paradise, Emily Swift

Neuropsychology

Dr Nicole Kochan &
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 has produced an automated neuropsychological norming tool aimed at improving the efficiency of a neuropsychological assessment by automatically calculating normative data and producing a summary report from a comprehensive range of gold standard neuropsychological tests. An important focus is identifying appropriate cognitive instruments for individuals coming from culturally and linguistically diverse backgrounds to enable a more accurate diagnosis of cognitive impairment in these individuals. A major project, the CogSCAN Study, is evaluating the reliability, validity and usability of computerised neuropsychological assessment for older adults in clinical and research settings to improve accessibility and diagnostic accuracy of neurocognitive disorders. We have established strong collaborative links with researchers in CHeBA and with international consortia such as IGEMS and ENIGMA, investigating associations between cognition and brain structure and function, and genetic and environmental contributors to cognitive performance in older adult populations.

Group Leaders: Dr Nicole Kochan, Dr Teresa Lee

Staff: Dr John Crawford, Dr Ben Lam, Dr Karen Croot, Dr Adam Bentvelzen, Josephine Bigland, Ashton Trollor

Students: PhD candidate: Zara Page; Masters in Clinical Psychology: Matilda Rossie

Risk Factors Group

Dr Louise Mewton
Group Leader

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 COSMIC Consortium 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 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.

Group Leader: Dr Louise Mewton

Staff: Virginia Winter, Sarah Davies, Rachel Visontay, Nicholas Hoy

Students: PhD Candidates: Rachel Visontay (USyd), Nicholas Hoy (UNSW Sydney)

Understanding Risk of Dementia and Alcohol Consumption

A 2022 study led by Dr Louise Mewton reignited the debate about whether low levels of drinking could be positive for health. The review, published in *Addiction*, showed that abstaining from alcohol completely can actually increase the risk of dementia.

Risk factor reduction is a fundamental strategy for the prevention of dementia – particularly in light of the absence of disease-modifying treatments for dementia. A 2020 report from The Lancet Commission for Dementia Prevention, Intervention and Care estimated that 40% of global dementia cases could be prevented or delayed if 12 key modifiable risk factors for dementia were eliminated – with excessive or harmful alcohol use in midlife newly listed as one of those factors.

Dr Mewton said the inclusion of alcohol as a key risk factor for dementia was based on consistent and robust evidence indicating that chronic heavy alcohol use was associated with dementia and cognitive decline.

"There is controversy over the impact of more moderate levels of alcohol use on the incidence of dementia," explains Dr Mewton.

"Even low levels of alcohol use have been associated with poorer health outcomes.

They have also been associated with atrophy in key regions of the brain linked to dementia, like the hippocampus."

However, in Dr Mewton's international study of nearly 25,000 community dwelling adults over the age of 65, it was consistently shown that abstaining from alcohol was associated with a higher risk of dementia.

"Our data came from 15 studies of healthy ageing participants across six continents, and robust assessment of alcohol use and dementia," said Dr Mewton. "Over the duration of the study 2,124 of the adults developed dementia."

The researchers found that individuals drinking up to four Australian standard drinks per day had a lower risk of dementia when compared with individuals who did not drink at all. The lower dementia risk associated with drinking alcohol was evident over and above the effects of demographic and clinical characteristics.

Senior author and Co-Director of CHeBA Professor Perminder Sachdev said that while light to moderate alcohol use may be associated with reduced dementia risk, even low levels of alcohol use may be harmful to the brain.

"What we can conclude from our study is that there doesn't appear to be a need to intervene in those older adults currently drinking in a light to moderate pattern if dementia prevention is the ultimate goal," said Professor Sachdev.

DOI: 10.1111/add.16035

Clinical & Care

"Through research, there is enormous hope for better clinical care of people living with dementia." Professor Henry Brodaty AO

ADNeT

The Australian Dementia Network (ADNeT), a collaboration connecting leading researchers, clinicians, and consumers from across 17 Australian institutions including CHeBA, was developed to create a network for dementia prevention, treatment and care, with three key initiatives:

- The establishment of a national clinical quality registry for dementia;
- The development of unified guidelines for the diagnosis and treatment of neurocognitive disorders and the creation of a network of memory clinics; and
- The development of effective therapies for the prevention and treatment of dementia through improved patient screening and trial participation.

Funded by the National Health and Medical Research Council (NHMRC).

Australian Dementia Network

REGISTRY. CLINICS. TRIALS.

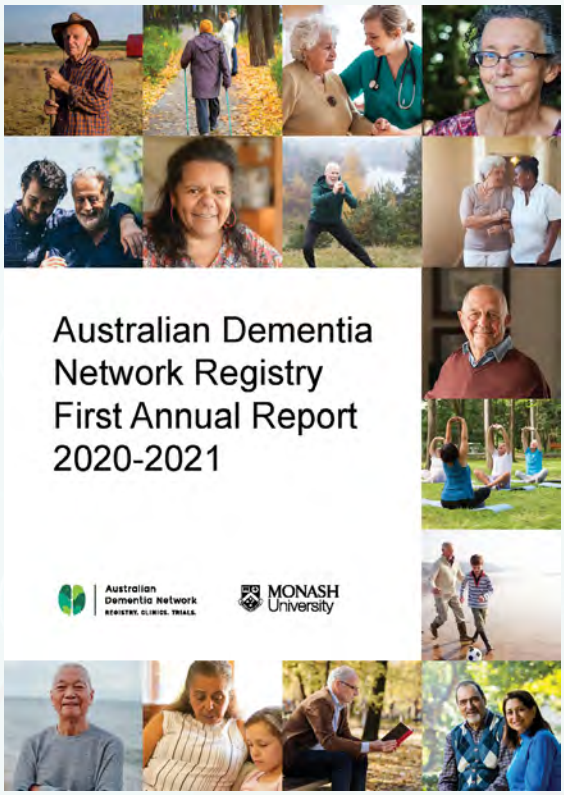
ADNet Registry Releases First Annual Report

Dr Stephanie Ward

This year the ADNeT Registry released its First Annual Report, providing a "Report Card" on the quality of care being delivered to Australians diagnosed with dementia and mild cognitive impairment.

Until now there has been no national, systematic, and coordinated approach to measuring the quality of dementia diagnosis and care. Having this type of data in a format that can be readily accessed will enable clinicians, healthcare providers and policy-makers to monitor quality of care and improve performance, and better understand the experience and outcomes from the perspectives of patients and their caregivers. The ADNeT Clinical Quality Registry for Dementia and Mild Cognitive Impairment was developed to fill this gap.

Dr Stephanie Ward, the ADNeT Registry Clinical Lead and Senior Research Fellow at CHeBA said, "the diagnosis and clinical care for dementia, and syndromes that may represent the prodromal phases of dementia, such as mild cognitive impairment, provides lots of challenges for clinicians. Providing good care is complex but participating in the ADNeT Registry allows us clinicians an important opportunity to benchmark our performance and understand the true experience of our community. The Registry supports clinicians like me to deliver the best possible care that we can."



Neuropsychology Tool Streamlines Cognitive Assessment, Diagnosis and Care

A major achievement this year from ADNet was the development of a new tool to accelerate a clinical diagnosis of Alzheimer's disease and other dementias.

Developed specifically for clinical neuropsychologists by the ADNeT Memory Clinics initiative, CHeBA, the University of Sydney's Brain and Mind Centre and the CSIRO, the tool promises to speed up the rate at which a potential diagnosis can be formulated and communicated to the client.

Currently, Australians can face delays of approximately three years on average between initial symptom presentation and a formal diagnosis of dementia. This increases to an average of seven years for some young-onset dementias, such as frontotemporal dementia.

Given neuropsychological assessment is essential for evaluating memory and other thinking skills that often decline early in dementia, the benefit of the tool is that it will speed up the assessment process by automatically calculating normative data and producing a summary report from a comprehensive range of gold-standard neuropsychological tests.

Ultimately, the tool will set a new standard for how neuropsychological evaluation can be conducted, with enormous benefit to both clinicians and clients.

ADNeT Deputy Director and co-lead of the Memory Clinics initiative, Professor Perminder Sachdev acknowledged the work of CHeBA's Dr Nicole Kochan, Dr Adam Bentvelzen, and Inga Mehrani in bringing this tool to its maturity.

Mindgardens FND Clinic

The Mindgardens Functional Neurological Symptom Disorders (FND) Clinic was established by CHeBA Research Fellow Dr Adith Mohan to provide short-term, post diagnostic multidisciplinary care to patients in New South Wales. This clinic will contribute to increasing FND awareness and knowledge among health-care providers, improve the management and care of these disorders in emergency, inpatient and outpatient settings, and develop treatment tools relevant to caring for patients across public and private sector settings. Collection of clinical data is a vital part of the Clinic.

Functional Neurological Symptom Disorders (FND) are a common and potentially reversible cause of neuropsychiatric disability. The highest prevalence is among young to middle-aged adults of whom more than a third are, as a result, forced out of the workforce and experience significant levels of disability.

The Australian-first Clinic is funded by the Mindgardens Neuroscience Network and will provide a multi-disciplinary assessment together with an intervention program suitable for patients.

The Clinic will operate from the Neuropsychiatric Institute (NPI) at the Prince of Wales Hospital, of which CHeBA Co-Director Professor Perminder Sachdev is Director.

The goal of the Clinic is to create and evaluate a model for gold-standard, evidence-based care provision for FND in Australia.

mindgardens
Neuroscience Network

Funding Success to Transform Care for Common Neurological Disorders

Dr Adith Mohan

Research Fellow Dr Adith Mohan was this year awarded a Maridulu Budyari Gumal, which is a Sydney Partnership for Health, Education, Research and Enterprise (SPHERE) grant to improve clinical outcomes for patients with Functional Neurological Symptom Disorders (FND).

The award will bring together a team of international experts in the field to address the gaps in the delivery of responsive, evidence-based services for FND across Australia and New Zealand.

Dr Mohan, leader of the Mindgardens FND Clinic said the creation of collaborative consortia of specialist clinics positively influence health outcomes in highly prevalent disorders.

This consortium for FND – the first of its kind and named CARE FND – will facilitate efforts to systematically collect epidemiological and clinical data that can be translated into gold-standard practice and shape policy development.

"This funding will allow existing services to come together to evaluate the current landscape of FND care provision and develop robust guidelines that can shape the development of pathways of care that engage primary health networks, private sector providers and NGOs alike in the assessment and management of FND."

Chief Investigator Professor Perminder Sachdev will provide expert guidance in the set up and governance of CARE FND.

DCRC

The Dementia Centre for Research Collaboration (DCRC), which had continuous funding since 2006 from the Commonwealth Department of Health and Ageing and then from the NHMRC, ceased operation at the end of 2021. DCRC funded many projects over the 15 years across Australia, promoted collaboration, provided practical research, which was implemented into practice, forged new partnerships, and encouraged novel research. Results were widely disseminated and made available on the DCRC website.

With the cessation of DCRC funding in 2021, the website was gradually wound down. Three topics, which were found to be extremely useful and well used by clinicians and researchers, were migrated to the CHeBA website during 2022.

The *Dementia Outcome Measurement Suite (DOMS)* provides a guide to scales and measures for assessment of cognition, staging (of severity), function, behaviours, delirium, and quality of life. The scales are rated using a traffic light system to rate psychometrics, user friendliness, time, and cost (if any). The actual scales and questionnaires are able to be downloaded free of charge; permission has been provided by the authors.

The 2012 *Clinician's Guide to Good Practice: Managing Behaviours and Psychological Symptoms Of Dementia (BPSD)* provides an evidence based guide for clinicians and family carers in understanding and assisting people who develop such behaviours. After general introduction and principles, the guide is arranged alphabetically from, aggression, agitation anxiety, apathy, depression, disinhibited behaviours, nocturnal disruption, psychotic symptoms (delusions and hallucinations), vocally disruptive behaviours and wandering. Descriptors, possible causes, differential diagnosis, effects on the person and those involved in their care, and management strategies are summarised for each behaviour. The guide is available online and as an App with separate formats for clinicians and family carers. An update of the 2012 guide is in preparation and will be available in 2023.

The General Practitioner Cognitive Assessment (*GPCOG*) is a short and efficient way to examine and assess cognition in primary care. Its psychometric properties are at least equivalent to use of the Mini-Mental State Examination (MMSE). A link to the GPCOG is provided on the CHeBA website.

Depression in People Living with Dementia

Research published in *Ageing Research Reviews* has confirmed that treating symptoms of depression in people living with dementia is most effective when a non-pharmacological approach is adopted.

Depression is a common psychological symptom associated with dementia and is estimated to occur in between 10% and 62% of people living with dementia. To date, pharmacological approaches continue to be used to treat depression in dementia, despite the failure of relying on medications being highlighted in large-scale studies.

The review and meta-analysis investigated a range of nonpharmacological approaches for symptoms of depression in dementia, identifying 37 relevant nonpharmacological studies from 27,126 articles published between 2012 and 2020.

Lead author and Postdoctoral Fellow Dr Claire Burley said that the findings support a positive link between nonpharmacological approaches and reduced symptoms of depression in people living with dementia.

According to Professor Henry Brodaty, the findings have statistical and clinical significance.

"We found there is great potential to reduce symptoms of depression in dementia – without the use of medications. This is even more relevant as randomised trials of antidepressant medications have not been shown to alleviate depression in people living with dementia."

"Pharmacological approaches should only be considered when psychosocial approaches have been proved to be ineffective or in cases of urgency."

CHeBA-led Consortia

"Bringing scores of international studies together for a common purpose will form the future of dementia research."
Professor Perminder Sachdev AM

COGNISANCE

Dr Meredith Gresham
Project Coordinator

Co-designing dementia diagnosis and post diagnostic care 'COGNISANCE' is an international consortium passionate about tackling the global issue of lack of post-diagnostic dementia support. In its third and last year, this project has involved translating and effectively communicating the growing evidence base around delivering a diagnosis of dementia with hope and providing information and resources that will enable people with dementia and their families to live positively and maintain, and potentially improve, their quality of life.

The first half of 2022 saw the continuation of our co-designed, social marketing campaign, "Forward with Dementia". Launched in October 2021, our Australian campaign has provided an ongoing series of webinars, podcasts, conference presentations, radio interviews, monthly newsletters, social media posts, and our 'hub', the co-designed, comprehensive website www.forwardwithdementia.au

The website is a central point for the campaign and contains three sections, one each specifically written for people recently diagnosed with dementia, their main supporter and health professionals. Within each section are short articles with up-to-date, evidence-based information and importantly, resources and actions to take to understand, better cope with and support living life positively. There are news items and stories from people impacted by dementia who have not only coped but flourished.

Project evaluation has been undertaken using the RE-AIM approach. This approach seeks to understand the project's Reach, Effectiveness, Adoption, Implementation and if the Forward with Dementia messages and resources are being Maintained. Comprehensive data collection has involved surveys, interviews, recording of project engagement, including downloading or ordering of printed project resources, Google Analytics, and social and traditional media analytics.

Initial results are positive.

Following a webinar one diagnostician remarked:

"I found that really refreshing and it made me kind of start to think about how we need to be changing our initial conversation, and perhaps kind of incorporating that positive energy into our kind of initial interaction". (AUS-HSCP3-W)

A person with younger onset dementia said:

"Love the suggestions & links under all the headings. So well organised. So positive! The language is simple and things are explained in a matter-of-fact way taking away from stigma or shame. The site is information rich, user-friendly and positive but I think some aspects of 'living with dementia' are in the real-world context. The website is a fabulous resource. I wish I had found it two years ago as I have spent a lot of time looking for what you have in one place." (AUS-CP5-55-W)

Our international teams' collective experience has been compiled into a Playbook to encourage delivery of similar campaigns in other countries. The Playbook will be launched at the International Psychogeriatric Association Congress in Lisbon, Portugal in June 2023.

Australian Staff

Professor Henry Brodaty, Chief Investigator

Dr. Meredith Gresham, Project Coordinator

Nora Wong, Research Officer

Collaborators

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 (UK), Newcastle University (UK), Maastricht University (Netherlands), Wroclaw Medical University (Poland), McGill University and Universities of Waterloo and New Brunswick (Canada).

What is Social Marketing?

Social marketing is an adaptation of contemporary commercial marketing theory and practice to influence positive social change for the benefit of individuals, groups, or society.

Definition adapted from Dann, S. (2010) Redefining social marketing with contemporary commercial marketing definitions. *Journal of Business Research* 63, 147-153.

What is co-design?

Co-design is a method that brings people living with dementia, families, health professionals and researchers together to design and improve services. It is about creating equal status between all group members. Co-design is based on the idea that by involving people with experience of relevant issues and problems it will result in outcomes that better meet needs.

Definition adapted from Agency for Clinical Innovation 2019. Patient experience and consumer engagement. A guide to build co-design capability. NSW Government: Agency for Clinical Innovation, 2019. https://aci.health.nsw.gov.au/

COSMIC

Dr Darren Lipnicki
Project Manager

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

By the end of 2022 there were 55 international studies participating in COSMIC. For a full list see *https://cheba.unsw.edu.au/consortia/cosmic/studies*

The major highlights for COSMIC in 2022 include:

Signing an MOU with 11 new studies:

- Five 10/66 studies, from Dominican Republic, Mexico, Peru, Puerto Rico, and Venezuela
- EpiFloripa Aging Study (Brazil)
- International Mobility in Aging Study (Albania, Brazil, Colombia, Canada)
- Neuroepidemiology of cognitive impairment in adults from marginal urban areas: a door-to-door population study in the Puente Piedra district (Peru)
- Northern Ireland Cohort for the Longitudinal Study of Ageing
- Taiwan Initiative for Geriatric Epidemiological Research
- Vallecas Project (Spain)

Four new projects were approved:

- Sex-specific risk and associated factors for transitions to mild cognitive impairment and dementia in diverse international cohorts of older adults from the COSMIC consortium.
- Associations of multimorbidity of cardiometabolic conditions with cognitive decline and dementia.
- Social health and cognitive health trajectories among healthy older adults.
- Nightmares, cognitive decline and dementia.

Three papers were published:

- Ding et al. Dose-response relationship between late-life physical activity and incident dementia: a pooled analysis of 10 cohort studies of memory in an international consortium. Physical activity and cognitive decline in older adults. *Alzheimers Dement*. 2023 Jan;19(1):107-122. DOI: 10.1002/alz.12628. Epub 2022 Mar 15.
- Mewton et al. The relationship between alcohol use and dementia in adults aged over 60 years: A combined analysis of prospective, individual-participant data from 15 international studies. *Addiction*. 2023 Mar;118(3):412-424. DOI: 10.1111/add.16035. Epub 2022 Sep 4.
- Samtani et al. A global collaborative population-based cohort study to examine relationships between social connectedness and cognition. *Lancet Healthy Longev*. 2022 Nov;3(11):e740-e753. doi: 10.1016/S2666-7568(22)00199-4. Epub 2022 Oct 20.

Presentations at international conferences, including

- Alzheimer Europe
- Alzheimer's Association International Conference
- International Society of Posture & Gait Research International Congress.

International collaborations with:

- The Institute for Health Metrics and Evaluation (IHME) at the University of Washington, where COSMIC has facilitated data provision from 17 cohorts for the Global Burden of Disease (GBD) study.
- The Davos Alzheimer's Collaborative (DAC), 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.
- COVID-19 study led by Dr Sarah Bauermeister (University of Oxford), to which around six COSMIC cohorts are contributing.

Dementia Platform Australia (DPAU)

- UNSW Sydney's sub-licence agreement with Monash Secure eResearch Platform (SeRP) was signed, allowing DPAU to utilise the SeRP as the data repository and analysis environment and proceed to execute Data Deposit Agreements with COSMIC studies.
- So far, 23 COSMIC studies have agreed to deposit data on DPAU, with six signing a Data Deposit Agreement and one study – the Sydney Memory and Ageing Study – being onboarded.

Staff: Professor Perminder Sachdev, Dr Darren Lipnicki, Dr John Crawford, Dr CP Ben Lam, Dr Louise Mewton, Nicholas Hoy, Rachel Visontay, Professor Henry Brodaty, Dr Suraj Samtani, Ashley Stevens, Gowsaly Mahalingam, Dr Jiyang Jiang, Dr Nicole Kochan, Jessica Lo, Dr Vibeke Catts, Rory Chen, Juan Carlo San Jose

Students: Dr Matthew Lennon, Annabel Matison

COSMIC Named to the Global Davos Alzheimer's Collaborative

In January 2022, the Davos Alzheimer's Collaborative (DAC) announced that COSMIC had agreed to be part of the DAC Global Cohort Development program, a ground-breaking data platform to accelerate the discovery, assessment, and delivery of precision interventions for Alzheimer's disease.

COSMIC is among the first to be named to the DAC and will bring data from eight countries to the new program – to help drive scientific discovery by providing researchers access to an extensive, truly international platform populated with brain related health data from broad and diverse populations. This data resource will help determine the causes, predispositions, and habits of people who develop Alzheimer's disease. It may also inform drug discovery and clinical care at a more rapid pace.

More of the COSMIC cohorts are expected to join DAC's strategic plan of expanding this concept worldwide.

SHARED

Dr Suraj Samtani
Study Coordinator

Highlights from 2022

We know that social isolation is a modifiable risk factor for dementia and accounts for about 4% of dementia cases worldwide. Cases of dementia are expected to double by 2050 and we need a greater understanding of each modifiable risk factor to inform the population and prevent this condition. Existing meta-analytic studies have used data from only North America and Europe and have used summary estimates from various studies all accounting for different sets of risk factors.

We wanted to answer the following questions: What kind and number of social connections do we need in order to slow down cognitive decline? Are these findings the same globally and not just in North America or Europe? Do these findings stay the same after accounting for all the known modifiable risk factors for dementia?

To answer these questions, the NHMRC and European Union Joint Programme - Neurodegenerative Disease Research funded a project called SHARED (Social Health and Reserve in the Dementia patient journey). Our team at CHeBA worked 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.

We harmonised data from 13 longitudinal cohort studies of ageing in North America, South America, Europe, Africa, Asia, and Australia. It is the largest meta-analysis on this topic (N = 40,006) and the first to include studies beyond North America and Europe. For the first time, we were able to answer the question of what kind and number of social connections we need to slow down cognitive decline. We found that living with others, being in a relationship, at least yearly community activities, and at least monthly friend/family interactions were associated with slower cognitive decline. This knowledge is useful for clinicians to recommend specific types and frequencies of social interactions, and for policy makers to drive prevention campaigns at a population level.

This article was published in *The Lancet Healthy Longevity* and has been featured on The Lancet podcast: https://www.buzzsprout.com/1746618/11655378.

We are now focusing on examining the link between social connections and risk of dementia and mortality. We hope to publish this next paper in the coming year.

Our take home messages are:

Try to see family/friends at least once a month.

Try to take part in community activities like volunteering, music groups, or walking groups at least a few times a year.

Stay physically, mentally, and socially active for healthy brain ageing.

Staff: Dr Suraj Samtani, Gowsaly Mahalingam, Dr CP Ben Lam, Dr Darren Lipnicki, Professor Perminder Sachdev, Professor Henry Brodaty

SHARED
Social Health and Reserve in the Dementia Patient Journey

STROKOG

Jess Lo
Study Coordinator

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 37 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.

In 2022, the following new studies joined STROKOG:

- Delirium and Risk of Vascular dementia after a Stroke (DRIVERS) from Nigeria
- Bulgarian SVD study from Bulgaria

We published a paper in *Stroke* titled 'Texture features of MR images predict post-stroke cognitive impairment: validation in a multi-centre study'. The project was led by Dr Nacim Betrouni, a collaborator from Lille, France. Dr Betrouni examined the reliability of using texture features of MRI to predict post-stroke cognitive impairment using data from three STROKOG studies. The study found that texture features obtained from routine clinical MR images are robust early predictors of poststroke cognitive impairment and can be combined with other demographic and clinical predictors to build an accurate prediction model.

Jess Lo submitted a paper to *Neurology* titled 'Short-term trajectories of post-stroke cognitive function'. The project included nine STROKOG studies and Jess found that the trajectory of cognitive function over the first year after stroke is heterogenous and that we can predict long-term cognitive outcome based on cognitive test results at around 3.6 months after a stroke event. Jess also found that older age, lower levels of education, diabetes, large artery strokes, and greater stroke severity are risk factors for lower cognitive performance over the first-year post-stroke.

There are eight other on-going STROKOG projects led by CHeBA researchers and external researchers. They include Dr CP Ben Lam (CHeBA) who is planning to submit his paper on post-stroke depression. Ben found that depression was frequent after stroke, and that female sex, less education, depression, more severe stroke and cognitive or functional impairment increases the risk of depression. Dr Lena Oestreich from the University of Queensland is leading a project on the comorbidity and interactions of neurobehavioral syndromes. Lena found that neuropsychiatric, cognitive, and functional complications of stroke are interrelated, and that novel interventions focused on alleviating worry and promoting independence may lead to overall improvement from post-stroke complications. Lena is finalising her paper and plans to submit early next year.

STROKOG is supported by an NHMRC Centre for Research Excellence grant. In addition to studies with stroke/TIA patients, the consortium will expand in 2023 to include studies with high vascular risk patients or intervention studies that aim to reduce the impact of cerebrovascular disease.

Staff: Professor Perminder Sachdev, Jess Lo, Dr John Crawford, Dr CP Ben Lam, Dr Darren Lipnicki

STROKOG

Longitudinal Studies

Maintain Your Brain

Maintain Your Brain (MYB) was 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 were addressed through coaching or information targeting 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. While data collection ended in October 2021, 2022 saw the data cleaned (a monumental task) and analyses got underway. We presented preliminary results in August 2022 and look forward to sharing results in 2023.

Staff: Professor Henry Brodaty, Professor Perminder Sachdev, Tiffany Chau, Fleur Harrison, Dr Megan Heffernan, Juan Carlo San Jose, Dr Nicole Kochan, Professor Michael Valenzuela, Dr Heidi Welberry

Older Australian Twins Study

Highlights from 2022

OATS data have contributed to 15 papers published in scientific journals, including the *Journal of Alzheimer's Disease, Nature Neuroscience, Human Brain Mapping*, and *The Journals of Gerontology Series A, Biological Sciences and Medical Sciences*. Annabel Matison presented a paper at the American Society of Nutrition Conference 2022.

OATS Online Journey 2 commenced in November 2021 and is expected to be completed in early 2023, with the last participants beginning their journey in late January. About 190 participants are expected to have completed OATS assessments by the end of Journey 2 data collection. Twelve new participants were recruited due to the OATS Online media launch in November 2021 from NSW, SA, ACT, and WA. Alongside the OATS Online participation, they also provided saliva samples for DNA analysis, ready for processing in 2023.

OATS Online Journey 2 assessments differed slightly from Journey 1, with more detailed questions about traumatic brain injury, sleep apnoea risk, female hormone use, resilience, and social and emotional loneliness. Two new telephone interviews were introduced: the Montreal Cognitive Assessment (MoCA) Blind for all participants to better estimate their cognitive status; and Self-rated Activities of Daily Living (ADLs) and Instrumental Activities of Daily Living (IADLs) for participants without an informant. Around 30 participants completed this new interview.

The OATS Online Platform (OOP) was updated with minor improvements thanks to OATS' Health Informatics Specialist, Juan Carlo San Jose. Better processes for preparing participants for consensus diagnosis and recording it in the OOP were introduced. A new feature was implemented that allows participants who have withdrawn from OATS to be introduced to the OOP.

Our contribution to the IGEMS (Interplay of Genes and Environment across Multiple Studies) consortium continued in 2022, with OATS data contributing to two papers being published by IGEMS researchers, co-authored by OATS researchers Dr Teresa Lee, Scientia Professor Perminder Sachdev, Dr Vibeke Catts, and Dr Adith Mohan. In June, the OATS team helped the UNSW Microbiome Research Centre recruit participants for The Healthy Optimal Australian Microbiome (HOAM) study. Over 60 OATS participants living in the HOAM catchment areas were invited to participate in HOAM.

Data collection for OATS will conclude at the end of Journey 2 in 2023, with Juan Carlo San Jose and the OATS study coordinator, Dr Amanda Selwood, leaving OATS at the end of 2022. Data collected from Baseline through OATS Online Journey 2 will continue to be entered, cleaned, and released for data analysis through the same channels.

OATS acknowledges funding from the National Health and Medical Research Council and the Dementia Momentum. OATS also gratefully acknowledges the contribution of Twins Research Australia, who facilitated the initial recruitment of OATS participants. The ongoing support of OATS' participants, project staff and many collaborators in Australia and worldwide is greatly appreciated.

Staff: Ongoing OATS staff include Scientia Professor Perminder Sachdev, Dr Vibeke Catts, Dr Amanda Selwood, Dr Teresa Lee, Professor Julian Troller, Juan Carlo San Jose, Dr Karen Mather, Dr Anbupalam Thalamuthu, and Scientia Professor Henry Brodaty. Dr Amanda Selwood and Juan Carlo San Jose will leave the OATS team at the end of 2022.

Students: In 2022, 11 PhD students, three Masters, and one Honours student used OATS data in their thesis projects. Completions in 2022 included Dr Rebecca Koncz, who submitted her PhD thesis, Anthony Liao, who submitted his Honours thesis, and the Masters students, who completed their projects. Ongoing PhD students include Toyin Abdusalam, Abdullah Alqarni, Chao Dong, Annette Spooner, Andrea Lammel, Annabel Matison, Jing Du, Emilie Westerline Kjeldsen, Ella Hopkins and Shizuka Hayashi.

Sydney Centenarian Study

The Sydney Centenarian Study (SCS) was launched in 2007, with 445 Sydney residents aged 95 and above recruited during two waves of recruitment, 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 completed 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 provided invaluable information on the biology of centenarians. 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.

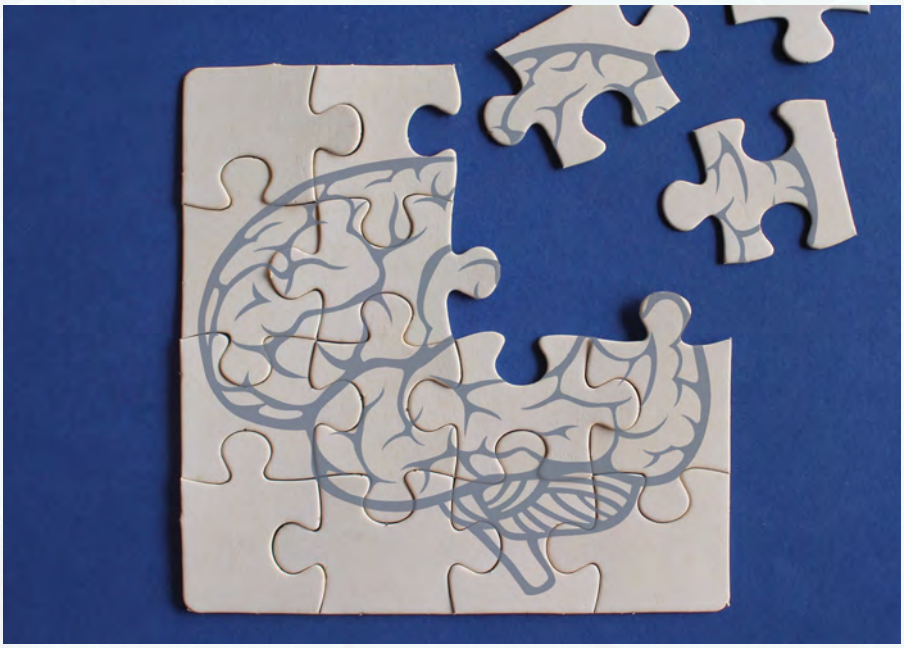
Fleur Harrison
Study Coordinator

Sydney Memory & Ageing Study

2022 was a year of endings and beginnings for the Memory and Ageing Study Team. We officially finalised and released all outstanding MAS data, along with scoring guides and norms, to our internal and external investigators. We were also granted permission to use MAS data for collaboration with industry partners, opening the door to several exciting new collaborations. In 2022, the original Memory and Ageing Study officially wrapped up. However, we also began an exciting new journey as our Team planned for and prepared to begin the Memory and Ageing Study – Part 2 (MAS2), whereby we will replicate and extend the original study's findings with a fresh cohort and innovative new questions and techniques with support from a successful NHMRC grant totaling over $3.3M.

The original Memory and Ageing Study (MAS1) began in 2005 and officially concluded at the end of 2020, making it one of the largest and longest running single cohort studies of ageing in Australia. MAS is renowned for its data nationally and internationally, largely because the study had followed the same cohort (i.e., 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. This longitudinal data allowed us to monitor individual changes over time and better understand what factors predict healthy cognitive ageing versus neurodegenerative diseases like dementia.

Lifestyle factors that promote cognitive health or predict risk of dementia may change over a generation. Each generation's experiences differ from its predecessor. While improvements in education, health care and work opportunities should lead to better cognitive, physical, psychological, and social health, results of studies are mixed. Knowledge of changes in health profiles are important for planning services. Understanding the drivers of good health and quality of life and risk factors of poor health can assist in targeting health promoting and preventative interventions. In summary, there are gaps in knowing what changes to expect in the rates of these conditions and in their risk and protective factors.



The NHMRC Clinical Trials and Cohorts Grant will allow us to refresh the MAS1 sample for an entirely new study (the Memory and Ageing Study Part 2 – MAS2), which will allow us to assess the generational change in four domains of health of older people - physical, psychological, social, and cognitive/brain health - by repeating comprehensive cross-sectional and longitudinal assessments of a defined population, and of associated use of health services. The wealth of knowledge gained from MAS1 perfectly positions us to examine whether risk factors associated with cognitive decline and dementia have changed over a generation so that we can make appropriate policy and healthcare recommendations. Our extraordinary team of international experts will be leading this effort with recruitment starting in early 2023.

Staff: Professor Henry Brodaty, Professor Perminder Sachdev, Dr Nicole Kochan, Professor Wei Wen, Professor Julian Trollor, Professor Brian Draper, Dr Karen Mather, Dr John Crawford, Dr CP Ben Lam, Dr Katya Numbers, Dr Vibeke Catts, Josie Bigland, Zara Page.

Students - PhD: Annabel Matison, Abdullah Alqarni, Dr Russell Chander, Sophie Chen, Choa Dong, Dr Jing Du, Li Li, Dr Premilla Chinnappa-Quinn, Fleur Harrison, Fatemah Khorshidi, Matthew Lennon, Nithin Manchery, Zara Page, Toyin Abdulsalam, Mary Revelas, Dr Gurjeet Kaur Virk, Dr Janet Mitchell, Shizuka Hayashi, Mary Revelas.

Students – Hons: Anthony Liao, Shafi Kalem, Jessica Sawang, Leilei Zhang.

Highlights from 2022

- NHMRC Clinical Trials and Cohorts grant to refresh the MAS Study (MAS2); a five-year grant totalling $3.3M.
- All Wave 7 data was cleaned, checked, and released with scoring notes to internal and external investigators.
- MAS received ethics approval to share previously collected data with commercial entities.
- MAS COVID-19 questionnaire was shared with German collaborators who collected ~900 responses from older Germans, facilitating cross-country comparisons.
- All Honours students using MAS data received HDs for their thesis projects and presentations; three have prepared and/or submitted their manuscripts for publication.
- MAS data contributed to 10 new manuscripts in high impact journals (e.g., *Lancet Global Health*; IF = 38.93), with an additional 8 manuscripts currently under review.
- MAS data contributed to 5 successful PhD theses and 4 successful Honours theses in 2022.
- MAS contributed data to 14 global dementia consortia projects in 2022 – with 5 publications in 2022 attributed to global consortia collaborations (COSMIC, SHARED, ADNI, etc.).

Students, Achievements & Awards

PhD Completions

Dr Janet Mitchell
Meaningful Relationships for People Experiencing Dementia-Associated Behaviours in Residential Aged Care

Meaningful relationships for people experiencing dementia associated behaviours haven't been prioritised in residential aged care. I found that residents engaged in meaningful relationships when supported to do so. Associated factors included care provider executive trained in and committed to relational person-centred care, care home management empowered to innovate, and all care partners supported and recognised e.g., sufficient time to engage with residents and each other, including socially. The study concluded that the quality of relationships is pivotal in dementia care.

I am extremely grateful for the opportunity to undertake my PhD within the supportive environment of CHeBA and the DCRC. Words inadequately express my gratitude to my supervisors who challenged and encouraged me, enabling a thesis that contributes to improvements in dementia care.

Dr Janet Mitchell was supervised by Professor Henry Brodaty, Professor Lynn Chenoweth, and Professor Jeffrey Braithwaite (now at Macquarie University)

Dr Gurjeet Kaur Virk
Blood based biomarkers for the identification of Alzheimer's disease using proteomics approaches

This work was to identify and validate the blood-based biomarkers from two different Alzheimer's disease cohorts. The study has expanded the knowledge of the plasma proteome profile of normal ageing and age-related neurodegenerative diseases for identification of potential biomarkers for early diagnosis and better patient care.

I am grateful for the opportunity to have undertaken my doctorate at CHeBA and BMSF, UNSW. Thanks to the incredible academic guidance, constant support, and facilities here, I have grown as a researcher and as an individual, and I will take the learnings and the journey forward.

Dr Gurjeet Kaur Virk was supervised by Professor Perminder Sachdev and Dr Anne Poljak

Dr Russell Chander
Social cognition in older adults: Associations with ageing, general cognition, and genetic, neuroimaging, and socio-environmental factors

Social cognition (the ability to read, interpret, and use social information in one's environment) has been shown to be affected in the ageing process and in dementia. My thesis clarified this relationship and demonstrated that healthy cognitive ageing was associated with some mild changes in theory of mind and emotion perception, while neurocognitive disorders were related to more far-reaching changes in these domains along with potential changes to social behaviour. Empathy was also related to brain changes in specific regions, but not related to genetic predispositions.

I am eternally thankful for the opportunity I had to work with CHeBA and my supervisors, advisors, colleagues, and friends on this thesis. Their support, guidance, and camaraderie have been invaluable to me, and they continue to be a source of inspiration and friendship.

Dr Russell Chander was supervised by Professor Perminder Sachdev, Associate Professor Wei Wen, and Professor Julie Henry (University of Queensland)

Dr Marina Ulanova
Towards early Alzheimer's disease diagnosis: development of amyloid-targeted magnetic nanoparticles for use as MRI/MPI tracers

Currently, a definitive diagnosis of Alzheimer's disease (AD) is only possible with positron emission tomography imaging of amyloid-beta or the analysis of cerebrospinal fluid for biomarkers of AD. My thesis sought to develop targeted superparamagnetic iron oxide nanoparticles which could permit visualisation of amyloid-beta pathology using magnetic resonance imaging or novel magnetic particle imaging technology and improve AD diagnostic methods.

I am grateful to have been able to undertake my PhD in CHeBA and for the support of my supervisors to learn new techniques, foster collaborations and to continually seek out novel ideas.

Dr Marina Ulanova was supervised by Dr Nady Braidy and Professor Perminder Sachdev

Dr Fatemeh Khorshidi
Brain Cell Viability and the Cellular Adaptive Response

The biphasic dose response to a substance, also called hormesis, is an effect with benefits at low doses while having toxicicity at higher doses. My PhD studies evaluated the dose-response relationship of several common dietary and/or endogenous compounds (resveratrol, alcohol, nicotinamide, and NAD+) on brain cells in culture using an astrocyte cell line. The cell survival, proteomic and metabolomic effects of these compounds were explored, as well as their multigenerational effects. While I faced many challenges during the course of my PhD, it was a wonderful opportunity to undertake my studies in CHeBA and learn so much about addressing scientific questions, particularly on this new and relatively controversial topic.

Dr Fatemeh Khorshidi was supervised by Professor Perminder Sachdev, Dr Anne Poljak and Dr Tharusha Jayasena

Other Achievements

PhD student Zara Page, who this year completed her Bachelor of Advanced Science (Honours) with Honours Class 1 in Neuroscience, was the recipient of the Josh Woolfson Memorial Scholarship to support her PhD which is looking at achieving culture-fair neuropsychological assessment for Mild Cognitive Impairment and dementia in the culturally and linguistically diverse (CALD) community.

The Josh Woolfson Memorial Scholarship supports research into modifiable risk factors of Alzheimer's disease, identifying and targeting at-risk groups and individuals, as well as developing intervention strategies for risk reduction.

UNSW's highly competitive Supervision Award was presented this year to Dr Katya Numbers, for her outstanding and expert guidance of multiple students through CHeBA.

CHeBA Publication Awards

Student: Rebecca Koncz

Koncz R et al. The heritability of amyloid burden in older adults: the Older Australian Twins Study. J *Neurol Neurosurg Psychiatry*. 2022 Mar;93(3)303-308. DOI: 10.1136/jnnp- 2021-326677

Early Career Research: Claire Burley

Burley et al. Nonpharmacological approaches reduce symptoms of depression in dementia: A systematic review and meta-analysis. *Ageing Res Rev*. 2022; 79:101669. DOI: 10.1016/j.arr.2022.101669

Professional Staff: Jess Lo

Lo et al. Long-term cognitive decline after stroke: An individual participant data meta-analysis. *Stroke*. 2022; 53:1318-1327. DOI: 10.1161/STROKEAHA.121.035796

Our Community

"The overwhelming support from our community drives us to advance our research toward healthier brain ageing for everyone."
Professor Henry Brodaty AO

The Dementia Momentum – Spokesman's Report

My journey with my wife Suellen concluded this year when she passed away peacefully on 23rd September.

Her passing, just two days after World Alzheimer's Day, had me reflecting heavily on our 12-year journey since she was diagnosed by Professor Henry Brodaty on 7 October 2010.

The earliest signs of young onset Alzheimer's disease were her lowering of interest in attending business functions, reduced confidence in group settings and less interest in household activities such as cooking. By her early to mid-50s it was clear we had an issue, but it took a good 5+ years of medical appointments before I was pointed to Henry Brodaty, who, with good fortune, accepted Suellen as a patient. The delivery of his diagnosis was devastating and yet empowering. We now knew we had to manage our way into this future, without any clear guideposts as to what suffering from this disease meant.

In that moment I could never have anticipated working so closely with Henry or becoming the Spokesman for an initiative that has generated so much support, and although my role has always been headed in the direction of this sad outcome, no amount of time and conversation prepares you for the reality of loss.

So, what of the facts? We know that the number of people diagnosed worldwide continues to rapidly increase. We also know that identification of risk factors is crucial for changing the social and economic impact of dementia. We know that once a diagnosis is made there is no cure, and yet despite estimates suggesting the cost of dementia to be USD1 trillion, research funding into protective factors still lags considerably. This means that despite advances in technology, there remain too few researchers working toward significant change.

The latest drug trials have seen some success, but even if a therapeutic treatment is discovered, it won't help millions of people who already have dementia. We know that research is expensive, especially brain research. A typical NHMRC grant is now $1.5 to 2 million over 3 years, and several such grants are needed. The USA governmental budget for dementia research is now $2.4 billion per year. We spend barely a few million a year. When the Abbott government provided $200 million over 5 years for dementia research – something I was proud to be able to announce at a Wipeout Dementia event - it was considered a breakthrough – but it was a one-off and has not been continued.

There is much to be done but there is also much to be celebrated. Through our work with The Dementia Momentum and its associated fundraising campaign Wipeout Dementia, we have generated a multitude of interest from like-minded individuals that will carry the torch and help drive the need for funding directed toward dementia research. This year particularly saw many successes, with the property industry leading the most successful fundraising event to date with $350,000 raised, KPMG and iPartners working in partnership for our annual lunch, and a number of significant research outcomes highlighted in this Report that were funded by our collective efforts.

It is with honesty that I say my journey with CHeBA and the role as Spokesman for the Dementia Momentum have been nothing short of a privilege. In perhaps a small way, we have seen the start of a movement that is shifting the prejudice that still exists, and have facilitated more dialogue about Alzheimer's disease.

Dr Richard Grellman AM

Dr Richard Grellman AM
Spokesman, The Dementia Momentum

KPMG Sydney Event for The Dementia Momentum and CHeBA 10 Year Anniversary

On 22 October, CHeBA celebrated 10 years of ground-breaking research.

As part of the 10 Year Anniversary celebrations, in-kind partner KPMG Sydney this year generously combined their annual lunch for The Dementia Momentum with this milestone. On Friday 28 October, partners, members, donors, and corporate fundraisers of The Dementia Momentum initiative gathered at the Barangaroo offices to pay tribute to CHeBA's achievements and research that has made an enormous impact on the future of Alzheimer's disease and other dementias. This annual event was this year sponsored by iPartners.

Guests heard from Spokesman Dr Richard Grellman AM, whose wife Suellen had lived with young onset Alzheimer's disease for 12 years and passed away just four weeks prior to the event. Dr Grellman gave a stirring presentation on the growing cost of dementia and the need for increased research funding.

In addition, David Gonski AC, Chancellor of UNSW Sydney, delivered an impactful keynote address, and Eileen Hoggett, National Managing Partner of Audit, Assurance and Risk Consulting at KPMG Sydney, shared the experience of losing her mother to Alzheimer's disease, aged just 66.

Professor Henry Brodaty and Professor Perminder Sachdev spoke about how philanthropic contributions were making a direct impact on current projects and CHeBA Ambassador PJ Lane recounted memories of his father, legendary entertainer Don Lane, who passed away following a diagnosis of dementia.

Finally, Chris Clarke of Watson Mangioni and Peter Clemesha of Avenor were both recognised with special awards for their long-term, ongoing contributions and involvement in The Dementia Momentum.

Looking ahead to the next 10 years, CHeBA hopes to reduce the burden of dementia, a disease which currently affects nearly 55 million people worldwide, and is estimated to cost a trillion dollars annually, with both these figures projected to rise significantly.

Wipeout Dementia

After a three-year hiatus due to the COVID pandemic, 2022 hailed the biggest and most successful Wipeout Dementia to date, with $350,000 raised to increase understanding about risk factors for dementia and reaching a milestone of $2 million raised for The Dementia Momentum.

Held at Bondi Beach on 25 March, this year's event saw 64 heavy hitters from the property industry get behind CHeBA with sponsors Morgans Financial, Avenor, Aoyuan International, AWM Commercial Furniture, Buildcorp, m3property, Sense Projects, Shape Australia, Winten Property Group together with event partners Colliers International, Kennards Hire and Hurley.

This year 1999 World Surfing Champion Mark Occhilupo competed in the event, generously auctioning off the board he rode in the 2019 Bells Beach Heritage Heat against American pro-surfer Tom Curren.

"The evolution of Wipeout Dementia across the property industry has been inspirational and humbling," said Spokesman for The Dementia Momentum and Ambassador, Dr Richard Grellman, whose wife Suellen recently passed away from young onset Alzheimer's disease.

A number of awards were announced on the day including the prestigious 'Gnarly Award', a Mark Richards 1980 replica twin fin surfboard which was awarded to highest fundraiser Michael Gordon, General Manager of Buildcorp Interiors.

In an extraordinary display of commitment Gordon personally raised over $30,000 for the cause and took his Buildcorp sponsored team to highest fundraising glory – with over $90,000 raised by the group. The team won a 5-hour private charter on a Sydney to Hobart winning yacht generously donated by Jim Cooney.

Co-Directors Professor Henry Brodaty and Professor Perminder Sachdev attended the event, which aims to increase awareness about the modifiable risk factors of Alzheimer's disease and other dementias while driving research funds to harness global research to prevent dementia.

A number of projects received a funding boost as a result of the March 2022 event, including the expansion of international studies under The Dementia Momentum initiative, particularly the continuation of research looking at successful brain ageing for those living to 100 and beyond.

Wipeout Dementia was created by CHeBA's Heidi Douglass. In 2023 CHeBA will once again run the property industry event at Bondi.

Blackmores Sydney Running Festival

On Sunday 18 September, 69 enthusiastic runners from eight partner organisations took to the streets of Sydney as part of the Blackmores Sydney Running Festival to raise almost $40K towards CHeBA's critical research.

This was CHeBA's feature fundraising event to celebrate the Centre's 10th anniversary, and the first time that a corporate partnership was secured for this campaign.

Nick Noonan, Partner at Henry William Lawyers, ran in honour of his father; rugby great Bill Noonan, who had early onset dementia and passed in December 2021, aged 74. A team of 19 runners and walkers from Henry William Lawyers joined Nick and raised over $10,000.

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

In 2023, the newly renamed Sydney Marathon will be a feature event for CHeBA. To find out more contact janelle.burns@unsw.edu.au.

The Brain Dialogues

The Reality of Dementia Series

As part of CHeBA's 10 Years of Research Appeal in October 2022, we ran a blog series called *The Reality of Dementia* – which highlighted some of our key partners and supporters and their challenging personal experiences. The impactful series was developed from candid interviews with KPMG's National Managing Partner of Audit, Assurance & Risk Consulting Eileen Hoggett, iPartners Head of Middle Markets Distribution Vito Abbonizio, bp Head of Reward Asia Pacific, Francesca Wood, Henry Williams Lawyer Jackson Skirka, Michael du Chateau and CHeBA Ambassador, and son of TV legend Don Lane, PJ Lane.

Eileen Hoggett

Jackson Skirka

Vito Abbonizio

Michael du Chateau

Francesca Wood

PJ Lane

CHeBA in the Media

An *Ageing Research Reviews* paper - authored by Dr Claire Burley and Professor Henry Brodaty – which covered non-pharmacological approaches to treating depression in people living with dementia, received extensive media coverage including: *Inside Ageing, Aged Care News, The Senior, Medical Xpress and Hospital & Healthcare*.

Dr. Claire Burley

CHeBA Visiting Lecture Series

In 2022, CHeBA hosted two interactive webinars, one of which was held in-person on UNSW campus for the first time since 2019.

On 27 April, Professor Anthony David from University College London discussed functional strokes as a new challenge for stroke services and neuropsychiatry.

On 15 November, Dr Clarissa Giebel from the University of Liverpool shared her findings on the long-term impacts of the pandemic on the mental health of carers of people living with dementia.

These webinars are available for viewing on the CHeBA website.

Professor Anthony David

Dr Clarissa Giebel

Public Forums

Ageing with Resilience

For the first time in three years, seniors from across Sydney were able to attend an in-house version of the annual forum hosted by the Eastern Suburbs Older Persons' Mental Health Service, in partnership with CHeBA, which seeks to encourage a paradigm shift in the approach to ageing.

The official opening of the Secrets of Ageing with Resilience forum was made by Deputy Chair of the South Eastern Sydney Local Health District (SESLHD) Dr Debra Graves, who acknowledged the importance of the theme and its relationship to positive mental health promoting healthy communities.

Dylan Parker, Mayor of Randwick, acknowledged the importance of these annual community events.

The free event, chaired by CHeBA Co-Director and Honorary Medical Officer of the Older Persons' Mental Health Service, Prince of Wales Hospital, Professor Henry Brodaty, provided practical strategies to combat adversity as well as heart-warming personal stories of courage and survival.

Geriatrician Professor Maria Fiatarone Singh AM spoke of the relationship between physical fitness – particularly muscle mass - and psychological resilience.

Holocaust survivor Peter Halas, who survived the Nazi occupation during the Second World War and the 1956 Soviet invasion of Hungary, attributes much of his resilience to support from his wife and children.

"I live my life day by day," says Halas. "Obviously I have stressors like everyone else but I'm a glass half full person."

Another incredible personal story of survival and hardship came from Wiradjuri and Gamilaroi Woman and Associate Professor Lynette Riley, who supports sustainable change for Aboriginal communities.

Lynette explained what it was like to live through the 70s when you were required to have a 'Certificate of Exemption' to be allowed to go to school. "It was effectively saying we were exempt from being Aboriginal," said Riley.

Final speakers were Elizabeth Chong AM and Professor Gordon Parker AO, who both advocated positivity and the need for accepting and embracing change in life.

Psychiatrist Professor Parker, author of 23 books and founder of the Black Dog Institute, defined resilience as the ability to bend but not break and to recoil from setbacks.

"Resilient people more readily tap into hope. Under pressure they demonstrate curiosity and keep moving forward," he said.

Professor Henry Brodaty AO, Professor Maria Fiatarone Singh AM, Dr Debra Graves, Associate Professor Lynette Riley, Mike Gasti (Service Director, Eastern Suburbs Mental Health Service), Daniella Kanareck (Clinical Manager, OPMHS), Professor Gordon Parker AO

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JPND research

Black Dog Institute

Foundations & Major Donors

Judy Harris Y Phil
J Holden Family Foundation

Sachdev Foundation
Estate of the late Roger Layton AM

The Howarth Foundation
Beryl (Liz) Woolfson

Donors 2022

In 2022, over 1,100 donations were made in support of our community and staff fundraisers who participated in the City2Surf, Blackmores Sydney Running Festival and Wipeout Dementia.

Vito Abbonizio
Chris Anictomatis
Ruth Armytage AM
Kylie Austin
Avenor
Guido Belgiorno-Nettis AM
Malcolm and Julie Beville
Martin Blake
Dr Andrew Blattman
Gahee Bong
Alyssa Brady
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Phil Butt
Philippa Byers
Lily Calderbank
Phil Cave AM and Judy Harris
Junchi Chen
Chris Clarke
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Benjamin Ware
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Jacqueline White
James Wilkinson
Will Wong
Henry Wong
Francesca Wood
X-Clusive Group

CHeBA Collaborators

Industry and Societies

Industry

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BaptistCare NSW/ACT

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Rhyolite Innovation

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

Dementia Australia

International Neuropsychiatric Association (INA)

International Psychogeriatric Association (IPA)

International Society of Vascular Behavioural and Cognitive Disorders (VASCOG)

National Prescribing Service Limited (NPS)

Royal Australian & New Zealand College of Psychiatrists (RANZCP)

RANZCP Faculty of Psychiatry of Old Age

RANZCP Section of Neuropsychiatry

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Sydney

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)

NSW Health (Older People's Mental Health OPMH)

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

St Vincent's Hospital

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

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Royal Melbourne Hospital

The Florey Institute of Neuroscience and Mental Health

Twins Research Australia

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Peking University, China

Renji Hospital, China

Shanghai Jiaotong University, China

Tianjin Huanhu Hospital (Department of Neurolgy), China

Tsinghua University, China

Wenzhou University, Wenzhou, China

Chinese University of Hong Kong, Hong Kong

Queen Mary Hospital, Hong Kong

Hong Kong Polytechnic University, Hong Kong

The University of Hong Kong, Hong Kong

CSI Holdsworth Memorial Hospital, India

Atma Jaya Catholic University, Indonesia

Keio University, Japan

Kyushu University, Japan

Osaka University, Japan

National Center for Geriatrics and Gerontology, Japan

Tohoku University, Japan

Kiang Wu Nursing College, Macau

University of Macau, Macau

Universiti Kebangsaan, Malaysia

Universiti Putra Malaysia, Malaysia

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University of Waikato, New Zealand

St. Luke's Medical Center, Philippines

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

Hallym University, Republic of Korea

Korean National Institute of Dementia (KNID), Republic of Korea

Seoul National University, Republic of Korea

Changi General Hospital, Singapore

National Neuroscience Institute, Singapore

National University, Singapore

National University Health System, Singapore

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Institut Louis Malardé, Tahiti, French Polynesia

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Forschungszentrum Juelich, Germany

Heidelberg University, Germany

Heinrich Heine University (Neuroscience Network Dusseldorf), Germany

Helmholtz Association (German Center for Neurodegenerative Diseases - DZNE)

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Maastricht University, The Netherlands

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Faroese Hospital System (Dept of Occupational Medicine & Public Health), Faroe Islands, Denmark

Southern Denmark University, Denmark

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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

Current Projects

Associations of multimorbidity of cardiometabolic conditions with cognitive decline and dementia

CHeBA staff

Darren Lipnicki, Perminder Sachdev,

Other investigators

Xin Xu, Xiaolin Xu, Xuhao Zhao, Yaguan Zhou (Zhejiang University), investigators from contributing COSMIC studies.

Aims

To examine the impact of different cardiometabolic multimorbidity profiles on (1) specific longitudinal cognitive trajectory patterns identified by group-based trajectory modeling (GBTM); (2) longitudinal cognitive decline (both global and domain-specific); and (3) incident cognitive decline. Cardiometabolic profile groups will be based on number of CMCs, and determined via the associations of particular CMCs with the cognitive outcomes.

Findings

Data being obtained.

Funding:

NIH.

Apathy in older community-dwelling persons: improving assessment, investigating its association with immune markers, differentiating from depression and fatigue and modelling its longitudinal course

CHeBA Staff

Fleur Harrison (PhD Candidate), Henry Brodaty, Julian Trollor

Other investigators

Moyra Mortby (NeuRA/UNSW), Adam Guastella (USyd), Andrew Lloyd (UNSW)

Aim/s

- To psychometrically evaluate the validity and appropriateness of available assessment tools for apathy in community-dwelling older people where they have not been sufficiently evaluated.
- To investigate the differential associations of a comprehensive range of biomarkers of immune functioning with apathy, fatigue, and depression. An underlying immune aetiology for depression, apathy and fatigue may exist, based on the recent understanding of links between immune system and psychiatric symptoms and syndromes. Apathy overlaps with fatigue and depression, and these three syndromes are difficult to differentiate. Identification of underlying biomarkers may assist but as yet there is scant research investigating such associations with apathy.
- To model longitudinal pathways of apathy, depression, and fatigue in order to distinguish their distinct and shared components, and their associations with the development of neurocognitive disorders. These three syndromes are associated in a multifactorial manner with cognition, function, physical health, medication use, and other determinants.

Findings

This work comprises a number of sub-projects, using data from the Sydney Memory and Ageing Study. The manuscript of the first sub-project has been prepared, with findings suggesting that apathy may be a determinant of multiple health behaviours in older adults, distinct from depression and fatigue. Symptoms of apathy were significantly associated with reduced physical activity and alcohol consumption, whereas symptoms of depression and fatigue had no or inconsistent relations with health behaviours. When multiple health behaviours were pooled into a combined risk index, only apathy was associated with greater risk of one or multiple risk factors (compared to zero). Apathy may be a target for health promotion activities, including interventions for dementia risk reduction.

Analyses and preparation of manuscripts for other sub-projects are ongoing. Findings will help better measure and characterise apathy, investigate its associations with inflammatory markers, and provide evidence on its longitudinal course and potential risk relationships with dementia and mortality.

Funding

Dementia Australia Research Foundation-Dementia Collaborative Research Centres; Brain Sciences UNSW; Josh Woolfson Memorial Scholarship, Kwan Fung and Yuet Ying Fung Healthy Brain Ageing Research Award Fund.

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, is also being examined. In a large collaborative study, 12 DNA methylation sites and 46 regions were associated with white matter hyperintensity burden. Gene set enrichment analyses suggested that these DNA methylation loci are linked to the immune response and the blood-brain barrier (Yang et al, 2022, Brain, doi: 10.1093/brain/awac290).

Funding

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

CELPI: a randomised trial of a carer end of life planning intervention in people with dementia

CHeBA staff

Lynn Chenoweth

Other investigators

A/Prof Glenn Arendts (UWA), Prof Christopher Etherton-Beer (UWA), A/Prof Barbara Hayes (Monash University), A/Prof Katrina Spilsbury (UNDA), Prof Meera Agar (UTS), Prof Kirsten Howard (USyd).

Aim

Test a Carer End of Life Planning Intervention (CELPI) co-designed by clinicians, content specialists and consumers to improve access to end of life care for older people with severe dementia (FAST 6d-7e), using an ED visit as a catalyst for recognising unmet needs and specialist palliative care referral where indicated.

Methodology

A randomised controlled trial (RCT) of CELPI model of person-centred ED discharge support to family carers and people living with advanced dementia. Random allocation of family carers and people living with dementia 'dyads' (N=440) to CELPI model versus usual post-discharge care, at six EDs Perth (n=2), Melbourne (n=2) and Sydney (n=2).

Primary outcome

Proportion of participants dying in their carer-nominated preferred location for death within 12 months of enrolment.

Secondary outcomes

Changes in carer (proxy) reported and self-ratings of quality of life (QUALID); comorbidities (Charlson Comorbidity Index); symptoms (Karnofsky Performance Status, Symptom Assessment Scale); number of ED attendances post enrolment and hospital in the home admissions; days spent in nominated preferred location of care post enrolment; number and type of medical interventions in last seven days of life e.g. IV fluids or antibiotics; bereavement risk in the carer; and carer strain. Patient and family recruitment, education, and data collection are in progress.

Publications/presentations

Arendts G, Chenoweth L, Hayes B, et al. CELPI: trial protocol for a randomised controlled trial of a Carer End of Life Planning Intervention in people dying with dementia. BMC Geriatri 22, 869 (2022). https:// doi.org/10.1186/s12877-022-03534-1.

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

Prof Julie Henry (University of Queensland), Prof Jacqueline Close (NeuRA), Prof David Bunce (Leeds University), A/Prof 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

In a group of 263 community-dwelling healthy older adults aged 60-95 years of age, attitudes towards computers and technology but not computer experience were related to test performance on three of four computerised neuropsychological instruments. Specifically greater computer anxiety/discomfort was associated with poorer performance. These findings suggest that it is important to consider a person's attitudes to technology when interpreting their performance on such tests.

Funding

NHMRC Boosting Dementia Research grant, UNSW Medicine Interlude Grant.

Determining the genetic and epigenetic factors linked to odour identification

CHeBA Staff

Karen Mather, Anbupalam Thalamuthu, Siddharth Raj (Medicine ILP student)

Other investigators

A/Prof Nicola Armstrong (Curtin University) (CHeBA Hon. Research Fellow), A/Prof John Kwok (University of Sydney; UNSW), Prof Peter Schofield (NeuRA; UNSW), Prof Margaret J. Wright (Queensland Brain Institute, University of Queensland), Prof 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 and identifying the epigenetic determinants of olfactory identification.

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

Dr Eduwin Pakpahan (workgroup leader), Prof Dame Louise Robinson, Prof 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 harmonised 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, Validation and Implementation of a Computerised Tool to Assess Instrumental Activities of Daily Living (C-STAM)

CHeBA staff

Simone Reppermund, Henry Brodaty, Katya Numbers, Nicole Kochan, Julian Trollor, Brian Draper, Ben Lam, Perminder Sachdev

Other investigators

Prof Lindy Clemson (USyd), Prof Kim Delbaere (NeuRA), Dr Jeewani Anupama Ginige (Western Sydney University), Dr Jacqueline Wesson (USyd), Dr Katharina Luttenberger (University of Erlangen), Mr Quoc Cuong Truong (University of Waikato), Dr Stephanie Ward (UNSW), Ms Claudia Woolf (St. Vincent's Hospital Sydney)

Aims

The aim of this project is to develop, validate, and implement a new, computerised diagnostic tool to assess functional ability in older people with and without dementia. The tool is a further evolution of our successful Sydney Test of Activities of Daily Living in Memory Disorders (STAM). The computerised STAM (C-STAM) will realistically simulate relevant IADL to assess functional performance in older people with cognitive impairment in clinical and research settings. The objectives of this study are to:

- Develop new items and refine existing items of the STAM for a computerised version in collaboration with consumers, carers, clinicians, and other subject matter experts
- Pilot/usability testing for feasibility and refinement of the C-STAM in older people with normal cognition, MCI, and dementia
- Validate the final version of the C-STAM in older people with normal cognition, MCI, and dementia
- Implement the C-STAM into clinical use

Project approved by HREC in 2022; participant recruitment will commence in 2023

Findings

Data under review

Funding

NHMRC MRFF Dementia Ageing and Aged Care Mission, UNSW Scientia Fellowship

Diet and late-life depression

CHeBA Staff

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

Other investigators:

Prof 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 *Ageing Research Reviews* (Matison et al., 2021, 70:101403). Further work has been undertaken to determine the heritability of fruit and vegetable consumption and to explore the shared genetic and environmental influences between fruit and vegetable intakes and depressive symptoms. Using OATS, vegetable intake was moderately heritable whilst there were no significant genetic or environmental correlations with fruit/vegetable intakes and depression. This work was presented at the American Nutrition Society 2022 Conference and has been written up for publication and is currently under review.

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

Dr Jong Bin Bae, Prof Ki Woong Kim (Seoul University Bundang Hospital), and 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.

Finding

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

Dr Hanna Jokinen and Dr 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.

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

A/Prof 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 2022, EADB published a study with over 110000 AD cases and 670,000 controls and found 75 risk loci, of which 42 were novel. Based on these results, a genetic risk score was positively associated with AD risk, over and above the effects of age and the major genetic risk factor for AD, the APOE ε4 allele (Bellenguez, C et al, 2022, Nat Genetics, 54, 412-536).

Funding

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

Examining brain ageing from transcriptomic and epigenomic perspectives

CHeBA staff

Karen Mather, Anbupalam Thalamuthu, Perminder Sachdev, Adith Mohan (PhD student), Fatemeh Amjadimoheb (PhD Student).

Other investigators

A/Prof Nicola Armstrong (Curtin University, CHeBA Hon. Research Fellow), Associate Prof John Kwok (University of Sydney; UNSW), Prof 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. Circular RNAs are also being examined.

Funding

NHMRC, Thomas Foundation, Rebecca Cooper Medical Research Foundation.

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

CHeBA staff

Alice Powell (PhD Candidate), Henry Brodaty, Perminder Sachdev

Other investigators

Prof Jacqueline Close (UNSW Sydney, NeuRA)

Aims

Explore how to best define exceptional cognition in older adults and its prevalence in an Australian sample, examine demographic and clinical predictors of exceptional cognition, review trajectories of cognitive maintenance or decline over time in these individuals, and examine interactions between exceptional cognition and physical and social successful ageing.

Funding

NHMRC postgraduate scholarship

Failure to identify particular odours predicts future dementia and mortality

CHeBA staff

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

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.

Genetics and epigenetics of longevity

CHeBA staff

Perminder Sachdev, Karen Mather, Anbupalam Thalamuthu, Mary Revelas (PhD student).

Other investigators

A/Prof Nicola Armstrong (Curtin University, CHeBA Hon. Research Fellow), Prof John Attia (University of Newcastle), A/Prof John Kwok (University of Sydney; UNSW), Dr Chris Oldmeadow (University of Newcastle), Prof Peter Schofield (NeuRA; UNSW); Prof David Ames (National Ageing Research Institute; Royal Melbourne Hospital), Prof 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. PhD student, Mary Revelas, found individuals with a high polygenic risk score for longevity had a healthy metabolic profile in studies from Australia, the UK and Sweden. This work has recently been published in Geroscience (Revelas et al., 2022).

Funding

Sachdev Foundation, NHMRC, Thomas Foundation

Genetics of white matter hyperintensities

CHeBA staff

Karen Mather, Wei Wen, Anbupalam Thalamuthu, Perminder Sachdev.

Other investigators

A/Prof Nicola Armstrong (Curtin University, CHeBA Hon. Research Fellow), Prof Paul Nqyuist (John Hopkins, USA), Prof David Ames (National Ageing Research Institute, Royal Melbourne Hospital), A/Prof John Kwok (University of Sydney; UNSW), Prof Peter Schofield (NeuRA; UNSW), Prof 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 in cohorts from around the world.

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/Prof Nicola Armstrong (Curtin University, CHeBA Hon. Research Fellow), Prof David Ames (National Ageing Research Institute, Royal Melbourne Hospital), A/Prof John Kwok (University of Sydney, UNSW), Prof Peter Schofield (NeuRA, UNSW), Prof 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 recent publications, Brouwer et al (2022) found genetic loci for changes in the morphology of 15 brain structures across the lifespan, using a sample of over 15,000 individuals. Interestingly, some of the variants were independent of age suggesting that they are important across the lifespan while others were age-dependent, with some associated with brain development and others associated with brain ageing *(Nature Neuroscience, 2022: Apr;25(4)421-432).* A review of the studies investigating the influence of copy number variants (CNVs) on brain structure in the ENIGMA Consortium was also undertaken. To date, the following CNVs have been associated with subcortical and cortical brain structures: 2q11.2, 16p11.2 distal, 15q11.2, and 1q21.1 distal (Sonderby et al., *Human Brain Mapping*, 2022:43:300-328),

Funding

NHMRC, Thomas Foundation.

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

CHeBA staff

Perminder Sachdev, Karen Mather, Anbupalam Thalamuthu, Wei Wen, Nicole Kochan, Teresa Lee

Other key investigators

A/Prof Nicola Armstrong (Curtin University) (CHeBA Hon. Research Fellow), Prof David Ames (National Ageing Research Institute, Royal Melbourne Hospital), A/Prof John Kwok (Sydney Univ UNSW), Prof Peter Schofield (NeuRA, UNSW), Prof 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 53,000 adults without dementia or stroke, novel genetic loci were identified for verbal short-term memory and verbal learning performance as well as the expected APOE locus (Lahti et al, 2022, Molecular Psychiatry, 27:4419-4431). Interestingly, the top results exhibited a range of functions in brain tissue, such as acting as expression quantitative loci (eQTLs) or being associated with tau or amyloid accumulation in the brain.

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

Prof Bernhard Baune (University of Münster), Dr Liliana Ciobanu (University of Adelaide), A/Prof Nicola Armstrong (Curtin University, CHeBA Hon. Research Fellow), A/Prof John Kwok (Sydney University; UNSW), Prof 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

Impact of mood and metabolic disorders on Alzheimer's disease: investigating sex specific interactions of chronic condition multimorbidity

CHeBA staff

Nady Braidy, Tessa Helman

Other investigators

Prof Nicolas Stapelberg (Bond University); Prof John Headrick (Griffith University)

Aims

- Reveal the sex-specific impacts of individual and commonly co-occurring disease states on cognition, anxiety and depressive behaviours;
- Investigate the sex-specific influences of co-morbid conditions on the density and distribution of amyloid-β plaque formation in brain slices;
- Identify sex-specific influences of co-morbid conditions on protein and lipid profiles within frontal cortex and hippocampal brain tissue;
- Assess sex-specific influences of co-morbid conditions on nervous system expression of key genes linked to neurodegeneration, neuroinflammation and oxidative stress;
- Evaluate the sex-specific influences of co-morbid conditions on circulating levels of inflammatory and metabolic markers.

Findings

Sexual dimorphic patterns of mood and metabolic disorders have been identified in both pre-clinical and clinical studies. In humans, women are more likely to be diagnosed with mood disorders such as anxiety and depression, while men are more likely to suffer from substance abuse disorders. Clearly dimorphic patterns are also apparent in animal models of disease. Previous pre-clinical research from our group has shown that chronic social stress induces distinct sex-specific behaviours, with male mice presenting with depressive-like behaviour and females with anxiety-like behaviour. In addition, prominent sex differences were observed for circulating and nervous system biomarkers linked to mood and metabolism. Importantly, sexual dimorphic patterns are also apparent in AD. Women are more likely to develop AD and experience more rapid cognitive decline . Similarly, female mice exhibit higher Aβ plaque burden and greater levels of phosphorylated tau and proinflammatory cytokines.

Funding

NHMRC, Rhyolite Innovations; UNSW Medicine Neuroscience, Mental Health and Addiction Theme and SPHERE CAG.

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

CHeBA staff

Karen Mather, Anne Poljak (Adjunct), Tharusha Jayasena, Henry Brodaty, Perminder Sachdev.

Aim

Inventory and aliquot samples for ready distribution to researchers.

Improve the safety of sample storage by aliquoting and transferring samples into -80oC and vapour phase storage.

Findings

Aliquoting of MAS samples (all waves which have plasma) has largely been completed, although ongoing plasma collections will require processing. Aliquoting of all waves of OATS has been completed, except the OATS2 (PET study), aliquoting of SCS samples is ongoing. Biobanking is an ongoing project for remaining stored CHeBA blood samples, as well as new samples coming for additional waves of existing projects or any new projects.

Funding

CHeBA Philanthropic Funds

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

A/Prof Anna Williams (UNDA), Dr Zhixin Liu (Stats Central, UNSW), Dr Patricia Reyes (SESLHD, UNSW), Ms Jane McGuire (SESLHD), Ms Genevieve Maiden (SESLHD), Ms Jacquelene Cook (PhD student 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 Jacquelene 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

Prof 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

Maximising 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

A/Prof Kay Deckers, A/Prof Sebastian Köhler, A/Prof Martin van Boxtel, Stephanie van Asbroeck (Maastricht University), and 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

Neuroprotective effects of sulfurophane and oleoylethanolamide in Alzheimer's disease

CHeBA staff

Perminder Sachdev, Nady Braidy, Chul-Kyu Lim (PhD candidate).

Aims

- Analyse the effects of oleoylethanolamide and sulforaphane in oxidative stress resistance, inflammation, cellular proteome and lipidome in human brain cells.
- Determine the outcome of administration of oleoylethanolamide and sulforaphane in behavioural performance in AD and aged rats.
- Analyse the change of protein expression related to AD by oleoylethanolamide and sulforaphane in rats.
- Analyse the change by oleoylethanolamide and sulforaphane in the brain of AD and aged rats.

Findings

Following results comparisons and evaluations, it was found that the oligomeric peptides used in this work were able to represent a concentration closer to the levels found in the AD brain, thereby offering a more physiologic impression of the effect of amyloid-beta oligomers on astrocyte glial lipid profiles. It was established that Sphingomyelins (SMs) were significantly elevated in astroglioma cells treated with Aβ42 oligomers compared to the non-treated cells ($p=0.0015$). However, this effect was found to be significantly attenuated by the endocannabinoid-like compounds Oleoethanolamide (OEA) and Sulforaphane in composition.

No significant differences were found in phospholipids except that the level of the Phosphatidylcholines (PC) and Phosphatidylinositol (PI) groups were higher in the Aβ42 groups ($p=0.0041$), which was consistent with the result found in human AD plasma samples. It was concluded that this was able to be reduced following treatment with the novel OEA/Sulforaphane formulation. Despite phosphatidylethanolamines (PE) and lyso-phosphatidylethanolamines (LPE) not being significantly different between the treated and non-treated cells, the ratio of PE/LPE was significantly increased in Aβ42 treated astrogliomas and was significantly reduced by treatment with the novel OEA/Sulforaphane formulation. Triacylglycerols (TG) were also increased in the Aβ42 group ($p=0.005$) and was rectified following treatment with the novel OEA/Sulforaphane formulation.

These results not only affirm the non-toxic advantages of OEA and Sulforaphane explored last year, but also address the hypothesis of plaque targeting due to this year's results showing effectiveness of treatment against Aβ42 in vitro. The outcomes pertaining to lipid activity were also encouraging due to the novel OEA/Sulforaphane formulation's efficacy in reducing and modulating them. It was overall concluded that the prototype may present as a potential therapeutic treatment for AD. That being said, the results had led to the hypothesis that further in vitro trials may be beneficial to explore alternative pathways and indicators of toxicity attenuation.

These findings were published in *Aging and Disease* with 3 manuscripts under preparation for submission.

Funding

NHMRC, Rhyolite Innovations.

Nightmares, cognitive decline and dementia

CHeBA staff

Darren Lipnicki, Perminder Sachdev,

Other investigators

Investigators from contributing COSMIC studies.

Aims

The primary aim of this project is to investigate if and how nightmares are associated with cognitive decline and dementia in the general older population, more comprehensively than done previously, using neuropsychological test data and consensus diagnoses of dementia. If sufficient data are available similar analyses will be performed for REM Sleep Behaviour Disorder and Restless Leg Syndrome.

Findings

Data being obtained.

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

A/Prof Costas Anastasiou (workgroup leader), Prof Nikolaos Scarmeas, Prof 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.

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

CHeBA staff

Perminder Sachdev, Jessica Lo

Other investigators

A/Prof Thibaut Dondaine, Dr Regis Bordet, Ms Florine Ruthmann (University of Lille)

Aims

The aims of the study are:

- to evaluate the influence of post-stroke anxiety on the cognitive disorders observed in patients,
- 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

Poststroke anxiety is a common condition, affects more women than men, and is related to other psychiatric and cognitive variables. Anxiety should be investigated after stroke to improve patients' outcomes and prevent comorbidities, especially in the cognitive domain. A manuscript draft has been circulated to CHeBA co-authors at the end of 2022.

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

Prof 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. Data harmonisation is continuing.

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

CHeBA staff

CP 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

To 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

Prof Maree Teesson, Prof Andrew Baillie, Prof Nicola Newton, Prof Cath Chapman, A/Prof 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.

These finding were published in *Addiction*.

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

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

Dr Lena Oestreich, Dr 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

Nine STROKOG studies contributed data to this project. Lena found that across cohorts and depression scales, a single network of interrelated post-stroke complications emerged. Networks exhibited dissociable depression, apathy, fatigue, cognitive impairment, and functional disability modules. Worry was the most central symptom in networks across all cohorts, irrespective of the scale used to measure depression. Items relating to activities of daily living were also highly central nodes. Follow-up analysis in two studies revealed that individuals who worried had more densely connected networks than stroke patients free of worry. Lena will submit a manuscript to a journal for review in early 2023.

Funding

Vincent Fairfax Family Foundation, NHMRC.

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

CHeBA staff

Abdullah Alqarni, Wei Wen, Jiyang Jiang, Perminder Sachdev.

Other investigators

None

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* (DOI: 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 Aging 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.

Our second study examined the moderation effects of hormonal factors on the relationship between vascular risk factors and WMH volumes. Results showed that in men with testosterone levels one standard deviation (SD) higher than the mean value, increased body mass index and pulse wave velocity, and smoking were associated with higher WMH volumes. The association between body mass index and WMH was more significant in the periventricular white matter regions, whilst the relationship between pulse wave velocity and WMH was restricted to deep white matter regions. Men with low testosterone levels (one SD below the mean level) showed a significant association between hypercholesterolemia and higher deep WMH volumes. Hypertensive women showed higher WMH volumes than women without hypertension regardless of whether hormone replacement therapy was used. However, higher WMH volumes, especially in the deep white matter regions, were found in women who did not use hormone replacement therapy or use it for a shorter duration. These findings highlighted the importance of considering hormonal risk factors in the prevention and management of WMH. The manuscript has been accepted for publication in Brain Imaging and Behavior.

The third study aims to examine the longitudinal changes of WMH using Sydney Memory and Ageing Study data. The manuscript is being revised internally.

Funding

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

Sex-specific risk and associated factors for transitions to mild cognitive impairment and dementia in diverse international cohorts of older adults from the COSMIC consortium

CHeBA staff

Darren Lipnicki, Perminder Sachdev,

Other investigators

Cuiling Wang, Mindy J. Katz, Richard B. Lipton, Carol Derby (Albert Einstein College of Medicine), investigators from contributing COSMIC studies.

Aims

Our overall aim is to examine the effects of sex on the transitions from cognitive normality to MCI and dementia, and whether these effects are impacted by age, education, race/ethnicity, ApoE genotype, SES and vascular factors. We propose to address the following specific aims:

- Examine the effects of sex on the risks of transitions to MCI and dementia, control for demographics and ApoE genotype. Differences of sex effects within different stages of progression will also be tested.
- Examine whether age, education and ApoE genotype modifies the effect of sex on the risks of transitions to MCI and dementia.
- Examine whether the effects of sex on the risks of transitions to MCI and dementia are further impacted by SES and vascular factors.

Findings

Data being obtained.

Funding

NIH.

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

CHeBA staff

Darren Lipnicki, Perminder Sachdev

Other investigators

Dr Seung Wan Suh (workgroup leader), Prof 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 cognitive health trajectories among healthy older adults

CHeBA staff

Darren Lipnicki, Perminder Sachdev, Henry Brodaty

Other investigators

Lisan Braas, Rene Melis (Radboud University Medical Center), investigators from contributing COSMIC studies.

Aims

1) Describe the heterogeneity and concordance of social and cognitive health trajectories among older adults initially without dementia, and 2) Describe these trajectories by geographic, sociodemographic and physical factors, such as gender and ethnicity.

Findings

Data being obtained.

Funding

NIH, European Union Joint Programme-Neurodegenerative Disease Research

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

CHeBA staff

Suraj Samtani (Study Co-ordinator), Henry Brodaty (Work Package leader), Gowsaly Mahalingam, Ben Lam, Darren Lipnicki, Perminder Sachdev.

Other investigators

Contributing COSMIC study leaders and associates, and SHARED consortium 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

We published our first meta-analysis paper exploring the associations between social connections and rates of cognitive decline in *The Lancet Healthy Longevity* (DOI:10.1016/S2666-7568(22)00199-4). We harmonised data from 13 longitudinal ageing studies (12 from COSMIC) with social connection data (N= 40 006). After controlling for known risk factors for cognitive decline, we found that living with others, being married/in a relationship, at least monthly interactions with family/friends, at least yearly community engagement, and never feeling lonely were associated with slower rates of cognitive decline. Our results provide specific recommendations for policy makers, health professionals and the community regarding the type and number of social connections needed for healthy cognitive ageing. Our next paper (currently in preparation) explores the associations between social connections and risk of dementia and mortality.

Funding

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

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

CHeBA staff

Perminder Sachdev, Jessica Lo, John Crawford.

Other investigators

Dr Clare Flach and A/Prof 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

Individuals who were cognitively impaired three months after stroke were at significantly increased risk of depression and disability in long-term follow-up. A number of drafts have been circulated with co-authors. Majed has submitted the results as a part of his PhD thesis.

Funding

Vincent Fairfax Family Foundation, NHMRC

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

Dr Phillip Tully, Dr Andrew Vincent (University of Adelaide), Dr 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

Prof 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

Ms Emma Nichols, Dr 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 NAD+ metabolome as a thereapeutic target for ageing and dementia

CHeBA staff

Nady Braidy, Tessa Helman

Aims

Uncover metabolomic signatures and define correlations of the NAD+ metabolome with healthy ageing and disease progression, sex and an unbalanced immune response and its onset retrospectively in mild cognitive impairment (MCI), AD and vascular dementia (VaD) (compared to cognitively normal control subjects), using cross-sectional and longitudinal data from multiple cohorts.

- To compare NMN and NR dietary interventions to determine if maintaining NAD+ levels reinstate cerebrovascular function and ameliorates AD pathology, and consequently cognitive and neuronal function in animal models.
- To carry out a human pilot study to determine whether NMN and NR can raise NAD+ levels and reduce pathological trajectories and cognitive decline in MCI patients.

Findings

This project considers a NADomics approaches to biomarker and drug target discovery using liquid chromatography mass spectrometry (LC-MS). Our preliminary NADomics screening of cognitively normal healthy adults has yielded markers of interest (e.g., NAD+, NADP+, NADH, nicotinic acid adenine dinucleotide (NAAD), N-methyl-nicotinamide (MeNAM) etc). NAD+ had the steepest age decrease average 4% standard deviation units decline per year. To confirm previous in vivo findings that these NAD+ precursors do not present toxic effects, we plan to begin a small-scale dose escalation study using wild-type C57bl6 mice. Provided the dose escalation study confirms lack of toxic or harmful effects, we will first define the NAD+ metabolome in plasma and brain homogenates in an animal model for AD (APP/Ps-1 mice), and correlate them with behaviour, immune status, and neuropathology at 4, 8, 12, and 18 months. Our earlier work indicated Alzheimer's like changes in this model, indicating its suitability

These findings were published in *Drugs and Ageing* with 3 more manuscripts are under preparation for submission.

Funding

NHMRC; Rhyolite Innovations.

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 2022, including:

- Beam, C.R., et al., Estimating Likelihood of Dementia in the Absence of Diagnostic Data: A Latent Dementia Index in 10 Genetically Informed Studies. *Journal of Alzheimer's Disease,* 2022. **90**: p. 1187-1201.
- Brouwer, R.M., et al., Genetic variants associated with longitudinal changes in brain structure across the lifespan. N*at Neurosci*, 2022. **25**(4): p. 421-432.
- Dong, C., et al., Parental Life Span and Polygenic Risk Score of Longevity Are Associated With White Matter Hyperintensities. *J Gerontol A Biol Sci Med Sci*, 2022. **77**(4): p. 689-696.
- Finkel, D., et al., Financial strain moderates genetic influences on self-rated health: support for diathesis–stress model of gene–environment interplay. *Biodemography and Social Biology*, 2022. **67**(1): p. 58-70.
- Hop, P.J., et al., Genome-wide study of DNA methylation shows alterations in metabolic, inflammatory, and cholesterol pathways in ALS. *Sci Transl Med* 2022. **14**(633): p. eabj0264.
- Jefferis, J., et al., The Heritability of Kidney Function Using an Older Australian Twin Population. *Kidney International Reports*, 2022. **7**(8): p1819-1830.
- Koncz, R., et al., The heritability of amyloid burden in older adults: the Older Australian Twins Study. *J Neurol Neurosurg Psychiatry*, 2022. **93**(3): p. 303-308.
- Lahti, J., et al., Genome-wide meta-analyses reveal novel loci for verbal short-term memory and learning. *Molecular Psychiatry*, 2022. **27**: p4419-4431.
- Li, S., et al., Early life affects late-life health through determining DNA methylation across the lifespan: A twin study. *EBioMedicine*, 2022. **77**: p. 103927.
- Li, X., et al., White matter hyperintensities segmentation using an ensemble of neural networks. 2022. *Hum Brain Mapp* **43**(3): p. 929-939.
- Matison, A., et al., Nature Versus Nurture – Studying the Relationships Between Diet and Depression in Older Adults. *Current Developments in Nutrition*, 2022. **6**(Supplement_1): p. 1118-1118.
- Restuadi, R., et al., Polygenic risk score analysis for amyotrophic lateral sclerosis leveraging cognitive performance, educational attainment and schizophrenia. *Eur J Hum Genet*, 2022. **30**(5): p. 532-539.
- Revelas, M., et al., High polygenic risk score for exceptional longevity is associated with a healthy metabolic profile. *GeroScience*, 2022. **45**(1): p399-413
- Sonderby, I.E., et al., Effects of copy number variations on brain structure and risk for psychiatric illness: Large-scale studies from the ENIGMA working groups on CNVs. *Hum Brain Mapp*, 2022. **43**(1): p. 300-328.

Funding

NHMRC.

The prevalence of poor mobility in older adults

CHeBA staff

Darren Lipnicki, Perminder Sachdev, Henry Brodaty, Nicole Kochan

Other investigators

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

Aims

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

Findings

Revised manuscript under review.

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

Dr 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 was obtained from COSMIC studies. We examined if there was a U-shaped relationship between blood pressure and dementia risk and whether treatment for hypertension in late life is associated with lower dementia risk.

Our preliminary findings in an IPD meta-analysis of 17 studies with a total of 43,258 from were that: 1. Unmedicated hypertensives had a 40% greater risk of dementia compared to medicated hypertensives and this relationship was not modified by age, sex or racial group. Those medicated hypertensive in early late-life (60 – 70 yo) had significant greater dementia risk compared to "healthy controls" but this attenuated with increasing age (>70).

There was a significant, U-shaped relationship between DBP, but not SBP, and dementia risk (lowest risk DBP 83 mmHg). Low DBP was associated with greater risk than high DBP.

The findings indicate that ongoing antihypertensive therapy throughout late-life is an important part of ongoing dementia prevention. Contrary to many previous studies it indicates that DBP, particularly low DBP, is a more important driver of dementia than SBP. Further investigation into the pathophysiological consequences and management of low DBP is needed. We will submit these findings for peer review and publication in 2023.

Funding

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

The Sydney Centenarian Study (SCS)

CHeBA staff

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

Aims

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

Findings

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

Funding

NHMRC.

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

CHeBA staff

Zara Page (PhD Candidate), Henry Brodaty, Nicole Kochan, Karen Croot

Aims

The overarching objective of this PhD project is to identify culturally-appropriate cognitive assessments for older Australians from culturally and linguistically diverse (CALD) backgrounds and create knowledge to guide the selection of the most suitable assessments for these individuals. Specific aims include:

- To systematically review literature to identify methods that aim to reduce construct and/or item bias associated with culturally, ethnically, or linguistically diverse status in pencil-and-paper neuropsychological assessment (PnPA) or computerised neuropsychological assessment (CNA) of older adults.
- To involve and engage older CALD community members in the design and implementation of an online survey validation of the CogSCAN Languages and Acculturation Questionnaire (CLAQ) through the introduction of a Community Working Group.
- To establish the factor structure of the CLAQ, as a tool to capture linguistic and acculturation variables to robustly characterise CALD status.
- To examine the relative importance of a range of linguistic and acculturation variables in explaining CALD performance on both PnPA and two CNAs.
- To compare the level and patterns of performance between English-speaking background (ESB) and CALD participants on PnPA and CNA measures.

Funding

DCRC PhD Scholarshi; The Josh Woolfson Memorial Scholarship

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

Prof Bernhard Baune (University of Münster), Dr Liliana Ciobanu (University of Adelaide), A/Prof Nicola Armstrong (Curtin University) (CHeBA Hon. Research Fellow), A/Prof John Kwok (University of Sydney; UNSW), Prof 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

- 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
- examine cross-ethno-regional differences.

Findings

Fourteen COSMIC studies from 10 countries contributed longitudinal data of 20,945 participants to this project. Five percent of all included participants suffered a stroke over follow up, which ranged from 3 to 15 years. Data harmonisation on stroke data, neuropsychological test scores and other data was completed in 2022. Data analysis will begin in 2023.

Funding

NIH, NHMRC

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

Prof Blossom Stephan, A/Prof Grazziela 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

Data being obtained and preliminary analyses underway.

Funding

NIH, UKRI.

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), PATH (Personality and Total Health Through Life Study), SLAS (The Singapore Longitudinal Ageing Studies), and Sydney MAS (Memory and Ageing Study). 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. We have now completed analyses in all datasets and have been summarising results into a manuscript. A PhD student, Mr. Keshuo Lin, is leading this study.

Funding

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

Completed Projects

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

CHeBA staff

Perminder Sachdev, Jessica Lo, Jiyang Jiang

Other investigators

Nacim Betrouni, Régis Bordet (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 obtained from routine clinical MR images are robust early predictors of post-stroke cognitive impairment and they can be combined with other demographic and clinical predictors to build an accurate prediction model. Results were published in the journal Stroke in 2022.

Funding

Vincent Fairfax Family Foundation; NHMRC

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

Findings

First draft of manuscript was completed in 2022.

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 (University of Melbourne).

Aim

The broad aim of this project was to design and establish a general framework for creating and computing novel diffusion weighted imaging (DWI) markers for examining 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 skeletonised 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 August 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: the Sydney Memory and Ageing Study (MAS) and the Renji Cerebral Small Vessel Disease Corhort Study (RCCS). Publications

Funding

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

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

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. 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 2023, it will be part of a new NHMRC CRE grant awarded to Prof Perminder Sachdev.

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 in 2022.

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 ε4 and common vascular risk factors.
- Examine the shared genetic basis between cerebral small vessel disease and β-amyloid burden.
- Investigate the relationship between amyloid burden and aspects of cognitive function.

Findings

- The heritability of global amyloid burden was moderate (0.41-0.52).
- APOE ε4 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.
- Results published in Koncz R, Thalamuthu A, Wen W et al. on behalf of the Older Australian Twins Study collaborative team. The heritability of amyloid burden in older adults: the Older Australian Twins Study Journal of Neurology, Neurosurgery & Psychiatry 2022;93:303-308
- There does not appear to be a shared genetic basis between β-amyloid and cognition, although larger studies are recommended. These finding have been published as a chapter in Dr Koncz's PhD thesis, submitted October 2022.

Funding

NHMRC.

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. Performance-Based vs Informant-Reported Instrumental Activities of Daily Living in Predicting Dementia. J Am Med Dir Assoc. 2022 Aug;23 (8):1342-1347.e9. doi: 10.1016/j.jamda.2021.09.020. Epub 2021 Oct 14.

Funding

NHMRC, UNSW Scientia Fellowship

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

Prof Kaarin Anstey (UNSW Sydney), ProfMaria Fiatarone Singh (University of Sydney), Prof Louisa Jorm (UNSW Sydney), Prof Nicola Lautenschlager (Melbourne University), Prof Anthony Maeder (Western Sydney University), Prof John McNeill (Monash University), Prof 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 commenced in 2021.

Publications

- Kochan NA, Heffernan M, Valenzuela M, Sachdev PS, Lam, BCP, Fiatarone Singh M, Anstey KJ, Chau T, & Brodaty H. Reliability, Validity, and User-Experience of Remote Unsupervised Computerized Neuropsychological Assessments in Community-Living 55- to 75-Year-Olds. *Journal of Alzheimer's disease : JAD*, 2022:90(4), 1629–1645. https:// doi.org/10.3233/JAD-220665.
- Almendrales 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 randomised controlled trial to prevent cognitive decline and dementia. *The British Journal of Nutrition,* 127(8),= 1259–1268. https://doi.org/10.1017/S0007114521001859

Future publications emanating from this project will be presented in the Publications Appendix of future reports.

Funding

NHMRC Dementia Team Research Grant

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), principal 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

Funding

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

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).

A plasma pre-analysis fractionation method has been developed which allows identification of >3000 plasma proteins, and this work has now been published. 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.

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 2022.

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., and a book chapter reviewing the role of lipids was also published (Sachdev PS, Poljak A) by Elsevier BV.

Funding

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

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

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), Henry Brodaty, Lynn Chenoweth.

Other investigators

Prof 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 relationships that are meaningful for people living with dementia who experience changed behaviours in residential aged care.
- Determine the factors associated with these meaningful relationships.

Findings

Residents experiencing dementia-associated behaviours engaged in meaningful relationships as evidenced by 'positive person' interactions.

Associated factors:

- Care provider executive trained in and committed to relational person-centred care;
- Care home management trained and empowered to innovate;
- Care partners trained, supported and recognised e.g., sufficient time to engage with residents and each other, including socially;
- Good connection between residents' family/close friend(s), care home staff and visiting personnel to the care home; and
- The contribution of lifestyle staff, who also acted as mentors to others, in attending to dementia-associated behaviours.

Funding

DCRC, CHeBA, and self-funded.

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 Aβ 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 Aβ fibrils, suggesting selectivity to bind plaque deposits in AD transgenic mouse and post-mortem human probable AD brain tissue sections.
- Our nanoparticles were shown to be safe and well tolerated in AD transgenic mice (APP/PS1) and wild type mice with no changes in liver and renal function tests and no observable changes in behaviour even at repeatedly high doses of 10 ng per kg weight of mouse.

Funding

Sachdev Foundation, The Yulgilbar Foundation, Australian Research Council Discovery Early Career Research Fellowship to Dr Nady Braidy.

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

CHeBA staff

Perminder Sachdev, Nady Braidy, Anne Poljak (Adjunct), Yue Liu (MSc candidate).

Other investigators

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

Aims

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

Findings

At present, the molecular basis of vascular dementia (VaD) remains elusive. Plasma samples were collected from Bankstown-Lidcombe hospital with VaD patients (n=50) and normal controls (n=50). Lipids were extracted and liquid chromatography coupled to mass spectrometry was used to comprehensively analyze the plasma lipidome in VaD and normal controls. The abundance of glycerides were significantly higher in VaD than in normal controls. Ceramides (Cer), cholesterol (CHE), phopholipids and lysophospholipids for VaD were significantly lower in VaD than for normal controls. Sphingomyelin was not significantly different between the 2 groups. Lipidomics can help to predict development of VaD. We also found the significant relation of global, old, acute/subacute and regional cerebral vascular pathologies, but not white matter rarefaction, to the onset and severity of Alzheimer's dementia. We also showed that late-life risk factors were found to have no relation with Alzheimer's dementia, and the increased risk of dementia with APOE ε4 is not mediated by CVD. The best interpretation of these findings is that CVD has a potential additive effect with AD pathologies in the development and progression of what is clinically diagnosed as Alzheimer's dementia. 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 four publications reporting on these findings and 2 more are under preparation for submission.

Funding

Australian Research Council Discovery Early Career Research Fellowship to Dr Nady Braidy; Mostyn Foundation

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.

Funding

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

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.

Experimental work to establish dose response curves and proteomics analysis using each of ethanol, resveratrol, nicotinamide, and NAD, were completed and Fatemeh is finalised her PhD experimental work and thesis chapters, and completed her PhD in September 2022.

Funding

NHMRC, Rebecca L. Cooper Medical Research Foundation.

The Sydney Memory and Ageing Study (MAS)

CHeBA staff

Henry Brodaty, Perminder Sachdev, Nicole Kochan, Wei Wen, Julian Trollor, Brian Draper, Karen Mather, John D Crawford, Ben CP Lam, Katya Numbers, Vibeke Catts, Russell Chander, Saly Mahalingam, Josephine (Josie) Bigland, Zara Page.

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 2022, including:

Further publications will be forthcoming and recorded in the Publications Appendix of future reports.

Funding

NHMRC

Upregulation of NAD+ Anabolism to Promote Lifespan

CHeBA staff

Nady Braidy.

Other investigators

Dr Kristine McGrath (UTS), Dr Mojtaba Golzan (UTS).

Aims

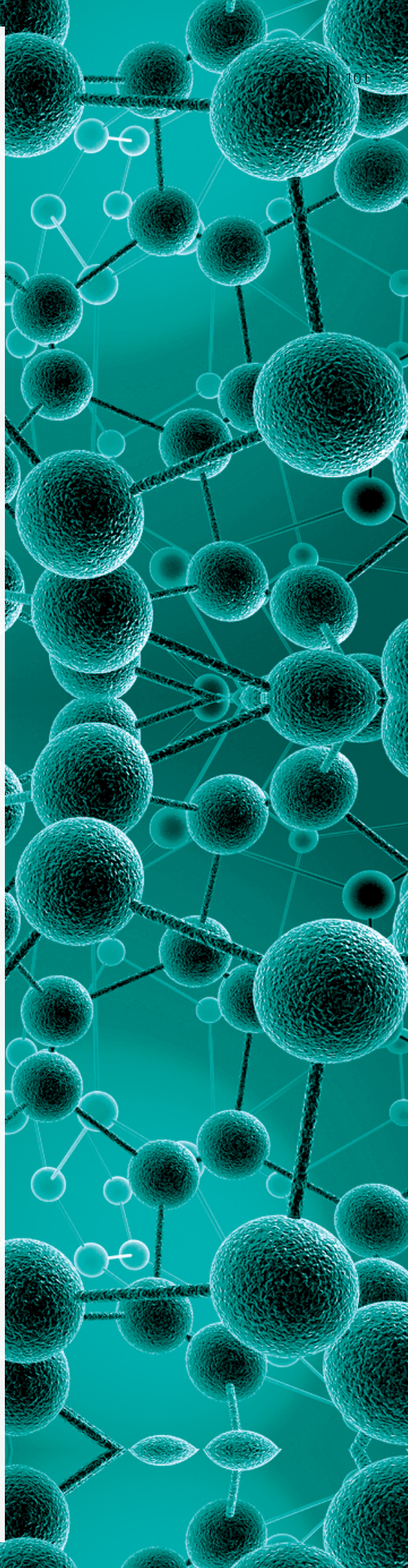
- Determine the effect of SIRT2 transgene on lifespan and underlying age-related degeneration in chow and high fat diet fed aged Wistar rats.
- Examine whether SIRT2 over-expression alters NAD+ levels and improves cognition in chow and high fat diet fed aged Wistar rats.
- Measure the changes in intracellular 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

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)*
Senior Research Associate, *Centres of Research Excellence for Vascular Cognitive Disorders (CRE-VCD)*

Nady Braidy
Research Fellow / *Leader Brain Ageing Research Laboratory*

Claire Burley
Postdoctoral Fellow / *PCC in Sub-acute care study*

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

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 (until 31 December 2022)*

Megan Heffernan
Postdoctoral Fellow / *Maintain Your Brain Trial Coordinator (until 31 December 2022)*

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*

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

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

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

Karen Mather
Senior Research Fellow / *Leader Genomics & Epigenomics Group*

Louise Mewton
Senior Research Fellow / *UNSW Scientia Program of Research*

Adith Mohan
Senior Lecturer / PhD Candidate

Katya Numbers
Postdoctoral Fellow / *Project Co-ordinator, Memory and Ageing Study (MAS)*

Matt Paradise
Senior Research Fellow / *Medical Fellow, ADNeT Project (ADNet-MC Initiative)*

Suraj Samtani
Postdoctoral Fellow / *SHARED Project Co-ordinator (until 31 December 2022)*

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 (until 30 November 2022)*

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

Professional & Technical Staff – Research

Nanmaran Anbupalam
Student Assistant (Casual) / *CHeBA Longitudinal Studies (until 30 June 2022)*

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

Josephine (Josie) Bigland
Research Assistant (Casual) / *CHeBA Longitudinal Studies*

Anne-Nicole Casey
Research Officer / *Update of Behavioural & Psychological Symptoms of Dementia (BPSD) Handbook Project (until 28 April 2022)*
Postdoctoral Fellow / *Maintain Your Brain (until 31 December 2022)*

Vibeke Catts
Research Manager

Tiffany Chau
Research Assistant / *Maintain Your Brain Trial (until 31 December 2022)*

Xinyue (Rory) Chen
Senior Project Officer / *Dementia Platforms Australia (DPAU) Project*

Ka Yue (Helena) Chui
Research Officer / Project Co-ordinator, *Vascular Cognitive Impairment (VCI) Study (until 26 September 2022)*

John Crawford
Senior Statistician / *CHeBA Longitudinal Studies*

Karen Croot
Research Officer / *CogSCAN Study (until 31 December 2022)*

Sarah Davies
Research Assistant / *Rethink My Drink Project*

Sumangali (Sumi) Gobhidharan
Research Officer / *Genomics & Epigenomics Group*

Danika Hall
Research Assistant (Casual) / *COGNISANCE Project (until 31 December 2022)*

Fleur Harrison
Research Assistant / *OAM Study; Patient Centre Care (PCC) in Sub-acute care study*

Shizuka Hayashi
Student Assistant / *CHeBA Longitudinal Studies*

Nicholas (Nick) Hoy
Research Assistant / *COSMIC Alcohol Study*

Sri Chandana Kanchibotla
Research Assistant / *Genomics & Epigenomics Group*

Gowsaly (Saly) Mahalingam
Research Assistant / *SHARED Project (until 31 December 2022)*

Niki McDonagh
Research Officer / *Social Cognition Intervention Project (until 1 August 2022)*

Inga Mehrani
Project Manager / *The Australian Dementia Network (ADNet) Project*

Zara Page
Student Assistant / *CHeBA Longitudinal Studies*

Juan Carlo San Jose
Health Informatics Specialist *(until 31 December 2022)*

Amanda Selwood
Research Assistant / *Study Co-ordinator, Older Australian Twins Study (OATS) (until 31 December 2022)*

Mayouri Sukhapure
Research Assistant / *Patient Centre Care (PCC) in Sub-acute care study*

Emily Swift
Research Officer / *Functional Neurological Disorders (FND) Project*

Ashton Trollor
Student Assistant (Casual) / *CogSCAN Study; CHeBA Longitudinal Studies (until 26 July 2022)*

Maria Villalva
Research Assistant / *Nanotechnology for the diagnosis and treatment of neurodegenerative disorders project (until 14 January 2022)*

Rachel Visontay
Research Assistant / *COSMIC Alcohol Study*

Virginia (Ginny) Winter
Research Officer / *Rethink My Drink Project*

Nora Wong
Research Officer / *COGNISANCE Project (until 31 December 2022)*

Professional & Technical Staff – Support

Janelle Burns
Engagement & Projects Officer / *CHeBA Operations Team*

Sophia Dean
Administrative Officer / *CHeBA Operations Team*

Heidi Douglass
Communications & Projects Officer / *CHeBA Operations Team*

Helena Hudson
Project Administrator / *CHeBA Operations Team*

Laurie Mock
Digital Communications Officer / *CHeBA Operations Team (until 20 December 2022)*

UNSW Adjunct & Conjoint Staff

Michael Connors
Adjunct Senior Lecturer

Tiffany Jessop
Adjunct Lecturer

Rebecca Koncz
Adjunct Senior Lecturer

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

Yvonne Leung
Adjunct Associate Lecturer *(until 1 July 2022)*

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

Kuldip Sidhu
Adjunct Associate Professor, *Co-Leader Molecular Biology & Stem Cells 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

Michael Valenzuela
Honorary Professor

UNSW Visiting Fellows

Jessica (Jess) Baker
Visiting Fellow

Heidi Foo
Visiting Academic

Satoshi Hosoki
Visiting Felloe

Jacki Wesson
Visiting Fellow (until 18 May 2022)

Qian Wu
Junior Visiting Research Fellow (until 30 November 2022)

CHeBA Honorary Research Fellows

Nicola Armstrong

Simone Reppermund

Appendix B: External Appointments

Dr Nady Braidy

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

Professor Henry Brodaty

- Scientia Professor, Ageing and Mental Health, (previously Professor of Psychogeriatrics, 1990-2010), School of Psychiatry, UNSW Sydney (2011-present)
- Montefiore Chair of Healthy Brain Ageing (2012-present)
- Head (and Founder), Memory Disorders Clinic, Prince of Wales Hospital (1985 -present)
- Senior Clinician, Aged Care Psychiatry, Prince of Wales Hospital (1990-present)
- Member, International Advisory Committee of the National Institute of Dementia, South Korea (2013-present)
- Honorary Professor, Kiang Wu Nursing College, Macau (2014-present)
- Chair, Australian Institute for Health and Welfare, Dementia Advisory Committee (2021-2024)
- Honorary Lifetime Vice-President, Alzheimer's Disease International (ADI) (2005-present)
- Honorary Medical Advisor, Dementia Australia NSW (1992-present)
- Ambassador for Dementia Australia (2015-present)
- Member, Australian Advisory Board for Nutricia, (2012-present)
- Ambassador, Montefiore Homes (2006-present)
- Chair, Clinical Advisory Committee, Montefiore Homes (2012-present)
- Expert Advisory Panel, NHMRC National Institute for Dementia Research (2016-present)
- Dementia Expert Advisory Panel, Commonwealth Department of Health (2022-present)
- Member, International Research Network for Dementia Prevention Advisory Group (2017-present)
- Member, Psychotropics Clinical Care Standard Topic Working Group, Australian Commission for Quality and Safety in Health Care (2022-2023)
- WHO Blueprint for dementia research working group and WHO mhGAP Guidelines Development Group – guidelines for mental health management especially for LMIC (2022-present)
- Editorial board member for the following journals: *Aging and Mental Health* (1996-present), *Alzheimer Disease and Associated Disorders: an International Journal* (1995-present), *Alzheimers and Dementia: Journal of the Alzheimers Association* (2005-present), *Australian and New Zealand Journal of Psychiatry* (1981-present), CNS Drugs (1999-present), *Dementia and Geriatric Cognitive Disorders* (2010-present), *Neurodegenerative Disease Management* (2010-present), *The Australian Journal of Dementia Care* (2012-present)
- Deputy Editor, *International Psychogeriatrics* (2017-present)

Dr Anne-Nicole Casey

- Research Coordinator, Susan Wakil School of Nursing and Midwifery, Faculty of Medicine and Health, University of Sydney, Evaluation study of the Meeting Centres Support Program (MCSP) Australian pilot
- Member, International Psychogeriatric Association (IPA) (2018-2022)

Dr Vibeke Catts

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

Professor Lynn Chenoweth

- Adjunct Professor in Medicine & Nursing; The University of Notre Dame Australia (2021-)
- Adjunct Professor in Nursing, Midwifery and Health; Western Sydney University
- Board Member, Australian Multicultural Aged Nursing Pty Ltd (AMAN)

- Member of the following research committees: Research Advisory and Review Committee, Dementia Australia; Human Research Ethics Committee B, UNSW; War Memorial Hospital Research Committee
- Research Grant Review panel member: NHMRC Health Services Research, Health Promotion & Ageing discipline Project Grants
- Editorial Board member in *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*

Fleur Harrison

- Student Member, Australian Psychological Society (2016-)
- Member, Alzheimer's Association International Society to Advance Alzheimer's Research and Treatment (ISTAART) (2011-)
- Member, Australian Association of Gerontology (2016-)

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, Speciality of Psychiatry, Faculty of Medicine and Health, The University of Sydney (2018-)
- Clinical academic neuropsychiatrist, Sydney Local Health District (2017-)
- Adjunct Senior Lecturer, Discipline of Psychiatry & Mental Health, UNSW Sydney (August 2020-)
- Fellow, Royal Australian and New Zealand College of Psychiatrists (RANZCP) (2017-)
- ember, "Motivation" taskforce, The Human Affectome Project (2017-)
- Member, COVID-19 Disability Community of Practice, NSW Ministry of Health (2020-)
- Member, Australian Association of Developmental Disability Medicine (2022-)

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 (2019-)

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

- Associate Editor in *Frontiers in Dementia* (Section: Aging and Risk Factors for Dementia)
- Review Editor in *Frontiers in Epidemiology* (Section: Neurological and Mental Health Epidemiology)

Dr Karen Mather

- Member of Australian Association of Gerontology and Alzheimer's Association International

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

Dr Katya Numbers

- Member of the Ageing Future Institutes Associate Investigator, UNSW (2020–Present)
- Member of the Australian Human Rights Institute, UNSW (2022–Present)
- Member of the Alzheimer's Association International Society to Advance Alzheimer's Research and Treatment (ISTAART), Alzheimer's Association (2019–Present)
- Member of the ISTAART Dyadic Patterns of Subjective Report Working Group, Alzheimer's Association (2019–Present)
- Member of the ISTAART Subjective Cognitive Decline PIA, Alzheimer's Association (2019–Present)
- Member of the ISTAART Alliance of Women Alzheimer's Researchers (AWARE) PIA, Alzheimer's Association (2019–Present)

Zara Page

- ISTAART Ambassador 2022 (March 2022- March 2023)
- ISTAART AWARE PIA Steering Committee (October 2022 – Present)

Dr Matthew Paradise

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

Dr Anne Poljak

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

Dr Simone Reppermund

- Editorial board member in Neurodegenerative Diseases
- NHMRC MRFF Dementia, Ageing and Aged Care Mission Grant Assessment Committee Member
- Postgraduate Coordinator for the Discipline of Psychiatry

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, 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, Neurocognitive Disorders Work Group for DSM-5 (2007-)
- Member of the International Advisory Group for the Revision of ICD-10 Mental and Behavioural Disorders and the International Advisory Group for the Revision of ICD-10 Diseases of the Nervous System, WHO ICD-11 Expert Working Group on Neurocognitive Disorders (2011-)
- President-Elect of the International College of Geriatric Psychoneuropharmacology (2012-)
- Executive Member of the International Society of Vascular Behavioural and Cognitive Disorders (VASCOG) (2012-)
- Member, Expert Advisory Panel, NHMRC National Institute for Dementia Research
- Founding Executive Committee Member of the Tourette Syndrome Association of Australia (1989-)
- Scientific Advisory Committee Member of the Alzheimer's Association of Australia (1995-)
- Committee Member on Psychotropic Drugs and Other Physical Treatments, Royal Australian and New Zealand College of Psychiatrists (1996-)

- Chair of the Medical Advisory Committee of the Tourette Syndrome Association of Australia (1996-)
- Chair of the Section of Neuropsychiatry, RANZCP (2005-)
- Fellow of the Australian Academy of Health & Medical Sciences (2015-)
- Fellow of the NHMRC Academy (2011-)
- Member of the NHMRC Assigner's Academy (2012-)
- Australian Advisory Board of Biogen (2018-)
- Alzheimer's Disease Advisory Board – Biogen Australia and New Zealand (2021-)
- Advisory Board of Roche Australia (2021-)
- Invited Member, Task Force of the International League Against Epilepsy (2011-) Neuropsychobiology Commission (2011-)
- Deputy Director, Alzheimer's Disease Network (ADNeT)
- Committee Member, Ageing Futures Institute, UNSW Sydney
- Member of the Dean's Advisory Committee, UNSW (1995-)
- Member of the Scientific Steering Committee, Neuroscience Institute of Schizophrenia and Allied Disorders (NISAD), Garvan Institute, Sydney (1996-)
- Chair of the Scientific Review Committee of the Division of Psychiatry, ESAHS Eastern Section (1996-)
- Member of the Ministerial Advisory Committee for Psychosurgery in NSW (1996-)
- Member of the Faculty of Medicine Research Committee, UNSW (2005-)
- Member of the Brain Sciences UNSW Executive Committee (2008-)
- Member of the Awards Committee at the School of Psychiatry, UNSW (2010)
- Overseas Ambassadors Advisory Group (2014-)
- Member of the UNSW Microbiome Research Centre's Advisory Committee (2021-)
- Editorial board member for the following journals: *Current Opinion in Psychiatry* (Neurocognitive Disorders section), *Middle Eastern Journal of Ageing, Middle Eastern Journal of Psychiatry & Alzheimer's, Brain and Mind Matters, The Open Neuroimaging Journal, International Psychogeriatrics, Alzheimer's & Cognitive Disorders*

Dr Suraj Samtani

- Member of Australian Psychological Society, Australian Clinical Psychology Association

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)

Mohammed Ali Saeed Alghamdi

PhD student
An investigation of the altered functional connectivity in relation to cerebrovascular burden
Discipline of Psychiatry and Mental Health, School of Clinical Medicine, UNSW Medicine and Health
Supervisors: A/Prof Wei Wen, Dr Jiyang Jiang

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

Fatemeh Amjadimoheb

PhD student
Circular RNAs as modulators of longevity and healthy aging
Discipline of Psychiatry and Mental Health, School of Clinical Medicine, UNSW Medicine and Health
Supervisors: Dr Karen Mather, Dr Anbu Thalamuthu

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

Gurpreet Kaur Hanstra

PhD student
Blood biomarkers for the diagnosis and prognosis of vascular dementia
Discipline of Psychiatry and Mental Health, School of Clinical Medicine, UNSW Medicine and Health
Supervisors: Prof Perminder Sachdev, Dr Anne Poljak, Dr Tharusha Jayasena

Shizuka Hayashi

PhD student
Automated rating of perivascular spaces in the ageing brain using deep learning
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, Prof Dadong Wang, A/Prof Yang Song

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

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

Adith Modhan

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 linguistic diverse (CALD) Discipline of Psychiatry and Mental Health, School of Clinical Medicine, UNSW Medicine and Health
Supervisors: Prof Henry Brodaty, Dr Nicky Kochan, 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

Heidi Welberry

PhD student
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
Supervisors: Prof Henry Brodaty

Jacqueline Wesson

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

Mark Yates

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

Completed

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)
Degree completed: 11 Oct 2022

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
Degree completed: 5 Sep 2022

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, Prof Lynn Chenoweth, Prof Jeffrey Braithwaite (Macquarie University)
Degree conferred: 5 Nov 2022

Marina Ulanova

PhD student
Towards early Alzheimer's disease diagnosis: development of amyloid-targeted magnetic nanoparticles for use as MRI/MPI tracers
School of Medical Sciences, UNSW Medicine and Health
Supervisor: Dr Nady Braidy, Prof Perminder Sachdev
Degree completed: 13 Oct 2022

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
Degree conferred: 23 Jul 2022

Honours and ILP Students 2022

Shalfi Kalam

Honours student
The relationship between olfactory function, depression and cognition in older people
Supervisors: Dr Simone Reppermund, Dr Katya Numbers, Dr Darren Lipnicki

Li Li

ILP student
Examining the relationship between cerebrovascular burden measured by DWI brain scans and risk factors using MAS cohort
Supervisors: A/prof Wei Wen, Dr Jiyang jiang, Dr Matt Paradise

Anthony Liao

Honours student
Genetics and Epigenetics of Neuroticism
Supervisors: Dr Karen Mather, Dr Sumi Gobhidharan, Dr Anbu Thalamuthu

Jessica Sawang

Honours student
Exploring the relationships between functional impairment, mood, and ageing perceptions in older adults with and without dementia
Supervisors: Dr Simone Reppermund, Dr Katya Numbers, Dr Ben Lam

Ellen Wang

Honours student
Lacune detection using random forests
Supervisors: A/Prof Pierre Lafaye de Micheaux, Dr Jiyang Jiang

Lei Lei Zhang

Honours student
Does functional impairment predict cognitive decline in older people without dementia?
Supervisors: Dr Simone Reppermund, Dr Katya Numbers, Prof Henry Brodaty

Appendix D: Awards & Promotions

Prof Henry Brodaty

- Fellow of the Academy of the Social Sciences in Australia

Dr Michael Connors

- Awarded the Basic Trainee Prize, Royal Australian and New Zealand College of Psychiatry (RANZCP) Faculty of Psychiatry of Old Age

Professor Lynn Chenoweth

- DCRC (Dementia Australia) World Class Dementia Grants ($536,000) for the project "Improving health outcomes, well-being and care for people living with dementia in the hospital setting" (Chenoweth L (CIA), Brodaty H, Williams A, Burley C, Liu Z, Reyes P, McGuire J, Maiden G)
- NHMRC targeted palliative care grant scheme ($3,000,000) for the project "CELPI: A randomised trial of a Carer End of Life Planning Intervention in people with dementia" (Arends G (CIA), Chenoweth L (CIB), Etherton-Beer C, Hayes B, Spilsbury K, Agar M, Howard, K)

Dr Meredith Gresham

- The Australia Association of Gerontology's 2022 Hal Kendig Research Development Award ($19,777) for a project "Living with uncertainty: What information do people with mild cognitive impairment and families need and want after diagnosis?"

Fleur Harrison

- Kwan Fung and Yuet Ying Fung Healthy Brain Ageing Research Award ($4,000)
- UNSW Development and Research Training Grant (DRTG) Scheme 2022 ($1,500)
- Discipline of Psychiatry & Mental Health HDR Funding ($1,500)

Dr Katya Numbers

- Arc PGC Research Supervisor Award – Faculty of Medicine & Health – 2022

A/Prof Simone Reppermund

- Promotion to Associate Professor
- Renewal of UNSW Scientia fellowship
- Best oral presentation award in Public Health and Prevention, Australian Dementia Research Forum 2022

Zara Page

- Josh Woolfson Memorial Scholarship (top up scholarship $10,000 per year for 3 years)
- Discipline of Psychiatry and Mental Health HDR Funding ($1,000)
- ISTAART Ambassador AAIC Travel Grant ($8,000)
- Emerging Researchers in Ageing (ERA) Travel Exchange Program Funding - International ($8000)

Scientia Professor Perminder Sachdev

- Named as one of Australia's Australia's research field leaders in health & medical sciences
- Ryman Prize, The Ryman Foundation, New Zealand

Dr Suraj Samtani

- Awarded the Early/Mid-Career Researcher Best Paper for 2022, Discipline of Psychiatry and Mental Health, Faculty of Medicine and Health, UNSW Sydney

Marina Ulanova

- CHeBA top-up scholarship

Appendix E: Research Grants & Funding

Grants

Understanding intergenerational change in the health and well-being of older adults and its effects: The Sydney Memory and Ageing Study 2 (MAS2)

Funding Source: NHMRC
Project ID: RG212928
Investigator/s: Prof Henry Brodaty, Prof Perminder Sachdev, Prof Colin Masters, Prof Maria Fiatarone Singh, Prof Annette Dobson, Prof Aletta Schutte, Prof Henry Cutler, Prof Carol Brayne, Dr Nicole Kochan, Dr Katya Numbers
Duration: 5 years: 2022-2027
Total Funds: $3,304,760

Nicotinamide adenine dinucleotide as a novel target for ageing and dementia

Funding Source: NHMRC/Investigator Grant
Project ID: RG210997 / RG210997-A
Investigator/s: Dr Nady Brady
Duration: 5 years: 2022-2025
Total Funds: $1,570,120

Exceptional cognition in old age and interactions with other aspects of successful ageing. Postgraduate Scholarship for Dr Alice Powel

Funding Source: NHMRC
Project ID: RG212082
Investigator/s: Prof Henry Brodaty, Dr Alice Powel
Duration: 5 years: 2022-2024
Total Funds: $124,846

A randomised trial of a carer end of life planning intervention (CELPI) in people dying with dementia

Funding Source: NHMRC
Project ID: RG214288
Investigator/s: A/Prof Glen Arendts, Prof Lynn Chenoweth*, A/Prof Barbara Hayes, A/Prof Katrina Spilsbury, Prof Kirsten Howard, Prof Meera Agar
Duration: 4 years: 2021-2025
Total Funds: $1,486,231 (*$98,802 only)

Vascular contributions to Dementia (VCD-CRE): a transformative approach to reducing the burden of cognitive disorders

Funding Source: NHMRC
Project ID: RG203943
Investigator/s: Prof Perminder Sachdev, Prof Amy Brodtmann, Prof Christopher Levi, Prof Michael O'Sullivan; A/Prof Andrew Bivard, Dr Vivek Gupta
Duration: 5 years: 2021-2025
Total Funds: $ 3,000,000

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

e-DIVA (empowering dementia carers with an iSupport visual assistant)

Funding Source: National Ageing Research Institute (NARI)/ NHMRC e-ASIA Joint Research Program
Project ID: RG203150
Investigator/s: A/Prof Tuan Nguyen, Prof Lily Dongxia Xiao, Prof Henry Brodaty*, A/Prof Bianca Brijnath, Dr Andre Andrade, Prof Adrian Esterman, Prof Susan Kurrle, Prof Maria Crotty, Prof Penelope Schofield, Prof Sunil Bhar
Duration: 4 years: 2021-2024
Total Funds: $1,883,366 (*$58,265 only)

Food for thought: preventing decline and improving cognition through diet and dietary advice in older people at risk (PURPLE Project)

Funding Source: University of Wollongong/DCRC World Class Projects
Project ID: RG203154
Investigator/s: Prof K Charlton, Prof Henry Brodaty*, Prof Kaarin Anstey, A/Prof Steven Roodenrys, Dr Katherine Kent
Duration: 3 years: 2021-2023
Total Funds: $599,552 (*$118,440 only)

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: 2021-2023
Total Funds: $536,000

Development of the WHO's blueprint for dementia research incorporating inputs from diverse stakeholders

Funding Source: World Health Organisation
Project ID: RG221723
Investigator/s: Prof Perminder Sachdev, Prof Henry Brodaty, Dr Adam Bentvelzen, Dr Nicole Kochan, Dr Karen Mather, Dr Nady Braidy, Dr Katya Numbers, Dr Louise Mewton, Dr Darren Lipnicki, Dr Suraj Samtani, Dr Ben Lam
Duration: 1 year: 2021-2022
Total Funds: $7,046

Update of behavioural and psychological symptoms of dementia (BPSD) Handbook

Funding Source:Ministry of Health/State Government Contract
Project ID: RG212282
Investigator/s: Prof Henry Brodaty
Duration: 1 year: 2021-2022
Total Funds: $86,826

Update to dementia behaviour management app – 4-GD95QC

Funding Source: Department of Health / Dementia and Aged Care Services Fund (DACS)
Project ID: RG211792
Investigator/s: Prof Henry Brodaty
Duration: 1 year: 2021-2022
Total Funds: $366,000

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: 2021-2022
Total Funds: $423,596

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: Flinders University / Department of Foreign Affairs and Trade (DFAT) National Foundation for Australia-China Relations
Project ID: RG203295
Investigator/s: Prof Henry Brodaty
Duration: 1 year: 2021-2022
Total Funds: $13,200

The Mindgardens functional neurological systems disorders (FND) Clinic

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

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

Funding Source: NHMRC / DCRC-Dementia Australia Research Foundation
Project ID: RG181322-A / RG203202-A
Investigator/s: Dr Suraj Samtani
Duration: 1 year: 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

The impact of the environment and pollution on cognitive health (EPOCH): building the knowledge base through international collaboration

Funding Source: Australian Catholic Uiversity/ UKRI-NHMRC Built Environment Prevention Research Scheme
Project ID: RG201875
Investigator/s: Prof Ester Cerin, Prof Fiona Matthews, Prof Kaarin Anstey, Prof Perminder Sachdev*, Dr Suzanne Mavoa, A/Prof Luke Knibbs, Prof Bin Jalaludin, Dr Yu-Tzu Wu, Dr Matthew Prina, Dr Benjamin Barratt
Duration: 3 years: 2020-2023
Total Funds $681,240 (*$116,925 only)

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 30 June 2023

The APPLE Tree programme: active prevention in people at risk of dementia through lifestyle behaviour change and technology to build resilience

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

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: 2019-2022*
Total Funds: $1,000,000

*Extended to 1 Dec 2022

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

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 2023

Towards a better understanding of the mechanisms of ageing and longevity in C.elegans and humans

Funding Source: UNSW/Chinese Academy of Sciences (CAS) Collaborative Research Seed Program – Mobility Grant
Project ID: RG192635
Investigator/s: Dr Karen Mather, Dr Shi-Qing Cai
Duration: 1 year: 2019*
Total Funds: $5,000

*Extended to 30 October 2023

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 2023

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: 2018-2023
Total Funds: $18,000,000 (*$926,393 / $231,598)

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: 2018-2023
Total Funds: $74,352

Maintain Your Brain (MYB)

Funding Source: NHMRC
Project ID: RG142234
Investigator/s: Prof Henry Brodaty**, A/ Prof Michael Valenzuela, Prof Perminder Sachdev, Prof John McNeil, Prof Anthony Maeder, Prof Nicola Lautenschlarger, Prof Louisa Jorm, Prof Maria Fiatarone Singh, Prof Kaarin Anstey, Prof Gavin Andrews
Duration: 3 years: 2018-2020*
Total Funds: $12,818,309 (**$4,272,769)

*Extended to 31 December 2022

COSMIC: An international consortium to identify risk and protective factors and biomarkers of cognitive ageing and dementia in diverse ethno-racial groups and geographical settings

Funding Source: National Institutes of Health (NIH) / National Institute on Aging (NIA)
Project ID: RG172507
Investigator/s: Prof Perminder Sachdev, Prof Mary Ganguli, Prof Louisa Jorm, Prof Henry Brodaty, A/ Prof Ronald C Petersen, Prof Richard B Lipton, Prof Karen Ritchie, Prof Ki Woong Kim
Duration: 5 years: 2017-2022
Total Funds: USD2,869,541

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

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 20 February 2023

Philanthropic

The application of nanotechnology to the diagnosis of Alzheimer's disease (AD) and vascular dementia (VD)

Funding Source: Andrew and Prue Kennard
Project ID: PS63654_PS63673
Awardee/s: Dr Nady Braidy
Total Funds: $250,000 (2021-25)

Retinal biomarkers in dementia

Funding Source: Sachdev Foundation
Project ID: PS63671_PS65013
Awardee/s: Prof Perminder Sachdev
Total Funds: $50,200

The application of nanotechnology to the diagnosis of Alzheimer's disease

Funding Source: Sachdev Foundation
Project ID: PS63669_PS65012
Awardee/s: Dr Nady Braidy
Total Funds: $45,000

New dietary interventions to promote healthy brain ageing

Funding Source: Rhyolite Innovation
Project ID: PS62564_PS62584
Awardee/s: Dr Nady Braidy
Total Funds: $200,000 (2021-23)

The Montefiore Chair of Healthy Brain Ageing at UNSW

Funding Source: Montefiore Home
Project ID: PS34587_PS34590
Awardee/s: Prof Henry Brodaty Prof Perminder Sachdev
Duration: 5 years: 2017-21*
Total Funds: $529,183

*Extended to November 2022

Magnetic Particle Imaging

Funding Source: John Holden Family Foundation
Project ID: PS59199_PS59205
Awardee/s: Prof Perminder Sachdev
Total Funds: $300,000 (2021-23)

Other

The Dementia Momentum

Funding Source: Miscellaneous Donor Contributions
Project ID: PS38235_PS38252
Awardees: Prof Henry Brodaty Prof Perminder Sachdev
Duration: Ongoing
Total Funds: $1,700,500*

*As of 31 December 2022

The Healthy Brain Ageing Fund

Funding Source: Miscellaneous Donor Contributions
Project ID: PS22384_PS41631
Awardees: Prof Henry Brodaty Prof Perminder Sachdev
Duration: Ongoing
Total Funds: $338,052*

***As of 31 December 2022**

The Kwan & Yuet Ying Fung Health Brain Ageing Research Award

Funding Source: Kwan & Yuet Ying Fung Estate
Project ID: PS36983_PS37138
Awardees: Prof Perminder Sachdev Prof Henry Brodaty
Duration: Ongoing
Total Funds: $104,788*

*As of 31 December 2022

The Josh Woolfson Memorial Scholarship Fund

Funding Source: Woolfson Family
Project ID: PS42978_PS42948
Awardees: Prof Perminder Sachdev, Prof Henry Brodaty
Duration: Ongoing
Total Funds: $154,812*

*As of 31 December 2022

Appendix F: Financial Statement

Statement of Financial Performance for Year Ended 31 December 2022

		Notes	2022	2021
Funds				
	Research Revenue		4,814,994	3,577,019
	Donation		1,016,538	1,249,395
	Fees		0	0
	Faculty Funds	3	0	0
	UNSW Contribution - Competitive	1	332,623	149,876
	UNSW Contribution - Strategic	2	0	0
	Sundry Other Revenue		160,285	15,070
Total Funds			6,324,440	4,991,360
Total Funds - Report Variance				
Costs				
	People Costs		5,552,016	5,005,890
	Scholarship Stipends		160,830	102,352
	Contract & Consulting Services		11,271	387,366
	Repairs and Maintenance		3,710	0
	Consumables		39,415	50,836
	Travel		27,322	3,737
	Equipment		25,901	5,288
	Other Expenses		217,989	332,995
	Internal Expenses		139,204	166,320
Total Costs			6,177,658	6,054,784
Operating result			146,782	-1,063,424
Operating result report Variance				
Opening Balance			1,505,883	2,569,306
Closing Balance			**1,652,665**	**1,505,882**

Notes to the Statement of Financial Performance

UNSW Contribution - Competitive relates to funding awarded to CHEBA from UNSW through various competitive schemes supporting activities and infrastructure

UNSW Contribution - Strategic relates to funding provided to CHEBA from UNSW as a strategic investment in the centre's research activities

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

Appendix G: Publications

Book Chapters

Bentvelzen A, Chander RJ, Foo H, Lee T, Lipnicki DM, Sachdev P. Neuropsychological Assessment of Cognitive Aging. In Boyle GJ, Goden CJ, Stern Y, Stein DJ, Sahakian B. (Eds.). *The SAGE Handbook of Clinical Neuropsychology, Volume 2: Clinical Neuropsychological Assessment and Diagnosis*. 2022; in press. Sage Publications.

Braidy N, Poljak A, Jayasena T, Adams S, Sachdev P. Glutamate in the Pathogenesis of Gliomas. In: Kostrzewa RM (ed) *Handbook of Neurotoxicity*. Cham: Springer International Publishing; 2022. p. 2029-41. DOI 10.1007/978-3-031-15080-7_149. ISBN: 978-3-031-15080-7.

Braidy N, Poljak A, Jayasena T, Guillemin G, Sachdev P. Ionotropic Receptors in the Central Nervous System and Neurodegenerative Disease. In: Kostrzewa RM (ed) *Handbook of Neurotoxicity.* Cham: Springer International Publishing; 2022. p. 747-68. DOI 10.1007/978-3-031-15080-7_126. ISBN: 978-3-031-15080-7.

Brodaty H, Jeon Y-H, Gresham M, Low L-F, Phillipson L. Non-pharmacological interventions for people living with dementia as part of post-diagnostic care. In: Gauthier S, Webster C, Servaes S, Morais JA, Rosa-Neto P, editors. *World Alzheimer Report 2022. Life after diagnosis: Navigating treatment, care and support*. London, England: Alzheimer's Disease International; 2022. p. 254-6.

Brodaty H, Gresham M, Low L-F, Phillipson L, Jeon Y-H, COGNISANCE Group. Campaigning for change: improving diagnostic conversations and post-diagnostic support. In: Gauthier S, Webster C, Servaes S, Morais JA, Rosa-Neto P, editors. *World Alzheimer Report 2022. Life after diagnosis: Navigating treatment, care and support*. London, England: Alzheimer's Disease International; 2022. p. 401-3.

Casey A-N, Burns K, Draper B, Brodaty H. Assessment and management of behaviours and psychological symptoms associated with dementia (BPSD): A handbook for NSW Health clinicians providing services for people experiencing BPSD, 2nd edition. *NSW Government Ministry of Health;* May 2022. ISBN: 978-1-76023-279-5.

Casey A-N, Burns K, Draper B, Brodaty H. Assessment and Management of People with Behavioural and Psychological Symptoms of Dementia (BPSD) - Summary Handbook. *NSW Government Ministry of Health*. Aug 2022. ISBN: 978-1-76023-280-1.

Jayasena T, Bustamante S, Poljak A, Sachdev P. Assay of Fatty Acids and Their Role in the Prevention and Treatment of COVID-19. In: Guest PC (ed) *Multiplex Biomarker Techniques: Methods and Applications for COVID-19 Disease Diagnosis and Risk Stratification*. New York, NY: Springer US; 2022. p. 213-34. DOI: 10.1007/978-1-0716-2395-4_16. ISBN: 9781071623954.

Journal Articles

Alqarni A, Wen W, Lam BCP, Crawford JD, Sachdev PS, Jiang J. Hormonal factors moderate the associations between vascular risk factors and white matter hyperintensities. *Brain Imaging Behav*. 2022 Dec 21. DOI: 10.1007/s11682-022-00751-5. PMID: 36542288 (Epub 2022 Dec 21).

Almendrales 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 randomised controlled trial to prevent cognitive decline and dementia. *Br J Nutr*. 2022 Apr 28; 127(8):1259-68. DOI: 10.1017/s0007114521001859. PMID: 34078487 (Epub 2021 June 4).

Arendts G, Chenoweth L, Hayes BJ, Campbell E, Agar M, Etherton-Beer C, Spilsbury K, Howard K, Braitberg G, Cubitt M, Sheehan C, Magann L, Sudharshan T, Schnitker LM, Pearce J, Gilmore I, Cerra N, duPreez J, Jaworski R, Soh SC, Celenza A. CELPI: trial protocol for a randomised controlled trial of a Carer End of Life Planning Intervention in people dying with dementia. *BMC Geriatr*. 2022 Nov 16; 22(1):869. DOI: 10.1186/s12877-022-03534-1. PMID: 36384478 (Epub 2022 Nov 16).

Barker AL, Morello R, Thao LTP, Seeman E, Ward SA, Sanders KM, Cumming RG, Pasco JA, Ebeling PR, Woods RL, Wolfe R, Khosla S, Hussain SM, Ronaldson K, Newman AB, Williamson JD, McNeil JJ. Daily Low-Dose Aspirin and Risk of Serious Falls and Fractures in Healthy Older People: A Substudy of the ASPREE Randomized Clinical Trial. *JAMA Intern Med*. 2022 Dec 1; 182(12):1289-97DOI: 10.1001/jamainternmed.2022.5028. PMID: 36342703 (Epub 2022 Nov 8).

Beard JR, Si Y, Liu Z, Chenoweth L, Hanewald K. Intrinsic Capacity: Validation of a New WHO Concept for Healthy Aging in a Longitudinal Chinese Study. *J Gerontol A Biol Sci Med Sci*. 2022 Jan 7; 77(1):94-100. DOI: 10.1093/gerona/glab226. PMID: 34343305 (Epub 2021 Aug 4).

Beam CR, Luczak SE, Panizzon MS, Reynolds CA, Christensen K, Dahl Aslan AK, Elman JA, Franz CE, Kremen WS, Lee T, Nygaard M, Sachdev PS, Whitfield KE, Pedersen NL, Gatz M. Estimating Likelihood of Dementia in the Absence of Diagnostic Data: A Latent Dementia Index in 10 Genetically Informed Studies. *J Alzheimers Dis*. 2022; 90(3):1187-201. DOI: 10.3233/jad-220472. PMID: 36213997 / PMCID: PMC9741742 (Epub 2022 Oct 6).

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Appendix H: Presentations

Conferences

Bentvelzen AC, Kessels RPC, Badcock NA, Savage G. Can neuropsychologists improve assessment of right-lateralised memory? Conceptual and experimental analysis. *College of Clinical Neuropsychologists (CCN) Conference*. 2022 Nov 4; Manly, NSW, Australia.

Bentvelzen AC, Mehrani I, Kochan NA, Michaelian J, Cespedes M, Fripp J, Naismith S, Sachdev P. Acceptability and use of an online normative calculator using a harmonised protocol in Memory and Cognition clinics: The ADNeT Neuropsychological Norming Tool (ANNT). *Australian Dementia Research Forum*. 2022 May 30; virtual poster blitz presentation and poster.

Brodaty H. Invited Speaker. Using cohort datasets for environmental health research. 3rd Sax *Institute Forum Sessions*. 30 Mar 2022; Sydney.

Brodaty H. Presidential Symposium: Healthy Ageing. *RANZCP 2022 Congress*. 15-19 May 2022; Sydney and online.

Brodaty H. Advances in dementia research, diagnosis, treatment and care. *RANZCP 2022 Congress*. 15-19 May 2022; Sydney and online.

Brodaty H. Panel member. Brain Health as a Global Priority hosted by *The George Institute*. 20 July 2022; Sydney and online.

Brodaty H. Invited Speaker. Secrets of ageing with resilience Public Forum. The Juniors, Kingsford; 26 Oct 2022.

Brodaty H. Invited Speaker. Prevention, Prediction and Personalisation. *Rising to the Challenge: Healthy Aging Forum 2022*, hosted by WuXi AppTec, Singapore's Agency for Science, Technology and Research (A*STAR) and Davos Alzheimer's Collaborative (DAC). 11 Jan 2022; Singapore and online.

Brodaty H. Invited Speaker. Telemedicine: Current challenges and future possibilities in care and diagnostics. *Alzheimer's Disease International Webinar*. 23 Mar 2022; virtual.

Brodaty H. Invited Speaker. Healthy ageing: the secrets of centenarians. *Joint JSPN/RANZCP symposium: Healthy Ageing*. 17 May 2022; Sydney, Australia.

Brodaty H. Plenary Speaker and Panellist.Translational research focus on aged care. *Australian Dementia Research Forum 2022*. 1 June 2022; Sydney, Australia.

Brodaty H. Part of the organising committee for the ADRF 2022 conference June 2022; Sydney, Australia.
Brodaty H. Invited Speaker. Should I be worried about my memory? *Australian Osseointegration Society (AOS) and Australian Society for Periodontology (AOP) conference*. Sydney; 2022 Aug 19.

Brodaty H. Invited Plenary Speaker. Interventions for reducing the risk of cognitive decline and delaying the onset of dementia. *39th Brazilian Congress of Psychiatry* held by the Brazilian Association of Psychiatry. 5 Oct 2022; Fortaleza, Brazil and online.

Brodaty H. Invited Speaker. Initiatives for dementia risk reduction in Asia Pacific: MYB. *Asia Pacific Regional Conference of Alzheimer's Disease International* (ADI-APRC 2022). 8-11 Dec 2022; Taipei, Taiwan and online.

Budiarto MD, Croot K, Rossie M, Allison K, Sachdev PS, Brodaty H, Lam BCP, Crawford JD, Lee T, Henry JD, Draper B, Close J, Ong MY, Turner J, Riches J, Kochan NA. CogSCAN at Home: Older adults' experience of computerised neuropsychological assessments at home. *Australian Dementia Forum*. 2022, 30-31 May 2022; online.

Burley C, Chenoweth L, Brodaty H, Williams A, Liu K, Reyes P, McGuire J, Maiden G. Improving health outcomes, well-being and care for people living with dementia in the hospital environment. *35th Global Conference of Alzheimer's Disease International*. 2022 June 9-11; London, UK.

Chenoweth L. Consumer and healthcare professional led priority setting for quality use of medicines in people with dementia: gathering unanswered research questions. *Australian Association of Gerontology 55th National Conference*. 2022 Nov 12; Adelaide, SA, Australia.

Connors MH, Seeher K, Teixeira-Pinto A, Woodward M, Ames D, Brodaty H. Dementia and caregiver burden: A three year longitudinal study. Invited presentation at the *Royal Australian and New Zealand College of Psychiatry Faculty of Psychiatry of Old Age Conference*. Nov 2022; Brisbane, QLD, Australia.

G**resham MD,** Low L-F, Phillipson, L, Jeon, Y-H, Wong, N, Hall D, Tan A, Swaffer K, Brodaty H. Forward with Dementia: Co-designing hope and changing the way we think about post-diagnostic dementia support. Invited presentation at the *Alzheimer's Western Australia Dementia Symposium*. 13 Nov 2022; Perth, WA, Australia.

Gresham MD, Low L-F, Phillipson, L, Jeon, Y-H, Wong, N, Hall D, Tan A, Swaffer K, Brodaty H. Talk honestly about dementia at diagnosis and offer support to move froward. *HammondCare International Dementia Conference*. 8 Sep 2022; Sydney, Australia.

Harrison F, Mortby M, Aerts L, Guastella A, Brodaty H. The link between apathy and depressive symptoms and healthy lifestyles in older community-dwelling adults. Poster presentation at the *Alzheimer's Association International Conference*, virtual, 31 July – 4 Aug 2022; virtual.

Harrison F, Aerts L, Mortby M, Brodaty H. Apathy and poorer engagement in multiple health behaviours: cross-sectional findings from the Sydney Memory and Ageing Study. Oral presentation at A*ustralasian Society of Behavioural Health and Medicine*. 2-4 Feb 2022; virtual.

Kochan NA, Croot K, Crawford JD, **Bentvelzen AC**, Allison KA, Rossie M, Brodaty H, Lam BCP, Henry JD, Lee T, Draper B, Close J, Ong MY, Sachdev P. Validation and user experience of computerised neuropsychological assessments in the CogSCAN study. *College of Clinical Neuropsychologists (CCN) Conference*. 2022 Oct 3; Manly, NSW, Australia and virtual on-demand presentation.

Kochan NA, Croot K, Crawford JD, **Bentvelzen AC**, Allison KA, Rossie M, Brodaty H, Lam BCP, Henry JD, Lee T, Draper B, Close J, Ong MY, Sachdev, P. Computer-administered neuropsychological assessment batteries: Validity, reliability, and user experience in an Australian sample of community-living older adults in the CogSCAN Study. *Alzheimer's Association International Conference (AAIC)*. 2022 Aug 8; San Diego, USA and online.

Koncz R, Pistilli C, Bessell E, Kim J-S, Thompson D, McDonald A. (2022). The effectiveness of Project ECHO in building capacity in clinicians working with adults with intellectual disability and comorbid mental health issues. *Royal Australian and New Zealand College of Psychiatrists (RANZCP) Congress*. 15-19 May 2022; Sydney, Australia.

Koncz R. The Statewide Intellectual Disability Mental Health Outreach Service (SIDMHOS). Invited presentation at the *Australian Association of Developmental Disability Medicine Conference*. 29 Aug 2022; Sydney, Australia.

Mitchell J, Brodaty H, Chenoweth L, Long J, Braithwaite G. Care home attributes supporting relational, person-centred care for residents living with dementia. 35th *Global Conference of Alzheimer's Disease International*. 2022 June 9-11; London, UK.

Mitchell J, Brodaty H, Chenoweth L, Long J, Braithwaite G. Re-envisioning dementia care through quality of engagement. *Australian Association of Gerontology 55th National Conference*. 2022 Nov 12; Adelaide, SA, Australia.

Mitchell J, Brodaty H, Chenoweth L, Braithwaite J. Relationality and well-being – people living with a dementia. *International Pyschogeriatrics Association (IPA) Conference 'The importance of old age mental health, an international overview'*. 2022 Sep.

Numbers K, Lam BCP, Crawford JD, Kochan NA, Sachdev PS, Brodaty H. Dyadic patters of subjective cognitive reports as predictors of incident dementia. Invited Talk presented as part of a Featured Research Session (FRS) at the *Alzheimer's Association International Conference (AAIC)*. 2022 Aug; San Diego, CA, USA, and online.

Page ZA, Croot K, Powell A, Lam BCP, Brodaty H, Kochan NA (2022, June 21-22). Methods of bias reduction for the neuropsychological assessment of culturally, ethnically, or linguistically diverse older adults: A systematic review (Poster presentation). *ISTAART Satellite conference AAIC 22: Addressing Health Disparities*. 2022 June 21-22; Washington DC, USA and online.

Page ZA, Croot K, Kochan N, Brodaty H. Growing a voice for Culturally and Linguistically Diverse Older Adults: Community Consultation about the Design and Implementation of an Online Survey in the CogSCAN Study (Conference presentation). *20th National Conference of Emerging Researchers in Ageing*. 2022 Nov 10; online.

Reeve E, Ailabouni N, Chenoweth L, Sawan M, Nguyen TA, Kalisch Ellett L, Gilmartin-Thomas J, Tan E, Sluggett J, Quirke LS, Hilmer S. Top 10 unanswered questions about quality use of medicines in people living with dementia. *Australian Association of Gerontology 55th National Conference;* 2022 Nov 12; Adelaide, SA, Australia.

Reppermund S, Walker A, Cvejic R, Srasuebkul P, Wand A, Draper B, Trollor J. Self-harm and dementia - using big data to improve outcomes and inform strategies for self-harm and suicide prevention. *Australian Dementia Research Forum*. 2022; virtual conference. This talk won an award for best oral presentation in Public Health and Prevention.

Reppermund S, Walker A, Cvejic R, Srasuebkul P, Wand A, Draper B, Trollor J. Self-harm and dementia. Protocol of an inclusive research project to inform strategies for self-harm and suicide prevention. *Society for Mental Health Research Conference*. 2022; Hobart, Australia.

Sachdev P. Invited Speaker. Title TBC. *22nd WPA World Congress of Psychiatry*. 3-6 Aug 2022; Bangkok, Thailand.

Sachdev PS. The many ages of man: Diverse approaches to assess the biological and psychological ages of the body and its systems. *Joint JSPN/RANZCP symposium: Healthy Ageing*. 17 May 2022; Sydney, Australia.

Sachdev P. Chair for the *Australian Dementia Research Forum (ADRF)* 2022. June 2022; Sydney, Australia.

Sachdev P. Invited Speaker. The current status of tardive dyskinesia. *22nd World Congress of Psychiatry (WPA)*. 3-6 Aug 2022; Bangkok, Thailand.

Sachdev P. Invited Speaker. The therapeutic impasse in psychiatry – Neuropsychiatry to the rescue. *22nd World Congress of Psychiatry (WPA)*. 3-6 Aug 2022; Bangkok, Thailand.

Sachdev P. Invited Speaker. Diagnosing Vascular Cognitive Impairment. *14th World Stroke Congress*. 26-29 Oct 2022; Singapore.

Ulanova M, Duong HTK, Gloag L, Bongers A, Tilley R, Sachdev PS, Braidy N. Immunotargeted magnetic nanoparticles as MRI/MPI tracers for early diagnosis of Alzheimer's Disease. Poster presentation at the *Society for Neuroscience Annual Meeting*. 13 Nov 2022; San Diego, CA. USA.

Seminars, Lectures & Workshops

Brodaty H. Prevention, Prediction, Personalisation. Invited presenter at the *Rising to the Challenge Healthy Aging Forum.* 2022 Jan 11; virtual

Brodaty H. Early Diagnosis of Dementia… Why Bother? Invited panelist at the Tonic Media GP webinar sponsored by Dementia Australia. Online webinar; 3 May 2022.

Brodaty H. Advances in dementia research, diagnosis, treatment and care. Invited Speaker for *RANZCP Podcast*. May 2022.

Brodaty H. Forward with Dementia. Invited speaker in a webinar hosted by Queensland Faculty of Psychiatry of Old Age. 2022 June 7.

Brodaty H. What's New in Dementia 2022. Invited speaker in a webinar hosted by One Day University, USA. 2022 Aug 1.

Brodaty H. Introduction to Dementia. Invited speaker in a webinar hosted by the Australian College of Nutrition and Environmental Medicine. 2022 Aug 19.

Brodaty H. Advances in dementia research, diagnosis, treatment and care. Invited Speaker in the Psych Matters Podcast hosted by RANZCP; 2022 Nov 11.

Brodaty H. Engineering personalised tissue implants for regenerative medicine. Invited moderator at the Australian Friends of Tel Aviv University Webinar Q&A. 28 Mar 2022.

Brodaty H. What's New in Dementia and Prevention. Invited speaker at the Honours Club, Friends of the Hebrew University. 25 May 2022; Sydney.

Brodaty H. What's New in Dementia. Invited speaker at the University of Third Age. 1 Apr 2022; Woollahra.

Brodaty H, Low L-F, Phillipson L, Gresham MD. Psych Matters RANZCP: Forward with Dementia. 17 Feb 2022; online podcast.

Brodaty H, Page Z, Numbers K. Publish or perish: trials, tribulations, triumphs… and a few tips. UNSW HDR Seminar. 2022 Sep 21; online.

Gresham MD. Research on how the current system is meeting the needs of people with moderate to severe dementia and their carers in the community? Invited presentation at the *Australian Dementia Forum*. 30 May 2022; online.

Gresham MD, Yeates, W, Szcześniak D, Cunningham C. Talking dementia: diagnosis and post -diagnostic support. *The Dementia Podcast, the Dementia Centre HammondCare*. 17 Feb 2022; online podcast.

Koncz R. Neuroimaging for Psychiatrists, for the Masters of Medicine (Psychiatry) program, The University of Sydney. May 2022; Sydney, Australia.

Lo J. Management and Curation of Health Data (HDAT9400) lecture. 2022 Nov 15; UNSW, Sydney.

Numbers K, Lam BCP, Mahalingam S. Intro to Statistics for Honours Students. Co-developed and led 8-week stats workshop for CHeBA Honours students. Discipline of Psychiatry & Mental Health, UNSW. 2022 March-June.

Numbers K. Understanding the Brain: Where we've been and where we're going. Invited talk at the Ku-ring-gai City Council. 2022 Sep.

Numbers K. The Brain: Past, present, and future. Invited talk at the Malabar City Council. 2022 Aug.

Numbers K. Emotional and Social Development. Invited lecture for Beginnings, Growth and Development. Discipline of Psychiatry & Mental Health, UNSW. 2022 June.

Numbers K. Assessing Personality. Invited tutorial for Personality. Discipline of Psychiatry & Mental Health, UNSW. 2022 June.

Numbers K & Page Z. Human Aspects of Living with Neurodegeneration. Invited practical presentation for Ageing and Endings B. Discipline of Psychiatry & Mental Health, UNSW. 2022 Oct.

Page Z. AASHA Community Talk – Healthy Brain Ageing & CALD Community Engagement. 200 Oct, Blacktown, Sydney.

Reppermund S. Assessment of Activities of Daily Living to detect early cognitive impairment: Differences between performance-based versus informant-reported measures. *Occupational Therapy Australia National Working with Older People Interest Group*. 2022; virtual webinar.

Sachdev P, Lennon M. Under PRESSURE: Looking down at the details of the blood pressure and cognition relationship. *CHeBA Seminar Series*. 11 May 2022; online.

Samtani S. Social connections: How to keep the mind and body healthy with ageing. Invited speaker at the *Older Person's Mental Health Service*. 7 Dec 2022.

Samtani S. Social Cognition, Connections and Health. *CHeBA Seminar Series*. 15 June 2022; online.

Samtani S. Adolescent Psychosocial and Brain Development. Invited lecture at the Children's Hospital.17 May 2022; Westmead, Sydney.

Ulanova M. Future Science Talks. East Village Sydney, Darlinghurst.

Ulanova M. Presenter at the Students of Brain Research X Youth Neuroscience Australia – Traversing Hemispheres: Brain Research Interstate.

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