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Centre for Healthy Brain Ageing (CHeBA)
Annual Report 2019

research

big data

positive ageing

prevention

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Co-Directors' Report

In 2019, we continued our ambition to make CHeBA a world-leader in brain ageing research. As this report shows, CHeBA has continued to expand its research activities to enhance the evidence base in relation to prevention, early detection, treatment interventions of cognitive disorders and the health care of people already impacted by dementia.

Our goal continues to be to make a major impact on the societal burden due to dementia and related disorders, in Australia and internationally.

The year 2019 was particularly marked by the fact that for the first time, all CHeBA researchers were brought together on the University's Kensington campus, after having spent many years across multiple locations. This has resulted in renewed energy and enthusiasm, and the flowering of several new collaborations, as the keen and able CHeBA researchers were able to rub shoulders with each other on a daily basis. Their vigour and innovativeness have been inspiring indeed!

The year marked the seventh anniversary of CHeBA. We were encouraged by a number of new funding grants in 2019, including a $2 million Boosting Dementia Research Grant in collaboration with the Garvan Institute to fund a clinical trial to repurpose a drug commonly used to treat diabetes for dementia prevention. CHeBA's Dr Louise Mewton was awarded funding from the UNSW-USyd Visible Partnership in Mental Health, Addiction and Neuroscience Research Seed Funding Scheme to adapt and pilot an online prevention program for risky drinking in older adults. A team of international researchers and clinicians, including Professor Henry Brodaty, was awarded $850,705 to contribute to the development of Vietnam's first National Dementia Plan. Several other grants, announced in 2018, came into fruition in 2019. These included two collaborative grants as part of the European Union Joint program for Neurodegenerative Diseases for the projects SHARED and COGNISANCE, an NHMRC project grant to support the international post-stroke dementia consortium (STROKOG), the Yulgilbar – DARF Innovation Grant on nanotechnology for dementia and a Rebecca Cooper Foundation grant to study lipids in brain ageing and dementia.

This funding, along with continued significant funding from Montefiore, the Vincent Fairfax Family Foundation, the John Holden Family Foundation, the Yulgilbar Foundation, the Mostyn Family Foundation and our incredible community and corporate donors, enables CHeBA to magnify its record of ground-breaking and innovative research in the fields of Alzheimer's disease and other dementias as well as healthy ageing.

We continue to be extremely fortunate to have the enthusiastic support of Richard Grellman AM, Spokesman for The Dementia Momentum and Ambassador for our Wipeout Dementia and Drive Out Dementia campaigns. This year we were delighted when the University's Chancellor, David Gonski AC, awarded Richard the University's highest honour – a Doctor of the University honoris causa - in recognition of his eminent services in support of CHeBA's research, fundraising and community activities.

The ongoing positive effect of his steadfast support on the expansion of our Centre and interest in our corporate activities is irrefutable, with the Wipeout Dementia campaign seeing its first and highly successful inter-generational event as well as its highest fundraising event to date with the property industry event in November generating over $210,000 in contributions. We extend our enormous thanks to all of Richard's fellow captains in the Wipeout Dementia campaigns – Rob Gillespie, John Cunningham, Mark Gross, Peter Clemesha, Craig Rodgers, Phillip Vivian, Darren Beasley and Steve Watson.

We also extend our gratitude for the ongoing support of Phil Cave in Drive Out Dementia and to KPMG Sydney and ARIA Restaurant, both partners of The Dementia Momentum since its launch in 2015. Colliers International Residential once again showcased their unwavering dedication to CHeBA, raising over $70,000 for Wipeout Dementia at their annual residential developers' luncheon.

"Our goal continues to be to make a major impact on the societal burden due to dementia and related disorders, in Australia and internationally."

-Professor Henry Brodaty AO &
Professor Perminder Sachdev AM

In 2019, CHeBA published several noteworthy research papers, including a major paper in Neurology from the STROKOG consortium identifying global prevalence and common risk factors for cognitive impairment following a stroke, as well as one from the COSMIC consortium published in PLOS Medicine, which investigated associations between risk factors and late-life cognitive performance on a global scale, using data from nearly 50,000 older individuals across 15 countries.

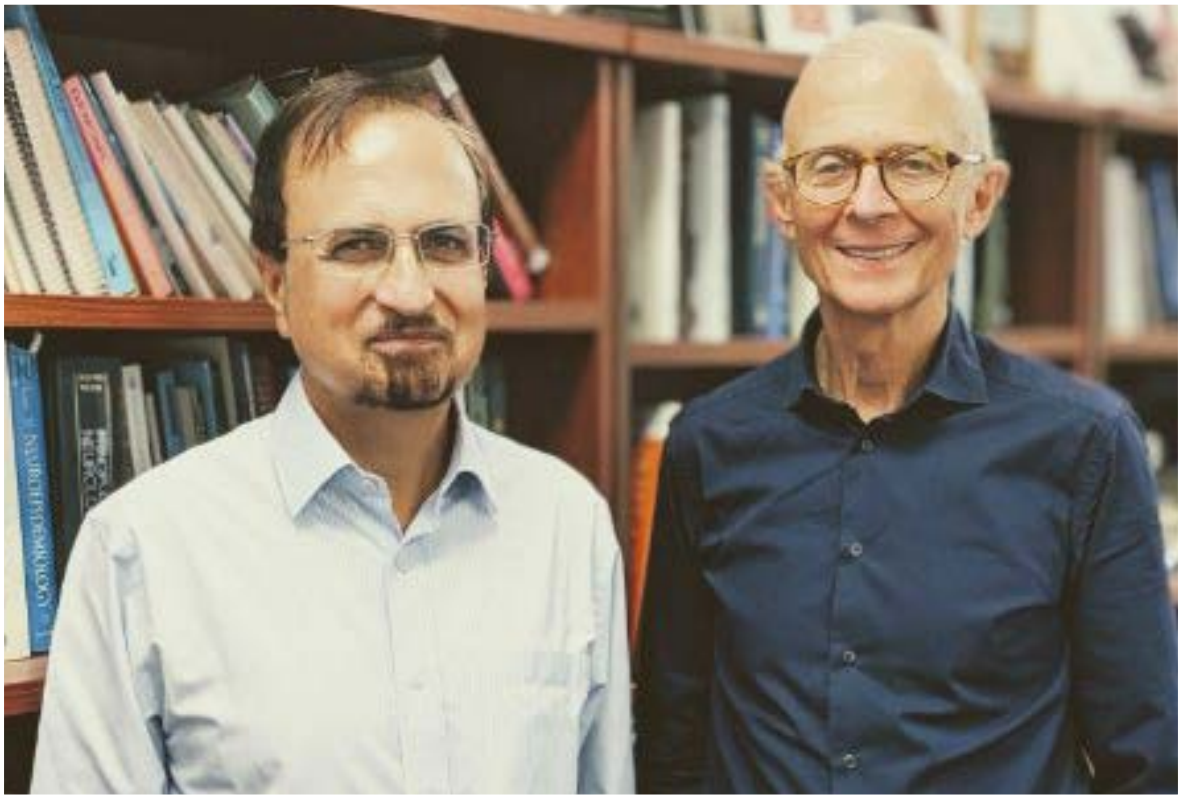
Other significant research outcomes included a collaboration with Garvan Institute which showed that statin use is protective against memory decline in some individuals at risk of dementia.

Ultimately, research is a team effort and our achievements throughout 2019 would not have been possible without a determined and capable group of colleagues across our Group Leaders, Study Co-ordinators, research assistants, PhD scholars and post-doctoral research associates, as well as our Centre Manager Angie Russell who manages to ensure CHeBA's operations run seamlessly.

Our thanks to Dr Sophia Dean who has continued to provide invaluable research and administrative support. We profusely thank Heidi Douglass and her incredible communications team for connecting CHeBA so well with the community and ensuring that CHeBA's work is accessible to everyone. As always, we gratefully acknowledge the instrumental contribution of our collaborators, supporters, fundraisers, volunteers and most of all our research participants. We look forward to continuing to deliver on CHeBA's vision and mission in 2020.

Scientia Professor Perminder Sachdev AM

Scientia Professor Henry Brodaty AO



About the Centre

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

Our 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

The functions of the Centre are to:

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

This will be achieved through:

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

Our Vision

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

Our Aims

Our aims are to conduct multidisciplinary research into ageing in health and disease and be involved in knowledge dissemination and translational research. In particular, CHeBA's focus is on the following:

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

SIGNIFICANT HIGHLIGHTS

"CHeBA is committed to pursuing ground-breaking research directions which can better explain dementia risk, identify protective factors and/or factors associated with dementia."

-Professor Perminder Sachdev AM

Research Key to Developing Global Dementia Prevention Strategies

Dementia is a worldwide problem that continues to grow. There are no effective treatments so identifying risk factors that can be avoided or modified may help to slow or prevent cognitive decline and the development of dementia.

This research, published in PLOS Medicine, investigated associations between risk factors and late-life cognitive performance on a global scale and used data from nearly 50,000 older individuals across 15 countries.

Lead author on the research, Dr Darren Lipnicki, said the study is unique in examining risk factors for cognitive decline across many diverse international sources, meaning the results can be generalised on a global scale.

"Improving the evidence base for modifiable risk factors is a research priority," said Dr Lipnicki, who is Study Co-ordinator of CHeBA's COSMIC (Cohort Studies of Memory in an International Consortium).

"Although no new risk factors were examined, the demonstration that certain risk factors are common across diverse populations is a significant new contribution," said Dr Lipnicki.

"Preventing or controlling diabetes and stroke, not smoking, and increased levels of education and physical activity are important across all populations," he said.

"This may help reduce the global burden of cognitive decline and dementia," said Dr Lipnicki.

Co-author on the research and Co-Director of CHeBA, Professor Perminder Sachdev, explained that the study was the first to comprehensively examine and compare the effects of risk factors on cognitive decline between white people and Asian people.

Professor Sachdev said the finding of differences between these groups suggest that modifiable risk factors such as smoking and diabetes differ in their impact in different ethno-regional groups.

"Diabetes appears to have a greater negative effect in Asian populations, which is of concern considering the prevalence of diabetes is rising in many countries," he said.

"The population-specific effects would help in developing dementia-prevention strategies in diverse settings around the world," said Professor Sachdev.

"Improving the evidence base for modifiable risk factors is a research priority."

-Dr Darren Lipnicki

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

$2 Million to Test Diabetes Treatment to Prevent Dementia

Professor Perminder Sachdev and Professor Henry Brodaty this year announced their involvement in a $2 million Federal funded clinical trial to test diabetes treatment for dementia.

The Boosting Dementia Research Grant has significant potential to help slow or stop cognitive decline and structural brain changes in people at risk of dementia.

The pioneering study, led by Garvan Institute of Medical Research's Professor Katherine Samaras, will assess whether metformin, a common type 2 diabetes treatment, can help prevent dementia from developing. Metformin is derived from French lilac and has been used safely to treat type 2 diabetes for 60 years.

Recently, metformin was shown to slow decline in cognition in a small clinical trial.

CHeBA's Co-Director Professor Perminder Sachdev said the study holds considerable potential to utilise this safe medication for dementia prevention.

"Australia's dementia statistics are sobering," said Professor Sachdev. "It is still the second most common underlying cause of death."

"Midlife obesity is associated with increased risk of cognitive deficits in later life, as is type 2 diabetes mellitus," said Professor Sachdev.

Studies have shown that diabetes and its precedents of insulin resistance and excess fatty tissue are strongly associated with Alzheimer's disease. This has enormous implications in Australia, where we have both a rapidly ageing population and in 2017 74% of people aged 65-84 were overweight or obese.

Fellow CHeBA Co-Director Professor Henry Brodaty said urgent actions were needed to address the epidemic of obesity in order to tackle the burden of dementia for the ageing Australian population.

"This study will conduct a large trial of metformin in participants at risk of dementia and assess their cognitive function over three years," said Professor Brodaty.

The study will also measure biomarkers of cognitive symptoms, conduct brain imaging to evaluate changes to the brain structure, connectivity and blood flow, and will assess health-related quality of life, functional independence and mobility and psychological health.

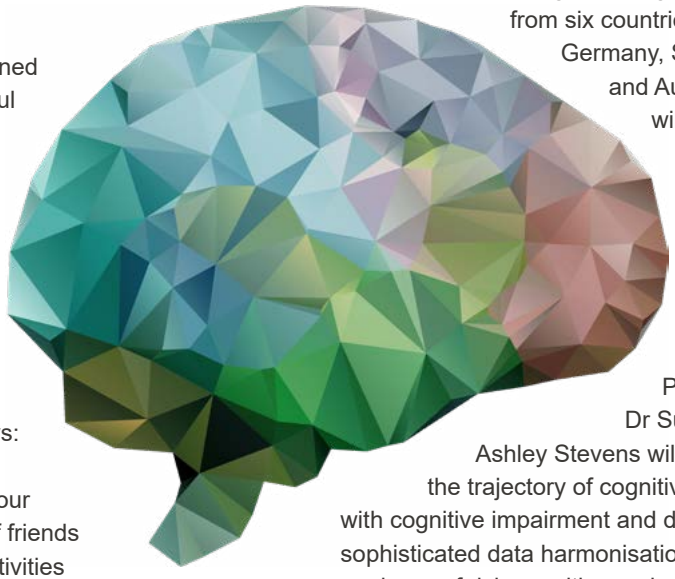
> "Midlife obesity is associated with increased risk of cognitive deficits in later life, as it type 2 diabetes."
>
> -Professor Perminder Sachdev AM

Chief Investigators of the funded project are Professor Katherine Samaras (Garvan Institute of Medical Research and St Vincent's Hospital); Professor Perminder Sachdev (CHeBA, UNSW Sydney); Professor Maria Fiatarone Singh (University of Sydney); Professor Henry Brodaty (CHeBA, UNSW Sydney); Professor Richard Day (UNSW Sydney); Professor Peter Macdonald (St Vincent's Hospital Sydney); Associate Professor Wei Wen (CHeBA, UNSW Sydney); Dr Nicole Kochan (CHeBA, UNSW Sydney); Dr Steve Makkar; and Professor Jose Luchsinger (Columbia University Medical Center).

JPND Grant to Analyse Interaction of Socialisation and Cognitive Decline

CHeBA Co-Director Professor Henry Brodaty AO was awarded an EU Joint Programme on Neurodegenerative Disease Research (JPND) grant of $724,254 funded by the NHMRC to analyse the interaction of socialisation and cognitive decline.

Poor social health has been shown to be a risk factor of dementia and good social health to be protective. However, the role of social health, particularly relating to the onset, disease course and prognosis of dementia, remains underexplored.



Social health is commonly defined as our ability to form meaningful relationships with other people and interact in healthy, positive ways. The way we connect to the people around us, adapt to different social situations, and experience a sense of belonging all contribute to social health[1]. Socialisation can be measured in many ways: the number of people we meet with each week, the quality of our relationships, the availability of friends to confide in, the number of activities involving other people that we engage in.

Social health affects our physical health and physical health influences our capacity to socialise. Think how much we feel like socialising when we have the flu or are in pain. There is also a bidirectional link between social health and cognitive health. Low levels of socialisation are associated with more dementia over time. Conversely, as people decline cognitively their ability to maintain socialisation and good social health declines. In other words, the bidirectional link acts across the entire path from cognitive health to severe dementia and manifests itself differently during various phases of disease.

Professor Brodaty's Social Health And Reserve in the Dementia patient journey (SHARED) project aims to unravel the interplay between social health and biological and psychological factors on the trajectory through dementia and to develop a framework for developing health and social care interventions.

"We will tease apart these two different trends by examining data from almost 150,000 persons across 40 global studies," says Professor Henry Brodaty

The JPND grant brings together researchers from six countries – Netherlands, Germany, Sweden, Poland, UK and Australia - each of whom will tackle separate work packages, coordinated by Dr Arfan Ikram, from Erasmus University Medical Center in Rotterdam. The Australian team of Professor Brodaty, Professor Sachdev, Dr Suraj Samtani and Ashley Stevens will focus on later periods in the trajectory of cognitive decline, namely those with cognitive impairment and dementia. They will employ sophisticated data harmonisation and complex statistical analyses of rich cognitive and social data sets. The Australian team will also interview people with dementia, their families and their health professionals to gain a deeper understanding of these links.

"Knowledge generated across various disciplines and work packages will be integrated into a system dynamics model on the role of social health during the entire patient journey," says Professor Brodaty.

"In turn, this will inform about modifiable pathways and targets for preventive interventions at both the population and individual level."

[1]https://yoli.com/what-is-social-health/

"Knowledge generated across various disciplines and work packages will be integrated into a system dynamics model on the role of social health during the entire patient journey."

-Professor Henry Brodaty AO

Richard Grellman Awarded Honorary Doctorate

Richard Grellman AM was awarded the University's highest honour in recognition of his eminent services to both the Australian community and to CHeBA.

At the UNSW Medicine graduation ceremony on Monday, 6 May, the University's Chancellor, David Gonski AC, awarded Richard Grellman a Doctor of the University, honoris causa, for his extraordinary support of the Centre's research activities, and his exemplary service to the broader community in promoting healthy ageing and destigmatising dementia.

"A powerful advocate for societal change, Richard has dedicated himself to campaigns that highlight the risk factors for dementia, particularly as Ambassador for the highly successful Wipeout Dementia," said Dean of Medicine, Professor Rodney Phillips.

Richard admits that watching his wife's deterioration has been a journey with no guiding compass, but with his characteristic determination he has, since 2014, channelled his remarkable energy toward seeking philanthropic support for research undertaken by CHeBA; which has assisted in the procurement of millions of dollars for the Centre.

"I have been blessed to have had the opportunity to support the work of UNSW in the field of dementia research. Through the wonderful work undertaken by CHeBA, its Co-Directors Scientia Professors Henry Brodaty and Perminder Sachdev and their highly committed colleagues, it has been and continues to be a privilege to play a small part. Given that my role as Spokesman for The Dementia Momentum has focused on corporate engagement and improving awareness of aspects of dementia and also fundraising for research, I needed a person within CHeBA to assist me and Heidi Douglass has been this person. A very significant part of what has been achieved is directly attributable to Heidi and her energetic and creative support.

I also acknowledge the many hundreds of people and organisations who have donated to this cause, some of whom are here today," said Mr Grellman.

In a heart-warming moment Mr Grellman dedicated his honorary doctorate to wife Suellen and acknowledged his children James, Sarah and Ben for their encouragement for his involvement with CHeBA as well as their active participation in events.

Mr Grellman spoke sincerely to the University graduates, acknowledging their milestone.

"This may be your own faith journey which, if you have a personal belief system, will only grow if you foster it. But I would broaden this area out to include anything that does not feed your bank account. Volunteering/community service/not-for-profits, environmental issues or supporting that elderly neighbour," said Mr Grellman.

"I encourage each of you to keep these thoughts in mind going forward. Whatever you call it, work/life balance is not just a quip; strive for it," he said.

"The ongoing involvement of Richard Grellman has been invaluable in championing our cause."

-Professor Henry Brodaty AO & Professor Perminder Sachdev AM

Adrian Cheng

"People between 90 and 99 are Australia's fastest-growing age group."

-Professor Henry Brodaty AO

People 95+ Have Greater Life Satisfaction Than Younger People

CHeBA researchers have explored the level of life satisfaction of near centenarians and centenarians to gain better understanding of ways to enhance the wellbeing of people with exceptional longevity.

This project is the largest study of its kind to examine the psychological health of 95+ year olds in Australia and was led by Medical Honours Student Adrian Cheng under the supervision of CHeBA Co-Director Professor Henry Brodaty, Study Co-ordinator of ICC-Dementia Dr Yvonne Leung and Research Assistant Fleur Harrison.

The research, which used data collected from 207 participants in CHeBA's Sydney Centenarian Study, compared the overall life satisfaction of near centenarians and centenarians with that of 1032 participants from a younger age group from CHeBA's Sydney Memory and Ageing Study (70-90 year olds).

The findings, published in the *Australian and New Zealand Journal of Psychiatry*, also investigated risk and protective factors for distress in centenarians and near centenarians.

Near centenarians and centenarians affirmed higher levels of distress than their younger counterparts from the Sydney Memory and Ageing Study. Among the older group increased psychotropic medication use and having contact with fewer relatives and friends were significantly associated with a higher level of recent psychological distress.

However, when participants were questioned about their overall satisfaction with their lives, it was the near centenarian and centenarian group that rated significantly higher than the younger-old.

"People aged between 90 and 99 are Australia's fastest-growing age group," said CHeBA Co-Director Professor Henry Brodaty and co-author on the research.

"This research indicates that a greater level of social connectedness through family and friends shows a higher level of life satisfaction in near centenarians and centenarians," said Professor Brodaty.

The research, for which Adrian Cheng received First Class Honours, contributes to the small body of research on the psychological health of the oldest-old.

"This research highlights the specific needs of the oldest-old and has implications for the prevention of psychological morbidity and interventions, such as development of services and improved care, to better understand the wellbeing of this special population," said Professor Brodaty.

Research Reveals No Link Between Statins and Memory Loss

Over six years, researchers evaluated the cognitive effects of statins in elderly consumers, revealing no negative impact and potential protective effects in those at risk of dementia.

Findings from more than 1,000 elderly individuals assessed over six years have revealed no links between statin medication and cognitive decline, such as memory loss, presenting new advice amidst some consumer concerns that statins may have a negative impact on cognitive health.

The collaborative study, led by researchers at the Garvan Institute of Medical Research and the Centre for Healthy Brain Ageing (CHeBA), UNSW Sydney, shows that statin use is even protective against memory decline in some individuals at risk of dementia.

The research is published in the *Journal of the American College of Cardiology*.

The authors of the current study assessed changes to the brain in 1,037 elderly individuals, measuring five areas of cognition using 13 different tests and MRI scans of the brain, over six years.

“Controlling for important and potentially contributory factors, such as age, sex and obesity, we found no difference in the rate by which memory and other aspects of cognition changed over time, between statin users and those who had never used the medication. There was also no difference in the change in brain volumes between the two groups,” says Professor Samaras of the Garvan Institute.

Further, the researchers found that in individuals with risk factors for dementia, including heart disease or diabetes, statin use slowed down cognitive decline, compared to those with the same risk factors who did not take statin medication.

The study used data from CHeBA’s Sydney Memory and Ageing Study; an observational study of older community-dwelling Australians that commenced in 2005 and that researches the effects of ageing on cognition over time.

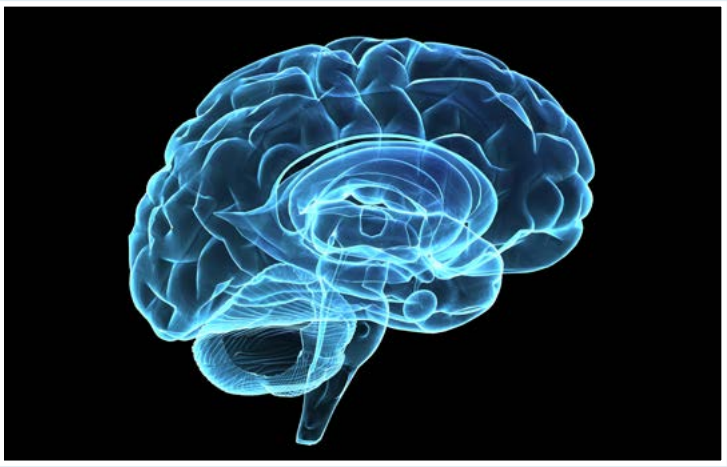
Senior author Professor Perminder Sachdev, Co-Director of CHeBA, says: “The Sydney Memory and Ageing Study is now in its 14th year and has permitted us to ask many important questions in relation to the brain health of the elderly.

“In this study our data reassuringly suggests that the use of statins to lower cholesterol levels is not likely to adversely affect memory function. Since it is an observational study, the findings should not be considered conclusive. However, the evidence is mounting that statins are safe in relation to brain health and this concern should not preclude their use in individuals who are likely to benefit from lower cholesterol levels.”

This research was supported by the Australian Government's National Health and Medical Research Council (Dementia Research Grant 510124).

“The Sydney Memory and Ageing Study is now in its 14th year and has permitted us to ask many important questions in relation to the brain ageing of the elderly.”

-Professor Perminder Sachdev AM



Research Highlights the Prevalence of and Common Risk Factors for Post-Stroke Cognitive Impairment

Latest research led by CHeBA has identified global prevalence and common risk factors for cognitive impairment following a stroke.

The research, published in *Neurology*, harmonised data from 13 international studies from Africa, Asia, Australia, Europe and the USA as part of the Stroke and Cognition Consortium (STROKOG). Led by CHeBA, STROKOG is an international collaboration which brings together post-stroke cohort studies. By performing joint analyses on combined datasets, the consortium aims to facilitate a better understanding of the determinants of cognitive decline and dementia after stroke, and to help improve the diagnosis and treatment of post-stroke cognitive disorders.

Jessica Lo, Study Co-ordinator of STROKOG, said this research aimed to address the variability in prevalence estimates and inconsistencies in potential risk factors for post-stroke cognitive impairment across diverse ethno-racial groups and geographical regions.

"This study is significant for practicing neurologists and clinicians because it presents a comprehensive profile of the cognitive performance of patients after stroke from around the world," said Ms Lo.

"Based on 3,146 patients admitted to hospital for stroke, we found that 44% were impaired in global cognition and 30 to 35% in each of five cognitive domains two to six months after stroke," said Ms Lo.

Diabetes and a history of past stroke were strongly associated with poorer cognitive function.

Co-Director of CHeBA and co-author on the research, Professor Perminder Sachdev, said that the research warranted attention in the development of prevention strategies.

"This research confirms that, globally, prevalence of impaired cognitive function is consistently high across diverse populations in stroke survivors, with diabetes being an important and independent risk factor for post-stroke cognitive impairment," said Professor Sachdev.

"This study is significant for practicing neurologists and clinicians because it presents a comprehensive profile of the cognitive performance of patients after stroke from around the world."

-Jessica Lo

This research was supported by the Vincent Fairfax Family Foundation (VFFF) and the National Health and Medical Research Council of Australia Program Grant. The funding sources were not involved with the study design, analysis or interpretation of data.

Established in 2012, STROKOG is one of four international consortia led by CHeBA to investigate risk and protective factors for dementia incidence and healthy brain ageing world-wide. Support for the consortia research is driven by CHeBA's major philanthropic initiative, The Dementia Momentum. Spokesman for The Dementia Momentum and Chairman of IPH Limited & FBR Limited, Richard Grellman AM says CHeBA is in an excellent position to make a world-wide difference to prevention, earlier diagnosis, and earlier and more effective interventions for dementia and related illnesses.

vfff Vincent Fairfax Family Foundation

RESEARCH HIGHLIGHTS

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

-Professor Henry Brodaty AO & Professor Perminder Sachdev AM

Digital Health Intervention to Maintain Your Brain

Research led by Professor Henry Brodaty has been highlighted in a special issue of the *Journal of Alzheimer's Disease*. The protocol paper showcases the significance of CHeBA's Maintain Your Brain trial in relation to dementia risk reduction and translation into practice. Protocol papers standardly are used to help improve the standard of medical research.

"As much as 30% of all late-life dementia could be associated with preventable lifestyle factors."

-Professor Henry Brodaty AO

Current estimates suggest that around the world there is a new case of dementia every 3 seconds. Unchanged, this will see the current number of 50 million people living with dementia triple by 2050.

Professor Henry Brodaty says that in the past 20 years there have been over 100 attempts at developing drug treatments for dementia but only four have been approved, all being symptomatic and not disease modifying. No new drug has been approved in almost 20 years.

"Given the scale of the issue and the challenging path to a cure, there is an increasing focus on prevention," says Professor Brodaty.

"As much as 30% of all late-life dementia could be associated with preventable lifestyle factors," he said.

Maintain Your Brain is a randomised controlled trial of an online multi-modal lifestyle intervention targeting these modifiable dementia risk factors with the primary aim being to reduce cognitive decline in people aged 55-77 years.

"The people in our trial are young enough to be able to prevent the accumulation of more pathology in their brain, and old enough that we can study the outcomes to benefit future generations," says Professor Brodaty.

The published paper details the protocol for this three-year trial which focuses on interventions built around four areas of physical activity, nutrition, cognitive training and mental health. Interventions are personalised so participants receive the most appropriate modules.

Lead author of the paper and Study Coordinator of Maintain Your Brain, Dr Megan Heffernan, says that the study finished recruitment in October 2018, with over 6,000 people volunteering to be involved.

"Our participants are currently completing their 12-month assessments.

"If successful, Maintain Your Brain will provide a model for not just effective intervention among older adults, but an intervention that is scalable for broad use internationally," says Dr Heffernan.

MAINTAIN YOUR BRAIN

International Study Examines Genetic & Vascular Risk Factors for Brain Infarcts

An international research team including brain scientists and genetic researchers from CHeBA has discovered two common genetic variants that link blood pressure with brain infarcts using the largest multi-ethnic genome-wide association study to date.

The findings, which utilised data from CHeBA studies was published in the eminent journal *Neurology*, highlight the importance of prioritising hypertension as a major modifiable risk factor.

Brain infarcts, clusters of dead brain cells resulting from insufficient blood supply, are associated with increased risk of stroke, cognitive decline and other negative health outcomes such as dementia. While

Improved Clinical Criteria for Diagnosing Vascular Cognitive Disorders

Researchers at CHeBA have investigated how certain criteria for identifying cases of vascular cognitive disorders compare, as well as how well they predict a change from mild impairment to dementia within five years.

Vascular cognitive disorders include vascular dementia and milder forms of cognitive impairment caused by problems with blood flow to the brain, often as a result of stroke, and the conceptualisation of vascular cognitive disorders has evolved significantly since the description of multi-infarct dementia in the 1970s. Previous criteria for diagnosing vascular cognitive disorders have focused only on dementia, and often did not provide clear guidelines for clinical decision making.

Lead author on the paper and Co-Director of the Centre for Healthy Brain Ageing (CHeBA), Professor Perminder Sachdev said that "other recent sets of criteria include Diagnostic and Statistical Manual of Mental Disorders and VICCCS; both of which have been widely used for clinical practice and research."

"These criteria have limitations," said Professor Sachdev.

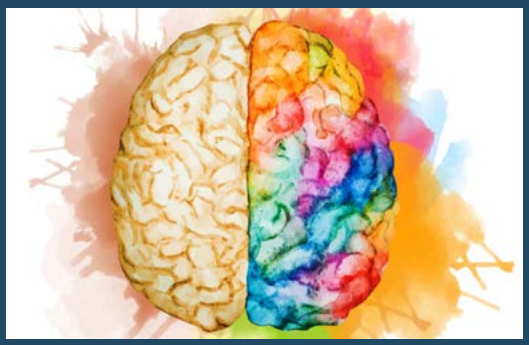
"Among other reasons, they emphasise dementia and exclude milder impairments, disregarding that early recognition of vascular cognitive impairment is important for prevention. Also, having memory impairment as a necessary criterion for diagnosis of dementia biases the diagnosis towards Alzheimer's disease," he said.

To overcome some of these limitations the Vascular Behavioural and Cognitive Disorders (VASCOG) criteria were developed.

"We investigated how VASCOG criteria compared with other criteria at identifying cases of vascular cognitive disorders, as well as how well they predict a change from mild impairment to dementia within five years, or mortality over 10 years," said co-author on the paper Dr Darren Lipnicki.

The findings, published in the *European Journal of Neurology*, showed that VASCOG criteria compare well in performance with other current criteria and predict mortality better than previous criteria.

"With detailed guidelines for accurately diagnosing vascular cognitive disorders, VASCOG criteria are appropriate for both clinical use and research application," said Professor Sachdev.



they are commonly found in up to 20% of healthy older adults, they are poorly understood.

This research was undertaken by the Cohorts for Heart and Aging Research in Genomic Epidemiology (CHARGE) consortium. This international collaboration investigated the contributions of genetic and vascular risk factors, such as blood pressure, to brain infarcts. Almost 21,000 older adults contributed to the research across eighteen studies from five ethnicities.

"CHeBA champions big data studies as crucial for rapidly and reliably identifying significant risk factors on a universal scale," said CHeBA's Co-Directors and co-authors, Professor Perminder Sachdev and Professor Henry Brodaty.

Co-author and Leader of CHeBA's Genetics & Epigenomics Group, Dr Karen Mather, said that "high blood pressure measures and their genetic risk scores were associated with brain infarcts."

"While further research is required to replicate the findings, this research emphasises the importance of reducing high blood pressure," said Dr Mather.

"This research emphasises the importance of reducing high blood pressure."

-Dr Karen Mather

The analysis study was supported by the National Institutes of Health USA and CHeBA's work by the NHMRC.

Review Highlights Need to Identify and Treat Pseudodementia

A systematic review by researchers from CHeBA and the Dementia Centre for Research Collaboration at UNSW Sydney has highlighted the significant burden of pseudodementia, which can have a similar effect on patients and their families as organic dementia.

The review, published in *Psychological Medicine*, identified 18 studies that followed patients from several weeks to 18 years.

Each year, a significant proportion of older people develop dementia i.e. problems with their memory and thinking that are severe enough to impair their ability to function in everyday life. Typically, this is due to Alzheimer's disease and other neurodegenerative diseases.

Lead author of the review, Dr Michael Connors, explained that other conditions, including depression and a number of psychiatric disorders, can also affect memory and thinking and, when severe, create a similar clinical picture.

"This phenomenon is known as "pseudodementia" – a psychiatric condition masquerading as organic dementia," said Dr Connors.

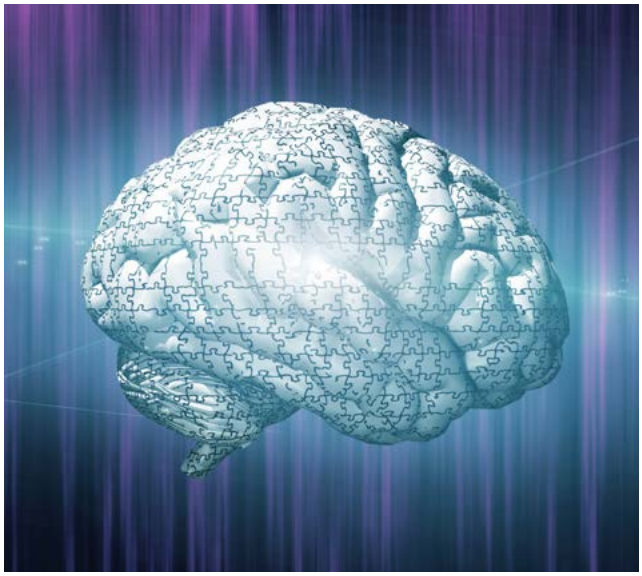
"It is not uncommonly encountered in clinical practice and is important to identify because it may be reversible with appropriate treatment," he said.

A significant question about pseudodementia is what happens to patients in the longer term. This has implications for how to manage patients, what advice to give to patients and their family, and how to conceptualise the disorder. Some research has suggested that people with pseudodementia eventually develop organic dementia and that there is little distinction between the two conditions.

"To address this, we conducted a systematic review in which we attempted to identify all studies that have been conducted on pseudodementia and which followed up patients over time," said Dr Connors.

Overall, 284 patients were studied, including 238 patients with depression, 18 with conversion disorder, 14 with psychosis, and 11 with bipolar disorder. Irrespective of diagnosis, 33% developed irreversible dementia at follow-up, 53% no longer met criteria for dementia, and 15% were lost to follow-up. Considerable variability was identified, with younger age at baseline, but not follow-up duration, associated with better outcomes. Electro-convulsive therapy (ECT) and pharmacological interventions were also reported to be beneficial, though findings were limited by the poor quality of the studies.

Co-author and Co-Director of CHeBA, Professor Henry Brodaty, said that overall, studies showed that patients with pseudodementia were at greater risk of later developing organic dementia.



"Importantly, however, not all patients did," said Professor Brodaty.

"Many patients remained stable or improved, albeit with many still impaired by their psychiatric disorder," he said.

In addition, studies also showed possible treatment benefits and differences with age, such that patients diagnosed with pseudodementia at a younger age had better outcomes.

"This may be a result of the difficulty discriminating pseudodementia from organic dementia in older patients, a group in which concurrent depression is also common," said Professor Brodaty.

Professor Brodaty said the findings highlight the significant burden of pseudodementia and the need to identify and treat the condition early.

"Given recent research tends to neglect the study of pseudodementia, the findings also reveal a clear need for further research with modern investigative tools, such as neuroimaging and genetic sequencing," said Dr Connors.

"Clinical trials to better understand underlying mechanisms and determine effective treatment strategies are also necessary," he said.

Lipidome Study Shows Link to Longer Lifespan

Researchers in the Brain Ageing Research Laboratory at CHeBA have discovered that low levels of blood lipids in people over 95 years of age could signify a unique lipid profile that may be associated with a longer lifespan.

The findings, published in *PLOS One*, examined how lipids in plasma are affected by age and sex in a group of healthy human individuals.

Lipidomics is an emerging field which involves the quantification of small molecules known as lipids. Lipids have important roles in cells, tissues and organ physiology due to their unique membrane organising properties – providing the cells with specialised sub-compartments. Lipids are also involved in energy storage, cellular signalling and hormonal regulation. Altered lipid metabolism has been associated with several age-related diseases including Alzheimer's disease.

Although lipidomics is becoming increasingly popular as a screening tool for understanding disease mechanisms, it is largely unknown how the lipidome naturally varies by age and sex.

The study used plasma from 100 subjects with an apolipoprotein E (APOE) E3/E3 genotype; aged between 56 to 100 years.

Lead author, CHeBA PhD student Matthew Wong, said that untargeted analysis was performed by liquid chromatography coupled-mass spectrometry and data processing using LipidSearch software.

Leader of the Brain Ageing Research Laboratory, Dr Nady Braidy, said the research found that plasma lipids change with age and are affected by sex in healthy individuals.

"Most lipids declined with age, more so in males than females," said Dr Braidy.

Females had higher levels of certain lipids such as low-density and high-density lipoprotein, total cholesterol, sphingomyelins and the phospholipid docosahexaenoic acid (DHA). DHA is important for maintaining brain health and cognition, and higher levels of DHA has been shown to reduce mortality due to late-life disease.

"It is likely that sex may have a major impact on lipids in age-related diseases such as Alzheimer's disease, affecting risk and severity," said Dr Braidy.

Surprisingly, the study found minimal association between lipid levels and body mass index (BMI) for most lipid classes.

"While BMI is typically associated with obesity and related conditions such as diabetes and cardiovascular disease, the exact relationship between BMI and lipid levels in 'healthy' individuals remains to be elucidated," said Dr Braidy.

Co-Director of CHeBA, Professor Perminder Sachdev, said the results suggested substantial age and sex-related changes in the plasma lipidome of healthy individuals during the second half of the human lifespan.

"Globally low levels of blood lipids in the 'oldest old' subjects over 95 years could signify a unique lipidome associated with extreme longevity," said Professor Sachdev.

Education Program Improves Care Quality in Aged Care

"Targeted education on family / staff relationships and collaboration can help raise awareness of its importance in delivering quality, family-friendly aged care services."

-Professor Lynn Chenoweth

An education program led by Professor Lynn Chenoweth at CHeBA has resulted in significant improvement in care service quality by promoting better understanding, relationships and collaboration between family members and direct care staff.

Findings from the pilot study, published in *Medical Research Archives*, suggest that relationship difficulties between direct care staff and families can occur when there is a mismatch between organisational structures and family expectations.

The 6-month education program, which was conducted across two leading Australian aged care homes was facilitated by 12 staff trainers across 61% of care staff and 45% of family members.

"Such education has the potential to promote better care delivery, particularly in improving communication between staff and families in making collaborative care decisions," said Professor Chenoweth.

Co-author and Co-Director of CHeBA, Professor Henry Brodaty, explains that moving into residential care is a stressful experience for many older people and their families which often gives rise to tensions between family and staff in relation to care service expectations.

"Residents lives are often complicated by long term chronic health conditions, including dementia," said Professor Brodaty.

This research was funded by Montefiore.

Funding for Evidence Base for Vietnam's Education Program

CHeBA Co-Director Professor Henry Brodaty, along with a team of international researchers and clinicians, have been awarded $850,705 to contribute to the development of Vietnam's first National Dementia Plan.

The project, which will be led by University of South Australia's Dr Tuan Anh Nguyen, aligns with the World Health Organization's initiative for every country to have a dementia plan to meet the burgeoning social and economic burden of the disease. The grant, "Strengthening responses to dementia: Building an evidence platform for the development of a Vietnam National Dementia Plan", will support creation of a coherent framework to direct resources for diagnosis and care for people with dementia, their carers and families.

By 2050, over 71% of people with dementia are predicted to be living in low and middle income countries. Professor Brodaty said advancing the mental health of older people in the Asia Pacific region was critical in the face of population growth and increased living standards resulting in longer lifespan. The average lifespan in Vietnam has increased by four years to 75 in the last two decades.

"We know dementia disproportionately impacts low and middle income countries so it is a privilege to be involved in helping equip Vietnam to meet these challenges," said Professor Brodaty.

The joint funding by the Australian National Health & Medical Research Council (NHMRC) and the National Foundation for Science and Technology Development of Vietnam (NAFOSTED) will support researchers from the University of South Australia, UNSW Sydney's CHeBA, South Australian Health and Medical Research Institute, University of Sydney, University of California, Davis, Hanoi Medical University and Vietnam National Geriatric Hospital to examine and strengthen Vietnam's response to the disease at the individual, organisational and national healthcare system levels.

"We know dementia disproportionately impacts low and middle income countries so it is a privilege to be involved in helping equip Vietnam to meet these challenges."

-Professor Henry Brodaty AO

OUR GROUPS

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

-Professor Henry Brodaty AO & Professor Perminder Sachdev AM

EPIDEMIOLOGY

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

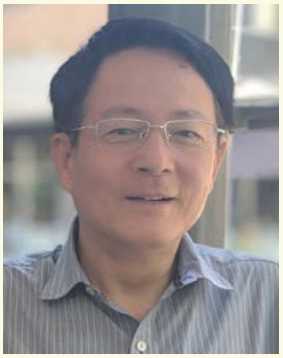
Group Leaders: Professor Perminder Sachdev, Professor Henry Brodaty
Staff: Emeritus Professor Gavin Andrews, Dr Nicole Kochan, Dr Karen Mather, Dr John Crawford, Dr Anbu Thalamuthu, Dr Darren Lipnicki, Dr Yvonne Leung, Dr Steve Makkar, Dr Vibeke Catts, Dr Ben Lam, Dr Louise Mewton, Dr Katya Numbers, Dr Catherine Browning, Jessica Lo

Group Leader:
Professor Perminder Sachdev

NEUROIMAGING

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

Group Leader: Associate Professor Wei Wen
Staff: Dr Jiyang Jiang, Yue Liu
Students: Abdullah Alqarni, Chao Dong, Jing Du, Heidi Foo



Group Leader:
Associate Professor Wei Wen

CHeBA Awarded Funding for Brain Scan Data

Research Manager of CHeBA, Dr Kristan Kang, and Leader of CHeBA's Neuroimaging Group Associate Professor Wei Wen have been awarded $14,000 to prepare over 4000 brain images collected over more than a decade for publishing.

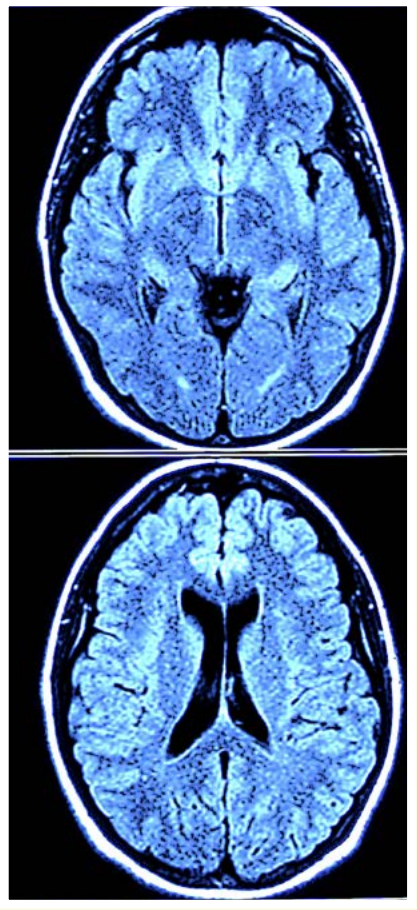
The funding, awarded by the UNSW eResearch Committee under the UNSW High Value Data Collections Publishing Scheme, will allow CHeBA's research data to be more available for use by the wider scientific community.

Dr Kang explains that brain scans are expensive to collect and of great value to health, ageing, biomedical and engineering projects.

"Brain scan data is especially powerful when paired with the extensive clinical data we have collected from our participants and already publish."

"The collections they form allow for the assessment of things like biomarkers and brain changes during ageing, including the progression into dementia and other neurological disorders with significant health economic impact," said Dr Kang.

Associate Professor Wei Wen, Leader of CHeBA's Neuroimaging Group, says that the brain scans can also be used in the assessment of new bioengineering methodologies. Consequently, these brain scans are high value "raw" data files which can be re-processed using new analytical techniques as they become available to answer new research questions.



GENETICS & EPIGENOMICS

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

Group Leader:
Dr Karen Mather

Group Leader: Dr Karen Mather
Staff: Dr Anbupalam Thalamuthu, Dr Sumangali Gobhidharan, Dr Naga Mutyala, Ms Sri Chandana Kanchibhotla
Students: Mary Revelas, Adith Mohan, Helen Wu, Jessica Lazarus, Siddharth Raj, Jun Woo Park

Seed Funding Awarded

Leader of CHeBA's Genetics & Epigenomics Group, Dr Karen Mather, has been awarded a UNSW-Chinese Academy Sciences Collaborative Research Seed Program Grant to have reciprocal visits with a Chinese investigator, Dr Cai, with the goal of establishing an innovative collaboration investigating ageing and longevity.

NEUROPSYCHOLOGY

The Neuropsychology Group is interested in investigating the cognitive changes associated with normal ageing, mild neurocognitive syndromes and dementia, and developing the most efficient and accurate methods for measuring cognitive decline. The group is developing normative data for several cognitive tests, and identifying appropriate cognitive instruments for individuals coming from culturally and linguistically diverse backgrounds. We also have projects evaluating the use of computerised neuropsychological assessment to improve accessibility and diagnostic accuracy of mild neurocognitive disorders and dementia. We have established strong collaborative links with researchers in CHeBA and with international consortia such as IGEMS and ENIGMA, investigating the associations between cognition with brain structure and function, genetics and environmental factors, medical comorbidities, inflammatory markers and falls in the older adult population.

Group Leaders:
Dr Nicole Kochan & Dr Teresa Lee

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

NEUROPSYCHIATRY

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

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

Group Leader:
Professor Perminder Sachdev

School of Psychiatry Academics Recognised by Royal Australian and New Zealand College of Psychiatry (RANZCP)

Two of UNSW's School of Psychiatry and CHeBA academics, Professor Brian Draper and Professor Julian Trollor, were acknowledged for significant contributions to psychiatry at the recent RANZCP Congress held on Monday, 13th May 2019.

Professor Brian Draper, a Chief Investigator on CHeBA's Sydney Memory and Ageing Study, was awarded the RANZCP's College Medal of Honour for his outstanding contribution to psychiatry as a clinician and researcher, and for his extensive and continuous service to the RANZCP.

Fellow awardee and neuropsychiatrist, Professor Julian Trollor, received the RANZCP Senior Research Award which recognises excellence in research in psychiatry and specifically acknowledges the Fellow or Fellows who have made the most significant contribution to psychiatric research in Australia and New Zealand over the preceding five years.

PROTEOMICS

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

Group Leader: Dr Anne Poljak
Staff: Dr Tharusha Jayasena, Scientia Professor Perminder Sachdev, Maboobeh Hosseini, Dr Fei Song
PhD Students: Gurjeet Virk (Scientia PhD candidate), Fatemeh Khorshidi (UPA PhD candidate), Rene Jezewski (Scientia PhD candidate), Toyin Ademola (Scientia PhD candidate)

Group Leader:
Dr Anne Poljak

BRAIN AGEING RESEARCH LABORATORY

Group Leader:
Dr Nady Braidy

This interdisciplinary group was formed to apply state-of-the-art molecular biology techniques to the advancement of research in the areas of normal ageing, Alzheimer's disease and other age-related neurodegenerative conditions. Our team consists of neuroscientists, protein and analytical chemists, psychiatrists, and bioinformaticians working in Australia and abroad.The Brain Ageing Research Laboratory was a sole recipient of a $1 million research grant from the The Yulgilbar Foundation to develop nanoparticles as nanodiagnostics and nanotherapeutics in Alzheimer's disease. The group utilises human and murine brain cell cultures and postmortem tissue for understanding the brain and the ageing process. The focus of the research group is: (1) to fully characterise metabolic biomarkers and develop simple tools to diagnose and detect severity and progression of neurodegenerative diseases and Alzheimer's disease in particular (Prognostics); and (2) to explore therapeutic strategies to attenuate cognitive decline and Alzheimer's disease pathology that can be translated into the clinic (Therapeutics). Our team fosters strong industry connections so that discoveries made in the laboratory can lead to new early diagnosis and treatments for people with dementia faster. This will bring a range of technological and intellectual approaches to the problem.

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

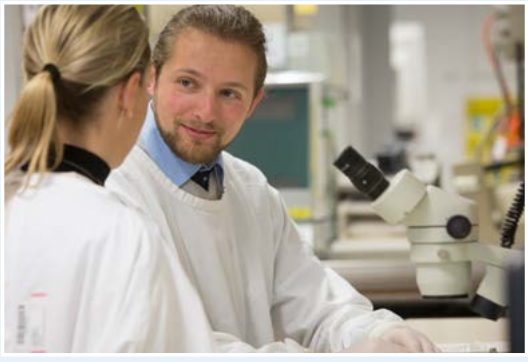
Group Leader: Dr Nady Braidy
Staff: Scientia Professor Perminder Sachdev, Ms Maria Villalva
PhD Students: Chul-Kyu Kim, Yue Liu, Marina Ulanova, Gurjeet Virk, Matthew Wong

Dr Nady Braidy Sponsored at Healthy Ageing Summit

Leader of CHeBA's Brain Ageing Research Laboratory, Dr Nady Braidy, was a sponsored presenter and panel member at the Healthy Ageing Summit and the APAC Summit in Singapore on 9-11 July 2019.

The conference, designed to bring together industry professionals across the globe to discuss pertinent issues impacting healthy ageing, included expert speakers on emerging food and nutrition solutions for today's older consumers, and the potential for reformulation and fortification. It also covered new innovations to improve the diets of the wider population in order to enjoy a healthier older age.

At the Healthy Ageing Summit, Dr Braidy – who was sponsored by FoodNavigator-Asia and NutraIngredients Asia – presented his research which shows how boosting NAD+ levels using the NAD+ precursor nicotinamide riboside can balance energy needs with supply.



CHeBA Promotion

Congratulations to Dr Nady Braidy who in July 2019 was promoted to Senior Research Fellow

Year 10 Students Attend Research Day at CHeBA

Aspiring Year 10 students from schools across New South Wales have been given a taste of research life in CHeBA's Brain Ageing Research Laboratory with Dr Matthew Wong, Dr Nady Braidy (Leader) and PhD students Yue Liu, Marina Ulanova and Gurjeet Kaur Virk.

Consortia Highlights

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

Study Coordinator: Professor Perminder Sachdev

In 2019, ICC-Dementia analysed the data from 18 brain ageing studies from 11 countries. We combined and analysed data from 4427 culturally and ethnically diverse centenarians and near-centenarians (aged 95 and above), which made our study the largest analysis of global dementia prevalence in the oldest-old to date. We estimated a global dementia prevalence of 53% in women and 45% in men. Risk of dementia was higher in women and it increases significantly with age, from 32% before reaching 100, 60% between 100 to 104 years old, to 73% beyond 105 years old. Education was a protective factor against dementia and cognitive impairment. We also found large differences in dementia prevalence across studies, which might be due to the variations in sampling strategies, sample size, and possibly also differences in culture, social resources and model of care in each country. These results were written up for publication.

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

COGNSANCE is a 10-university, 5-country consortium focused on improving the way in which a diagnosis of dementia is communicated to patients and families and support that is provided post-diagnosis.

Study Coordinator: Dr Meredith Gresham

Across the globe, while there are many national clinical guidelines on evidence-informed or best-practice diagnosis and post diagnostic support, the experience of diagnosis and post diagnostic support is less than optimal from the perspectives of people with dementia, their care partners and health care practitioners. Diagnosis is often not well communicated, with fewer than half of GPs routinely informing patients of their diagnosis. People with dementia and families often receive insufficient information about dementia and support after diagnosis is lacking.

COGNISANCE commenced in August 2019 to drive improvement through an innovative implementation project. Our research teams are bringing together codesign groups consisting of a range of stakeholders to develop two toolkits, one for people with dementia and one for health and social care professionals. Toolkits will provide information and resources to foster a collaborative practitioner-patient and family relationship to better communicate diagnosis and address living well with dementia. The project will be using innovative collaborations with an international marketing company to co-design social marketing campaigns to promote use of the toolkits.

Over 2019, research teams have been developed in each region and formative research consisting of surveys and focus groups has commenced. Chief investigator, Professor Henry Brodaty delivered a key note address “After the diagnosis… what next?” at the meeting of Alzheimer’s Europe in October.

Our partners are the Universities of Sydney and Wollongong in Australia, University College London and Newcastle University in the UK, Maastricht University in Netherlands, Wroclaw Medical University in Poland and two new Canadian Universities, New Brunswick and Waterloo joined with McGill University. External partners, the World Health Organisation, Dementia Alliance International (a global voice of people living with dementia) and Alzheimer’s Disease International complete this consortium awarded by the European Union - Joint Programme for Neurodegenerative Disease Research.

COSMIC (Cohort Studies of Memory in an International Consortium) is an international consortium to combine data from population-based longitudinal cohorts studies to identify common risk factors for dementia and cognitive decline. By the end of 2019 there were 40 international studies participating in COSMIC.

Study Coordinator: Dr Darren Lipnicki

In 2019, a number of new studies joined, including:

- Faroese Septuagenarian Cohort – Faroe Islands, Denmark
- Ibadan Study of Ageing – Nigeria
- Leiden 85+ Study – The Netherlands
- Shanghai Aging Study – China

The major highlights for COSMIC in 2019 include:

1. MOUs were signed with 4 new studies.
2. 13 new projects were started, led by either CHeBA researchers or international workgroups:
   a. The relationship between alcohol use trajectories and health, mortality and cognition in older adults;
   b. Sleep, mild cognitive impairment and dementia in elderly cohorts with ethno-racial diversity;
   c. Risk of MCI and dementia after cancer, and vice versa;
   d. Nutrition and cognitive health in the older population: emphasis on food group consumption and dietary patterns;
   e. The relationship between blood pressure and risk of cognitive decline;
   f. Development and validation of risk models for the prediction of dementia in low and middle-income countries;
   g. The associations among education, occupational complexity, and late-life cognition;
   h. Rates of progression to dementia;
   i. Does parity matter in women's risk of dementia?
   j. Parity and the risk of incident dementia;
   k. The association between cardiovascular risk factor variability with dementia risk and cognitive impairment;
   l. Maximizing dementia risk reduction: the impact of demographic/diversity factors on a modifiable dementia risk score;
   m. Physical activity and cognitive impairment.
3. Publications:
   a. Lipnicki et al. Determinants of cognitive performance and decline in 20 diverse ethno-regional groups: A COSMIC collaboration cohort study. *PLoS Med*. 2019;16:e1002853;
   b. Three other papers were submitted for publication or in press.
4. Conference presentations: oral presentations of COSMIC projects at:
   a. Alzheimer's Association International Conference (AAIC), Los Angeles;
   b. AAIC Satellite Symposium, Sydney;
   c. Congress of the International Federation of Psychiatric Epidemiology, Sao Paulo;
   d. Deutsche Gesellschaft für Psychiatrie und Psychotherapie, Psychosomatik und Nervenheilkunde, Berlin.
5. COSMIC collaborators meeting during AAIC, Los Angeles: 25 members and associates from 9 countries discussed current projects and future directions for the consortium.
6. COSMIC and 23 of our individual studies were listed on the Maelstrom Catalogue, with 15 studies having searchable meta-data: https://www.maelstrom-research.org/mica/network/cosmic

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

STROKOG

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

Study Coordinator: Jessica Lo

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

In 2019, the following new studies joined STROKOG:

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

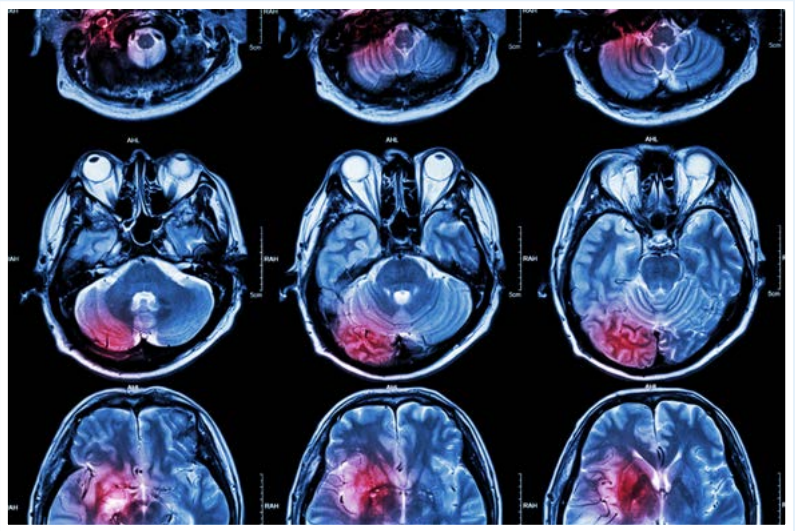
In 2019, the prestigious *Neurology* journal published the first STROKOG research paper written by CHeBA researchers. The paper focuses on the profile of and risk factors for post-stroke cognitive impairment in diverse ethno-regional groups. We found that diabetes, a history of past stroke, and to a lesser degree, hypertension, smoking and atrial fibrillation are related to poorer cognitive function at 1-6 months after stroke.

Three external researchers from the UK and from Finland collaborated with CHeBA and worked on three separate STROKOG projects in 2019. Dr Eugene Tang from Newcastle University, UK led a project on validating dementia risk score models. Dr Tang found that dementia risk prediction models developed for the general population do not perform well in individuals with stroke. His paper is due to be published in 2020. Dr Clare Flach from King's College London, UK has been examining stroke recovery associated with cognitive impairment. Dr Hanna Jokinen from the University of Helsinki in Finland is investigating domain-specific cognitive impairment and depression as determinants of post-stroke functional disability. The latter two projects are ongoing.

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

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

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



SHARED

SHARED (Social Health And Reserve in the Dementia patient journey) is a project designed to uncover the links between social and brain factors connected to cognitive decline. It was jointly funded by the National Health and Medical Research Council ($750,000) and European Union's Joint Program for Neurodegenerative Disorders (€2.5 million). It is the first international effort to harmonise work on social variables and examine their link to the onset and course of cognitive decline.

Study Coordinator: Dr Suraj Samtani

The SHARED project commenced on May 15-16 2019. This project brought together teams of geriatricians, physicians, psychiatrists, psychologists, epidemiologists, and other researchers from 7 universities: Erasmus Universitair Medisch Centrm (Netherlands), Radboud MC Nijmegen (Netherlands), Karolinska Institutet (Sweden), UNSW Sydney (Australia), University College London (United Kingdom), University of Bremen (Germany), Wroclaw Medical University (Poland). The teams are divided into subgroups called Work Packages, each with a specific focus.

The Radboud MC team comprise Work Package 2 (trajectories) and are focusing on identifying trajectories of social and cognitive health across the lifespan. The Swedish and UK teams comprise Work Package 3 (pre-clinical phase) and are examining the risk/protective social factors associated with cognitive decline in healthy adults. The German and Polish teams comprise Work Package 5 (model building) and are developing theoretical models linking social factors with brain health and cognition. The CHeBA team comprise Work Package 4 (clinical phase) and are focusing primarily on individuals who have cognitive impairments and tracking their progress over time through the stages of dementia. Their focus is on causation and examining what factors mediate the relationship between social and cognitive health.

CHeBA's Co-Directors Professor Henry Brodaty and Professor Perminder Sachdev and COSMIC Study Co-ordinator Dr Darren Lipnicki comprise the original Australian arm of the research team. The COSMIC studies represent a consortium of 40 longitudinal ageing studies from around the globe. A Postdoctoral Research Fellow and Clinical Psychologist (Dr Suraj Samtani) was hired in August 2019 as the SHARED Study Co-ordinator at CHeBA.

The SHARED project commenced monthly telephone/zoom meetings in November 2019 with a focus on agreeing upon the scope of the project and the conceptualisation of Social Health and deciding on appropriate measurements. Dr Samtani led the development of a meta-data inventory of the COSMIC studies: a task involving cataloguing all the questions in these studies in order to select datasets with a high-quality data on cognitive and social health. The team developed hypotheses about causal links between social and cognitive health, which will be analysed in 2020.

PhD Completions

Dr Matthew Wong

Thesis: Natural Variation in the Human Plasma Lipidome Signature using Mass Spectrometry: Relevance to Healthy Ageing

Lipids have crucial physiological functions, and while traditional lipids (LDL/HDL-cholesterol, total triglycerides) are commonly used to survey health and disease, the contribution of individual lipid species is less clear. Mass spectrometry-based lipidomics is an analytical tool that enables identification and detection of these individual lipids. My research used lipidomics to survey lipid profiles of plasma from subjects enrolled in CHeBA's longitudinal ageing studies and found a global reduction in lipids among the oldest age group. Further, I identified a class of lipids associated with the apolipoprotein (APOE) e2 allele, that could explain neuroprotection against Alzheimer's disease. Finally, I assessed heritability of lipids (genetics vs environment) in Older Australian Twins, finding that heritable lipids were associated with gene transcripts of genes with immune function and cell signalling. Our data suggest many factors regulating variation in plasma lipids in healthy ageing.

Dr Matthew Wong was supervised by Dr Nady Braidy, Professor Perminder Sachdev and Dr Anne Poljak.

Dr Helen Wu

Thesis: The Role of Reripheral Blood MicroRNA as a Biomarker of Alzheimer's Disease

My research aimed to identify novel microRNA (miRNA) biomarkers for the early detection of Alzheimer's disease. MiRNAs are epigenetic markers and their dysregulation have been implicated in a number of diseases. Using blood samples from a number of cohort studies including the Sydney Memory and Ageing Study, the Older Australian Twins Study and the Australian Imaging, Biomarker and Lifestyle Study of Ageing, I examined differential blood miRNA expression in individuals with Alzheimer's disease, mild cognitive impairment (MCI) and normal cognition. A number of dysregulated miRNAs were identified and these candidate miRNA biomarkers for Alzheimer's disease were further investigated for their biological pathways and relevance to Alzheimer's disease pathology.

Dr Helen Wu was supervised by Dr Karen Mather, Professor Perminder Sachdev, Professor Henry Brodaty and Dr Anbupalam Thalamuthu.

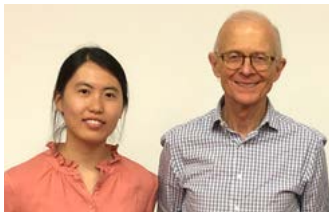
Funding: NHMRC post-graduate scholarship and Henroth Investments.

Honours

Zara Page

Zara Page

Neuroscience student, Zara Page, has achieved first class Honours using data from CHeBA's Sydney Memory and Ageing Study and CogSCAN project to explore culture-fairness of computerised neuropsychological testing for culturally and linguistically diverse older Australians. *Supervisors: Dr Nicole Kochan, Leader Neuropsychology Group and CogSCAN.*



Tally Zhou & Professor Henry Brodaty

Tally Zhou

Tally Zhou achieved Honours investigating the effects of head injury on cognitive decline and dementia by analysing longitudinal data from CHeBA's Sydney Memory and Ageing Study. *Supervisors: CHeBA Co-Director Professor Henry Brodaty and Dr Karen Croot.*

Sylvia Seah

Sylvia Seah's Honours investigated whether the quality of services in a convenience sample of seven Australian aged care homes, which claimed to be person-centred, aligned with person-centred indicators (VIPS). Data were obtained via semi-structured interviews with a volunteer sample of 12 aged care residents, 15 of their family members and 18 staff members in various roles. Data were analysed deductively with a-priori reference to the VIPS. *Supervisors: Professor Lynn Chenoweth and CHeBA Co-Director Professor Henry Brodaty.*

ILP Students

ILP students develop fundamental research skills and learn about current issues in brain ageing research. An understanding of brain ageing research will help students in their future careers as health practitioners.

Grace Wong

Grace Wong's ILP investigated the effects of medication, specifically their anticholinergic burden, on cognitive decline and dementia by analysing longitudinal data from CHeBA's Sydney Memory and Ageing Study.
Supervisors: CHeBA Co-Director Professor Henry Brodaty and MAS Study Coordinator Dr Katya Numbers.

Tally Zhou, MAS Study Co-ordinator Dr Katya Numbers and Grace Wong

Alice Yan

Alice Yan's ILP examined the utility of dual task walking, namely walking while simultaneously performing a cognitive task like counting, as a potential screening tool for cognitive impairment and dementia, by analysing data from CHeBA's Sydney Memory and Ageing Study.
Supervisors: Dr Nicole Kochan, Co-Leader of CHeBA's Neuropsychology Group and MAS Study Coordinator Dr Katya Numbers.

Ashwini Kumar

Ashwini Kumar's ILP investigated the extent to which cognitive reserve built up throughout life via education, complex mental activities, reading vocabulary etc, can explain late-life cognitive abilities in our exceptional oldest-old individuals from CHeBA's Sydney Centenarian Study.
Supervisors: Dr Nicole Kochan, Co-Leader of CHeBA's Neuropsychology Group and Dr Yvonne Leung, Post-Doc Research Fellow.

Dansen Ken-Gin Cho

Dansen Ken-Gin Cho ILP assessed the longitudinal changes in memory performance and their association with brain volumetric changes in older Australian twins.
Supervisors: Dr Vibeke Catts, Study Coordinator of CHeBA's Older Australian Twins Study, Dr Teresa Lee, Co-Leader of CHeBA's Neuropsychology Group, and CHeBA Co-Director Professor Perminder Sachdev.

Ching Ho

Ching Ho's ILP investigated the older person's recognition, experiences and management of self-identified sensory changes. Data were obtained through one-on-one semi-structured interviews with a convenience sample of thirteen consenting community-dwelling adults 65 years and older. Data were analysed deductively through the lens of goal-directed behaviour theory.
Supervisors: Professor Lynn Chenoweth and CHeBA Co-Director Professor Henry Brodaty.

Cognitive Reserve as a protective factor for late-life cognition in centenarians and near-centenarians

Ashwini Kumar, a fourth-year medical student joined CHeBA for 2019 and worked with Dr Nicole Kochan and Dr Yvonne Leung to explore whether cognitive reserve is protective for cognition in centenarians.

Cognitive reserve refers to a process whereby an individual's background and lifestyle choices such as education and occupation can influence the likelihood of maintaining good cognitive function in later life.

The cognitive reserve hypothesis may explain instances where we see well-preserved cognitive function in individuals who show significant changes in the brain associated with disease such as Alzheimer's disease. Evidence from several studies supports the idea that cognitive reserve built throughout a person's lifetime can reduce dementia risk. However, it is not known whether cognitive reserve remains protective in the oldest old. Therefore, this study aimed to examine the relationship between cognitive reserve and cognitive performance

as well as rates of dementia in Sydney Centenarian Study participants. Education, occupational attainment, engagement in mental activities through life and reading vocabulary were used as proxy measures of cognitive reserve.

As expected, the study found that almost all the cognitive reserve measures were associated with higher cognitive scores. However, years of education was an exception. This is interesting as education in other studies was protective of cognition.

The study also found that mental activities and reading vocabulary combined together had a stronger association with cognitive performance than the combination of occupation and education. This suggests that cognitive reserve predictors that can be built throughout life like mental activities and literacy had the strongest protective effects on late-life cognition.

LONGITUDINAL STUDIES

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

-Professor Perminder Sachdev AM

SYDNEY CENTENARIAN STUDY

The Sydney Centenarian Study was launched in 2007 and to date has included over 445 Sydney residents aged 95 and above. The project examines the cognition, physical health, psychological health, functional independence, nutrition, brain structure and genetics of Australia's oldest.

Centenarians and near-centenarians are seen as exemplars of successful ageing, and the study is identifying factors that are important to longevity and maintenance of physical and cognitive health. Participants are interviewed at baseline and every subsequent six months. Some of our participants up are to their sixth follow-up assessment. Each assessment covers: medical history, medications, cognitive performance, subjective memory complaints, psychological distress, falls, physical activity, mental activity, social integration, and diet. Participants also complete a brief physical exam. 64% of participants have provided a blood sample for genetics and proteomics analysis; 10% of participants have undergone structural brain imaging (MRI). An informant (i.e. someone that knows the participant well) is interviewed after each assessment to corroborate the information provided by the participant as well as comment on their degree of functional independence.

HIGHLIGHTS FROM 2019:

- We welcomed new participants from the Inner West of Sydney. Our biggest recruitment effort to date is planned to roll out in January 2020 inviting eligible individuals aged 85 and over to join the study from three local government areas in the eastern suburbs of Sydney.
- Five participants were featured on ABC Catalyst with CHeBA Co-Director Professor Perminder Sachdev interviewed as part of the program which focused on the secrets of ageing healthily.
- Research paper published in *Genes* showed genetic risk for cardiovascular health not necessarily linked to exceptional longevity. Revelas, M et al. (2019). Exceptional longevity and polygenic risk for cardiovascular health. *Genes*, 10(3), E227.
- Poster presentation by Dr Jiyang Jiang at the Organisation of Human Brain Mapping (OHBM) annual meeting. Jiang, J., Sachdev, P. S., Liu, T., Theobald, A., Brodaty, H., & Wen, W. Stronger functional connectivity in the oldest old. (2019).

Tale of the Century

This article was published in Montefiore LIFE

Every year, the likelihood of living to 100 and beyond increases. The possibility of achieving this exceptional age is on the one hand exciting – after all, throughout history, humankind has been intrigued by the fountain of youth concept. However, longevity can come with significant challenges.

Peter Singleton of Woollahra with SCS Study Coordinator Dr Catherine Browning

The Sydney Centenarian Study aims to determine which factors contribute to successful ageing. Study Coordinator Dr Catherine Browning says we know that genes play a significant role in longevity, but lifestyle and environmental factors can influence the way they behave.

"The Study is interested in shedding light on these lifestyle factors so we can take charge of the way our bodies and brains age," she explains.

To date, over 400 participants have been involved in this study, including many Montefiore residents such as Mr Peter Singleton.

"When I'm asked to do something that I think may help then I'm always happy to be involved," says the 96-year-old, who has enjoyed taking part in the study. Peter has lived at Woollahra for three years and remains active through long walks, and regular exercise sessions at Randwick.

Each participant in CHeBA's Sydney Centenarian Study is invited to take part in an interview in their home, to answer questions about their history, health, diet, memory and lifestyle. A brief physical examination includes measurements of height, weight and blood pressure.

"It doesn't matter if participants have memory, hearing, visual, or mobility difficulties – we can accommodate individual needs, says Dr Browning. "By seeing participants with a wide range of abilities, we get a more accurate picture of what it means to be a Sydney Centenarian."

And to all the people considering joining the study? Peter Singleton says: "Just do it!"

OLDER AUSTRALIAN TWINS STUDY

Commenced in 2007 as a collaboration between CHeBA, the National Ageing Research Institute (NARI) and the Queensland Institute of Medical Research (QIMR), the Older Australian Twins Study (OATS) has assessed a total of 727 participants on up to four occasions - totalling over 1600 assessments in the past decade. Today OATS is managed entirely at CHeBA, UNSW Sydney.

The main objective of OATS is to identify genetic and environmental factors that contribute to healthy ageing, especially healthy brain ageing. Studying twins provide a unique opportunity to do so, as identical twins have the same genetic code, whereas non-identical twins share 50% of their genetic code (in a similar fashion to other siblings). Using special analysis techniques, this genetic difference between identical and non-identical twin pairs allows us to determine the relative contribution of genes and environment on specific outcomes. The assessment that twins undergo as part of OATS involves many questionnaires on their life experiences, current lifestyle and diet, physical and mental health, brain scans, blood sample analysis and providing DNA for genetics analysis.

Over its lifetime, OATS has contributed to 51 scientific publications, with 5 published in 2019. A minimum of 17 students have utilised OATS data for their research projects. In 2019 this included three medical doctor trainees, who performed small research projects as part of their medical degree. We were also proud to see three students graduate with PhD degrees in 2019. Currently, 10 Higher Degree students continue to analyse OATS data in their studies.

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

HIGHLIGHTS FROM 2019:

- Three PhD students who utilised OATS data for their studies graduated. This takes the tally of PhD studies utilising OATS data to 8. OATS would like to congratulate Dr Matthew Wong (supervised by Nady Braidy, Perminder Sachdev, Anne Poljak) for his PhD titled Comprehensive Identification of Natural Variation in the Human Plasma Lipidome Signature Using Mass Spectrometry: Relevance to Promoting Healthy Ageing; Dr Helen Wu (supervised by Karen Mather, Perminder Sachdev, Henry Brodaty, Anbupalam Thalamuthu) for her PhD titled The Role of Peripheral Blood microRNA as a Biomarker of Alzheimer's Disease; and Dr Liliana Ciobanu (supervised by Bernhard Baune and Catherine Toben) for her PhD titled Investigating the Transcriptome Signature of Depression: Employing Co-expression Network, Candidate Pathways and Machine Learning Approaches.

- OATS contributed to two major publications in 2019, which outlined some of the genetic determinants of brain morphology. The papers were published by the ENIGMA Network, which is an international effort by world-leading researchers in neurology, psychiatry, imaging and genomics to understand brain structure and function, based on MRI and genetic data from many populations around the globe. The network includes studies from Europe, North America and Australia, but also from South America, Africa and Asia, continents often under-represented in many research studies. The adage that the brain is a static, non-changing organ is no longer considered true. In fact, the brain and its components change across the lifetime, and particularly so in young and older age. As OATS has longitudinal data from many of our participants, we are uniquely positioned to contribute to the understanding of trajectories of normal change and change associated with disease and functional impairment. This knowledge is essential to understand disease mechanisms and identifying ways to prevent or intervene during decline.

- OATS also participated in the IGEMS (Interplay of Genes and Environment across Multiple Studies) consortium, which is an expanding collaboration between 18 twin studies, including OATS, and represents over 76,000 twin participants. In 2019 a lot of effort went into collating data across these studies and ensuring different measures of health and cognition used in different studies are comparable and able to be analysed together. This groundwork has set the foundation for many important analyses to proceed going forward.

- In 2019, the OATS team continued to work towards an online project, aiming to give the study access to more participants, particularly those living in non-metropolitan areas. This involved a collaboration with the School of Computer, Data and Mathematical Sciences, Western Sydney University, who provided the expertise to build the platform where questionnaires are delivered and cognitive testing is performed in a secure online environment. Of the 727 participants assessed as part of OATS until today, nearly 500 may be available for further assessment. The OATS team started contacting participants again this year to engage them in this next phase of assessment. For some participants, this will be their fifth wave of participation in OATS. The OATS team is extremely grateful for the time and effort our participants selflessly provide to the study.

Cycling Without Age with Dr Vibeke Catts

CHeBA's Older Australian Twins Study Co-ordinator, Dr Vibeke Catts, has joined over 13,000 Cycling Without Age volunteers worldwide in piloting purpose-built trishaws, which provide seniors the opportunity to get into the outdoors and (again) experience wind in their hair.

A generous private donation to Montefiore Randwick provided the funds to purchase a trishaw. Throughout 2018, Mr Adrian Boss from BIKEast worked alongside Montefiore's Leisure & Lifestyle and Volunteers departments to train volunteer pilots and get the program up and running. Now there is a queue of residents wanting to join Dr Catts, and other volunteers from BIKEast, on rides around Centennial Park on Monday mornings.

Worldwide, more than 60,000 elderly people have been on rides and the Cycling Without Age trishaws cover more than 2.2 million kilometres each year – that's 53 times around the globe.

This volunteering endeavour doesn't just provide the opportunity for seniors to be outdoors, but is also significant in providing enriching social engagement. A healthy social life is now being acknowledged as an important factor in reducing risk of dementia.

> "The relevance of social connectedness in relation to healthy brains cannot be underestimated."
>
> -Dr Vibeke Catts

"The relevance of social connectedness in relation to healthy brains cannot be underestimated," said Dr Catts, who was born in Denmark and whilst growing up, rode a bicycle as her main mode of transport. Her own pleasure in riding and being in green spaces is a key motivation for her to volunteer with Cycling Without Age, and it is already very evident that residents of Montefiore enjoy the social outings and the experiences, such as sights and sounds, from the front seat of the trishaw.

SYDNEY MEMORY & AGEING STUDY

The Sydney Memory and Ageing Study (MAS) was initiated in 2005 to complement the worldwide effort to study predementia syndromes such as MCI. The primary objectives of MAS are to determine the clinical characteristics and prevalence of MCI in non-demented older Australians, and to determine the rate of change in cognitive function over time for those with and without a baseline diagnosis of mild cognitive impairment (MCI).

Additionally, the study aims to determine the features of MCI that best predict decline to a diagnosis of dementia. To do this, we examine features of MCI and predictors of cognitive decline from sociodemographic, clinical, neuropsychological, neuroimaging, biochemical, genetics, and proteomics perspectives. This multivariable approach not only increases our understanding of the prevalence of MCI and incident dementia in a community-based sample, but also sheds light on how best to use MCI diagnostic criteria in a clinical setting. Taken together, MAS' comprehensive methodology and well-validated outcome variables provide valuable data for future intervention strategies targeting individuals at greater risk of developing dementia.

The MAS baseline cohort consisted of 1037 older adults (aged 70-90) recruited from Sydney's Eastern suburbs who did not have a current diagnosis of dementia. Participants underwent comprehensive biennial assessments (called "Waves") comprised of neuropsychological tests, medical assessments, interviews, and questionnaires about sociodemographic, health status, lifestyle, and related data. A knowledgeable informant (close friend or family member) was also interviewed. MAS generally conducts more extensive in-person assessments every 2 years, with a briefer phone interview completed in the intervening years.

Presently, MAS is three-quarters of the way through Wave 7 data collection – 15 years out from baseline – and still has an active cohort of approximately 300 participants and their informants. The MAS study will wrap up in December of 2020 with the completion of Wave 7. To date, MAS data has contributed to 168 publications in in respected international scientific journals, with 13 of those being published in 2019 alone. There are currently 25 higher degree students and postdoctoral fellows who are using MAS data for as part of their research.

Subjective Cognitive Complaints and Dementia

Study Co-Ordinator of CHeBA's Sydney Memory and Ageing Study, Dr Katya Numbers, was invited to present on participants' subjective experience of cognitive decline at the 4th Annual Australia Dementia Forum 2019 Conference (ADF) in Hobart in June.

Dr Numbers showcased cross-sectional data from the inaugural year of the Memory and Ageing Study (baseline) as well as longitudinal data from year 6 of the study.

"At baseline, we found that participants' subjective cognitive complaints were not related to their actual performance on neuropsychological tests or their current clinical diagnosis," explained Dr Numbers.

"However, we were able to predict who would convert from normal cognition or mild cognitive impairment to dementia six years later based on participants' baseline subjective cognitive complaints," she said.

Dr Numbers argued that some of the ambiguity about whether these complaints are really a marker of preclinical dementia is due to the cross-sectional nature of many studies. However, when examined longitudinally, a reliable association between subjective cognitive complaints and cognitive decline is often observed. And, the further out from baseline, the more predictive they become.

"Having the chance to speak to consumers, their families and their carers about the research process from their point of view was really eye opening."

-Dr Katya Numbers

HIGHLIGHTS FROM 2019:

• Data from MAS made headlines this year as the most comprehensive analysis of cognition in older statin users to date was published. Findings from over 1,000 MAS participants, followed-up over six years, found no links between cholesterol-lowering statin medication and cognitive decline, presenting new advice amidst consumer concerns that statins may have a negative impact on cognitive health. Up to half the individuals prescribed statin therapy do not fill their prescription largely due to this concern, which carries a significant impact on public health. In fact, the authors found that statin use might even be protective against cognitive decline. This study provides reassurance older adults to feel more confident about their statin prescription (Samaras et al., American Journal of Cardiology).

• Perivascular spaces surround small blood vessels as they penetrate brain tissue and are a common MRI finding in older adults. Using data from MAS participants with MRI data, a CHeBA researcher has developed a new rating scale to understand the relationship between perivascular spaces and dementia. The new rating scale is easy to use, quick, has good psychometric properties and performs better than existing. Accurate identification and quantification of perivascular spaces will help with understanding the relationship between small vessel disease and dementia, as well as assist with diagnosis and prognosis of dementia (Paradise et al., Journal of Neurological Sciences).

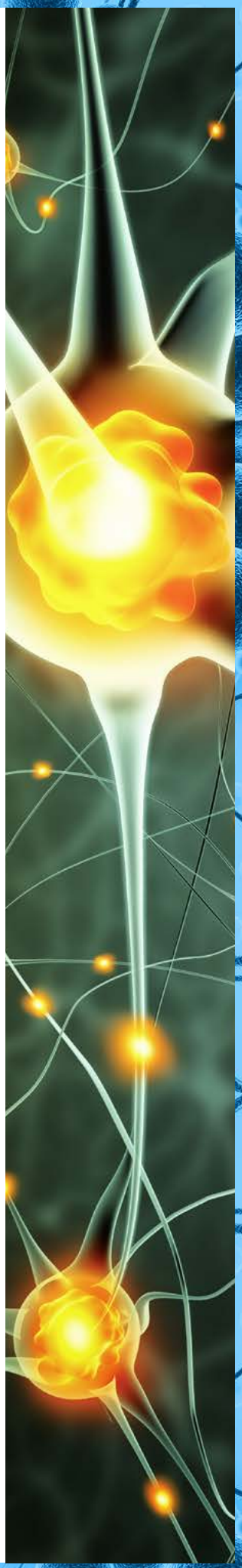
• MAS contributes important data to several large, ongoing, consortia projects. One such consortia project, comprised of over 48,000 individuals from around the world, found education, smoking, physical activity, diabetes, and stroke all have strong associations with late life cognitive decline. Importantly, these are all modifiable lifestyle factors that can be targeted for early prevention strategies. Different effects between Asian and white cohorts were found for smoking and diabetes, suggesting that any global strategy may need to consider ethno-regional differences (Lipnicki, et al., PLOS Medicine).

• Early-life stress (ELS) has previously been identified as a risk factor for cognitive decline, mainly in clinical groups. A recent study using MAS data found no relationship between global cognitive function and overall experiences of ELS. However, those who have had experienced physical neglect were found to have poorer global cognition compared to those who had not. This suggests that the relationship between ELS and cognition in older age may be dependent on the nature of the trauma experienced (Grainger, et al., International Psychogeriatrics).

• Telephone-based cognitive screens, such as the Modified Telephone Interview for Cognitive Status (TICS-M), have great potential for increasing older adults' access to cognitive screening. This seminal study found that cognitive data gathered from telephone interviews correlated well with established face-face cognitive screens and neuropsychological tests. Cut-off scores produced from this data also reliably distinguished between those with and without a dementia diagnosis. This study will help improve the accessibility and cost-effectiveness of cognitive testing for older adults (Bentvelzen et al., Journal of the American Geriatrics Society).

• Dementia is a known risk factor for falls and injury-related hospitalisations, but it is not clear whether individuals with mild cognitive impairment (MCI) have elevated falls risk. This study compared injury-related hospitalisation rates for older adults with normal cognition, MCI, and dementia in Australians. People with MCI had higher injury rates than people with normal cognition and lower injury rates than people with dementia. For individuals with MCI and dementia, the most common fall-associated injuries were non-fracture head injuries. These findings suggest falls-risk screening and prevention initiatives may be useful for older people with MCI (Harvey et al., Archives of Gerontology and Geriatrics).

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



OUR COMMUNITY

"Such solid and ongoing support from our community allows us to extend our research objectives to create lasting social change around dementia."

-Professor Henry Brodaty AO & Professor Perminder Sachdev AM

The Dementia Momentum

Spokesman's Report

We are all aware that with a rapidly expanding ageing population, dementia is set to bring an enormous challenge to health, aged care and social policies.

Dementia is estimated to cost Australia more than $15 billion in 2019 and is predicted to increase to more than $18.7 billion by 2025 and close to $40 billion by the middle of the century. Globally, we are looking at an estimated cost of around $820 billion.

In both economic and social terms, the future of dementia has the potential to be devastating to all Australians.

When I first became Spokesman of The Dementia Momentum initiative in 2015, there were reportedly 342,000 Australians with dementia. In just a few years, this statistic has increased by 100,000 to over 440,000 people with dementia.

Dementia is now the single greatest cause of disability in older Australians and its impact continues to worsen.

Despite this, dementia research receives only about 13 per cent of the amount of money for cancer research, an imbalance that must be righted.

The scale of this problem is compounded by the fact that the pursuit of effective drug treatments has hit a brick wall. Even if the search for early intervention to prevent dementia or slow its development becomes a reality through some dramatic breakthroughs, it will not help the thousands of people like my wife Suellen who already have dementia. Our society appears condemned to live with dementia for several future generations.

With one in 10 Australians over the age of 65 now with a diagnosis of dementia and with the average delay between the onset of symptoms and a diagnosis of the disease being approximately 2 years, clearly, we need research across the full spectrum of the disease beyond drug treatments, to include prevention strategies in early and mid-life to reduce modifiable risk factors associated with dementia, more timely diagnosis, better post-diagnostic support and effective end of life care for patients and their families.

The importance of lifestyle intervention trials must not be underestimated. Evidence indicates that Alzheimer's disease develops over a 20-30 year period, which provides us a significant window of opportunity to expand research around risk and protective factors during early and mid-life. The undeniable truth is that this research needs to be conducted at a larger scale to establish more robust findings.

We also need to address the prejudice still associated with dementia and recognise that our cognitive abilities do not necessarily define us. With dementia set to impact more and more of the population we must establish a collective means to support the dignity of those affected and stamp out discriminatory behaviour, intended or otherwise.

My wife Suellen did not choose to have dementia but we have an opportunity to choose how we, as a nation, respond to people in our lives and our community who are diagnosed with dementia.

It is my great hope that the research under The Dementia Momentum initiative – which is combining and harmonising data from around the world to determine which modifiable risk factors are specific to particular demographics and which are worldwide – will generate enough output to inform and create significant policy change in this country.

To ensure robust research findings, we need more funding sources, particularly additional support from corporate and philanthropic sectors, which can be difficult to attract due to persistent stigma about the disease. My hope is that donors recognise the value of funding research into prevention and end of life care, in addition to drug therapies, if we are to change the future of dementia and benefit all Australians.

> "Dementia is now the single greatest cause of disability in older Australians, and its impact continues to worsen."
>
> -Richard Grellman AM

Richard Grellman AM is Chairman of IPH Limited, FBR Limited and Spokesman for The Dementia Momentum.

the dementia momentum

We have had an enormously successful year with The Dementia Momentum; notably delivering the first ever inter-generational Wipeout Dementia event at Queenscliff which raised close to $100,000, as well as a tremendously successful property industry event in November which raised the highest amount to date with over $210,000 in donations.

I am grateful to my fellow captains and surfers – both new and unwavering – who have shown such extraordinary commitment to the success of this event. I am also extremely grateful to my dear friend Phil Cave for his significant support hosting the Drive Out Dementia events, our corporate partners at KPMG Sydney and ARIA Sydney and to Peter Chittenden of Colliers International Residential for humbling ongoing annual support at their developers' luncheon.

On their behalf, and on behalf of my wife Suellen, I urge all Australians to ponder the reality of dementia in this country and support research endeavours that have direct relevance to your health and that of the entire community around you, including your children and your grandchildren.

Richard Grellman AM
Chairman, IPH Limited & FBR Limited

Phil Cave AM, Richard Grellman AM & Luke O'Neill

Drive Out Dementia

The Drive Out Dementia event held in August 2019, sponsored by Anchorage Capital, raised close to $30,000 for The Dementia Momentum initiative.

CHeBA extends enormous thanks to Spokesman Richard Grellman AM, Phil Cave AM and Luke O'Neill for generously pooling their skills and resources in a bid to address the growing number of dementia diagnoses. The Drive Out Dementia events were an elite one-day opportunity for motoring enthusiasts to test their luxury vehicles on a purpose-built 5km private road in the name of dementia research. The events were held over three years and successfully raised awareness and significant funding support for CHeBA's research.

Inter-Generational Wipeout Dementia

CHeBA led its first-ever inter-generational **Wipeout Dementia** aged between 10 and 70 years of age at Queenscliff beach in May raising over $90,000.

The event was sponsored by Morgans Financial, Kennards Hire, SkiJapan, Cunninghams and Colliers International Residential.

Morgans was represented by Mark Gross and his 10-year-old son Ben, Colliers by Managing Director Peter Chittenden and his 14-year-old son Lachlan, SkiJapan by CEO Peter Murphy and 15-year-old son George. Cunninghams was represented by Managing Director John Cunningham and nephew Sam Wright as well as James Haywood and 13-year-old son Alby.

Ambassador for Wipeout Dementia and Spokesman for The Dementia Momentum, Richard Grellman, said this was the ninth Wipeout Dementia, which saw Ambassador and 1978 World Surfing Champion Wayne “Rabbit” Bartholomew introduce 15-year-old son and surfer for Billabong, Keo, to the cause.

A 1980 retro Mark Richards ‘Gnarly Award’ for highest fundraiser was taken by Tony Holt and 16-year-old daughter Stella Holt, who raised over $14,000 in the event and incorporated outreach support from St Vincent’s School which Stella attends.

> “Our vision is for the younger generation to have long and fulfilling lives characterised by physical, mental and cognitive wellbeing.”
>
> -Professor Henry Brodaty AO & Professor Perminder Sachdev AM

Special thanks go to Simon Liddy and 26-year-old daughter Eloise Liddy who were the other second highest fundraisers of this round of Wipeout Dementia; raising over $11,000 in this event and over $30,000 across a number of events.

A competition Mick Fanning DHD was awarded to Mark Gross (of sponsor Morgans and first-time captain of Mark’s Mavericks) and his Ben Gross for their fundraising success and School outreach. Over a number of events Mark has raised close to $50,000 for the cause.

Other top fundraisers in this round were Richard and son Ben Grellman who raised close to $10,000, Rob Gillespie and Chris Clarke who raised over $5,000, Richard and 14-year-old daughter Eliza Gerahty who raised $4,500.

With the longest ride of the day and a skilful board headstand saw regular participant Heath Sims take home 'Wave of the Day' and fan favourite Tony Camphin took home Best Wipeout.

The tag team surf contest saw father-son, father-daughter duos competing in four 20-minute heats to start the event. Geoff and 16-year-old son Lachlan Nesbitt, Phillip and 13-year-old Hugh Waddington, Stephen Lennard (substitute for John Cunningham) and Sam Wright, and Richard and Ben Grellman made it to the semi-finals, along with finals surfers - Wayne "Rabbit" and Keo Bartholomew, Peter and George Murphy, Chris Clarke and Rob Gillespie and Ian Freestone and Heath Sims. It was Ambassador "Rabbit" and son Keo that took home the ultimate glory and led Grellman's Evergreens to their first win since May 2015.

Both CHeBA Co-Directors, Professor Henry Brodaty and Professor Perminder Sachdev, attended the event and expressed their gratitude to Richard Grellman and all regular and new surfers for their incredible and generous support.

"Such community spirit, which has brought together 32 surfers across the age spectrum, is inspiring for us to continue our vision toward reduced dementia incidence in Australia and internationally," said CHeBA Co-Directors.

HWL Ebsworth Lawyers Support Wipeout Dementia

HWL Ebsworth has continued its outstanding record of support of CHeBA's Wipeout Dementia campaign by nominating CHeBA at their monthly employee charity event held on Friday, 5th April.

To date, HWL Ebsworth has previously committed and provided significant pro bono trademarking support to the Centre.

Senior Partner Simon Liddy's personal fundraising achievement is close to $25,000 over the 2016 and 2017 Queenscliff events, which has positioned him as second highest fundraiser in both events.

Mr Liddy said he was proud to support CHeBA's research.

"The level of support for this cause has been inspiring," said Mr Liddy, who surfed the first ever inter-generational Wipeout Dementia with daughter Eloise in May.

"I was delighted to have my daughter surfing alongside me in Wipeout Dementia and help promote the relationship between physical activity throughout life and brain health in late life," he said.

"My fellow partners and I are committed to corporate social responsibility. Supporting dementia research, particularly risk reduction and prevention, is an area we are proud to be involved in," said Mr Liddy.

Property Industry Wipeout Dementia

45 heavy hitters from across Australia's property industry led the most successful Wipeout Dementia to date in November 2019, raising over $210,000 for CHeBA's research.

> "The expansion of Wipeout Dementia across the property industry to embrace social change and support research has been astonishing."
>
> -Richard Grellman AM

The event was sponsored by Morgans Financial, Aoyuan International, Colliers International Residential, m3property and Winten Property Group, and saw all surfers take to the water at the same time for the contest's first ever Battle Royale.

The event, held on 22 November at Sydney's iconic Bondi Beach, was the tenth run by CHeBA and continued the initiative's track record of success according to Spokesman for The Dementia Momentum and Ambassador, Richard Grellman AM, Chairman of IPH Limited and FBR Limited, and former Chairman of The Association of Surfing Professionals (International) Limited.

"This year we saw our first interstate surfers from m3property's Melbourne and Sydney offices," said Mr Grellman.

"The expansion of Wipeout Dementia across the property industry to embrace social change and support research has been astonishing.

Over ten events Wipeout Dementia has generated more than $1.6 million for The Dementia Momentum, with industry representatives in the 2019 event joining from CBRE, Shape Australia, Avenor, Bates Smart, Charter Hall, Steve Watson & Partners, Aoyuan International, FDC, Ray White Commercial, Stamford Capital, Sense Projects, Haigs Builder Brokers and many more.

In a major upset, the 2019 winning team was led by first time captain Darren Beasley, second highest fundraiser and Deputy General Manager of sponsor Aoyuan International, who took his team to glory in the contest as well as highest overall fundraising team in the event.

The title was taken from reigning champions Cliff's Carvers, captained by Craig Rodgers of Charter Hall who instead boasted the most points in the first ever Wipeout Dementia Battle Royale, which saw 45 surfers take to the water at once to compete for waves. Fellow Wipeout Dementia Ambassador and 1978 World Surfing Champion Wayne 'Rabbit' Bartholomew AM said that he was "exceptionally proud of all the surfers in the property industry that have generated such a swell of support for Wipeout Dementia."

Anthony Scotts of AWM Commercial Furniture, who spoke at the event alongside brother-in-law Mike DuChateau, said he was also proud to be part of an industry getting behind a cause so important to him.

Mr DuChateau, whose wife has young onset Alzheimer's disease, labelled the disease a 'thief' and said that attending the event and seeing the extraordinary support behind research had given him a renewed sense of hope for the future.

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 Josh Millard of Parkview. In an incredible display of dedication Mr Millard personally raised over $22,000 for the cause.

A Mick Fanning competition DHD surfboard signed by Ambassadors Richard Grellman and Wayne 'Rabbit' Bartholomew went to Darren Beasley, Pip de Rohan, Director of Project One and Brett Newman, CEO of Parramatta Council who were the other top fundraisers in this round (raising $14,229, $11,502 and $11,465 respectively), with Mike Gordon of Buildcorp and Anthony Scotts of AWM Commercial Furniture each close to the $10,000 mark. David Kemp of Buildcorp, Peter Clemesha of Avenor, Will Rothwell of Winten, Steve Watson of Steve Watson & Partners, Craig Rodgers of Charter Hall, Philip Vivian of Bates Smart, Phillip Wicks of Shape Australia and Peter Kleijn of Winten Property Group were all acknowledged for raising above their targets of $5,000.

During the post Surf Off Awards Ceremony it was a $5,000 donation at the event from Corporate Interior Projects took the campaign over the $200,000 goal.

A score of 8 won Winten Director Will Rothwell 'Wave of the Day', while Craig Shelsher from Custance Associates took home the almighty 'Wipeout Award' with the contest's major drop in. Final awards went to architect Nikki Mote, who returned after being the first ever female to surf Wipeout Dementia in 2016, Mike Gordon for his awareness outreach and acquiring most number of donations, Craig Rodgers for his second highest wave score of the day, awareness outreach and greatest personal donation and to Anthony Scotts who took out the 'Campaign Champion' award for driving significant support over a number of years.

Most Valuable Player awards as voted by the Captains, went to Pip de Rohan in Watto's Wavehunters, Lucy Ford of Capital Bluestone in Daza's Drop Ins, Peter Kleijn of sponsor Winten in Phil's GOATS, Joel Ducey of sponsor m3property in Clemo's Diehards and Anthony Scotts of Cliff's Carvers.

CHeBA Co-Director, Professor Henry Brodaty attended the Surf Off. He expressed his appreciation to all participants, Ambassadors Richard Grellman and Wayne 'Rabbit' Bartholomew, and said that funds raised through the property industry Wipeout Dementia events have supported research and infrastructure costs for CHeBA's international consortia harnessing "big data" to identify risk and protective factors for dementia.

"Wipeout Dementia fundraising has been the launch pad for a significant number of priority research projects across CHeBA's international consortia spanning more than 30 countries," said Professor Brodaty.

A number of projects received a funding boost as a result of the November event including the relationship between education, certain genes and cognitive impairment; social health and reserve in dementia; nutrition and cognitive health in the older population and global prevalence and common risk factors for post-stroke cognitive impairment.

Wipeout Dementia is held in honour of Richard's wife Suellen, who has advanced young onset Alzheimer's disease and has been in high care since December 2015 - and whose 69th birthday coincided with the 10th Wipeout Dementia event.

In-kind event awards were donated by: Hurley, Dripping Wet, Prevention Australia, Samsonite, Destination Towels, Australian Healthy Food Guide, Three Blue Ducks and Bistecca.

Photography by Sprout Daily

Aoyuan International Hosts Launch Event

Aoyuan International generously hosted the launch event of the 2019 Property Industry Wipeout Dementia event at their offices on 31 October. Team captains Peter Clemesha, Craig Rodgers, Philip Vivian and Steve Watson and their surfers in the 2019 event attended the event, with General Manager and fellow team captain Darren Beasley Master of Ceremonies. Guest speakers were Richard Grellman AM, Peter Clemesha and Professor Henry Brodaty AO.

ARIA Restaurant Sydney Continues Strong Support

ARIA Restaurant Sydney hosted its fifth annual senior executives' corporate luncheon to support The Dementia Momentum initiative on 20 March.

PJ Lane, CHeBA Ambassador and son of entertainment icon Don Lane was MC for the event.

Spokesman for The Dementia Momentum Richard Grellman AM and CHeBA Co-Director Professor Henry Brodaty also delivered talks.

"With Alzheimer's disease and other dementias heading to epidemic proportions our future will be impacted greatly by the work being done at CHeBA through The Dementia Momentum," said PJ Lane.

PJ Lane thanked Richard Grellman for sharing his journey and also Bruce and Barbara Solomon and the staff at ARIA for their generous hosting of this event.

CHeBA Ambassador PJ Lane

The Dementia Momentum Spokesman Richard Grellman AM

$10,000 FOR CHeBA TO HONOUR DAD'S FIGHT WITH DEMENTIA

Martin Gregory is an adventure seeker. He has travelled 400 miles inside the Arctic Circle with a team of 8 dogs, scaled Cotapaxi Volcano in Ecuador, travelled 4,200 kilometres across Africa, travelled 1,200 kilometres through the Himalayas and trekked across the Owen Stanley Mountain range on the infamous Kokoda Track.

Clearly, Martin enjoys a challenge but 2 years ago he was faced with one of his greatest challenges to date when father, Richard Paul Gregory, was diagnosed with dementia.

"My Dad was an exceptionally encouraging father," says Martin, who runs his own Consulting business that uses adventure as a background for developing High Performing Teams and improving the way leaders make decisions. Martin facilitates that type of experiential learning session on the General Manager Executive Education program through his partnership with AGSM at UNSW Sydney.

CHeBA Research Fellow
Dr Adith Mohan with Martin Gregory

In 2018 Paul Gregory passed away which prompted a desire in Martin to honour his father's battle with dementia by raising funds for key research at CHeBA. His highly challenging fundraising endeavour was to compete in three rounds of boxing as part of a tournament through Corporate Fighter, at The Star in Sydney on Friday, 5th April in front of approximately 600 attendees.

When asked what his Dad would have thought of him participating in the Corporate Fighter event Martin believes he would have said boxing was a daft idea but, would have supported him regardless.

Martin exceeded his extraordinary target of raising $10,000 for CHeBA's research into Alzheimer's disease and other dementias and said that the event was always in honour of his Dad's own fight with dementia.

24 HOUR EXTREME CHALLENGE FOR CHeBA

On June 8th, Dr Claire Burley, an adventure-addicted scientist who is passionate about raising awareness of dementia and other brain health related conditions, spent 24 hours of pushing her body to extreme limits in the OCRWC Enduro (Obstacle Course Racing World Championships). Her goal was to raise money $1,000 for CHeBA's research while promoting evidence-based awareness that physical activity has a direct and positive impact on brain health.

"I have several personal stories I could share relating to dementia, clinical depression, eating disorders and addiction, amongst others," says Dr Burley, who is a Research Fellow with the Dementia Centre for Research Collaboration (DCRC).

"The significance for me, however, is that brain health and mental health is something that affects every single one of us."

Dr Burley is clearly very passionate about understanding brain health - both personally and professionally. At the University of Birmingham in the UK, she completed a PhD looking at measuring brain health, ageing and fitness.

"Understanding brain health is crucial in diagnosing, preventing and treating neurocognitive conditions such as dementia," explains Dr Burley.

"However, the literature reveals discrepancies around the interpretation of brain health and differences between populations. My PhD investigated several brain health measures from different disciplines (imaging, cognitive performance and well-being) in different age and fitness groups," she said.

Dr Burley says there is still much we all need to do to reverse stigma, develop early interventions and provide better models of care.

"CHeBA is a fantastic Sydney-based research group, which I am honoured to be closely aligned with at UNSW Sydney. They are dedicated to advancing scientific knowledge and improving health services for people experiencing brain related health conditions, particularly Alzheimer's and other dementias."

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VISITING LECTURE SERIES

CHeBA's Visiting Lecture Series continues to bring highly acclaimed international researchers to the UNSW community. In 2019 we were honoured to host Professor Vladimir Hachinski and Professor Charles de Carli.
To receive event updates email cheba@unsw.edu.au.

Professor Henry Brodaty & Professor Vladimir Hachinski

Professor Vladimir Hachinski

Talk Title: Can we Begin Preventing Dementias Now?

Professor Vladimir Hachinski, CM, MD, FRCPC, DSc, FRSC, Doctor honoris causa is Distinguished University Professor, Professor of Neurology & Epidemiology, past Richard & Beryl Ivey Chair, Department of Clinical Neurological Sciences, Western University, Canada. He coined the term brain attack to stress the urgency of stroke and discovered the key role of the brain's insula in control of the heart that when awry, can lead to sudden death. He is a leading advocate, contributor and thought leader of the vascular (treatable) component of dementia, crystallizing the concepts and coining the terms multi-infarct dementia, leukoaraiosis, brain at risk stage, vascular cognitive impairment, devising the eponymic Ischemic Score that identifies the treatable component (over 3700 citations).

Pathophysiological studies suggest a close link between Alzheimer and cerebrovascular disease. A hypothesis free, data driven analysis of the Alzheimer Disease Neuroimaging Study (ADNI) identified the first pathological biomarkers in Late Onset Alzheimer Disease (LOAD) were vascular dysregulation, a surprising and promising finding. Clinical studies also suggest that some dementia might be preventable. The FINGER Study showed for the first time that multiple interventions can result in cognitive improvement among individuals at risk of developing dementia, even when they are APOe4 positive. A Swedish study involving 80,948 patients with atrial fibrillation (AF) showed that anticoagulation decreases the risk of dementia by 48%. Targeting high blood pressure to a systolic of 120 mmHg compared to 140 mmHg results in a 19% reduction of the risk of mild cognitive impairment. Population, clinical and pathophysiological studies suggest that we can begin preventing some dementias now.

Meetings at the World Health Summit in Berlin in 2018 have produced a scientific blueprint for "Preventing dementia by preventing stroke". The time has come not only to recognize the dementia tsunami, but to do something more about it.

Professor Charles DeCarli

Talk Title: Biomarkers of Silent Cerebrovascular Disease Across the Age Range: Implications for Injury Mechanisms and Cognitive Impairment

Professor Charles DeCarli is the Victor and Genevieve Orsi Chair in Alzheimer's Research and Distinguished Professor of Neurology at the University of California, Davis.

His research focuses on using advanced structural and functional brain imaging to study normal aging, mild cognitive impairment, and dementia, and the role of genetics, cerebrovascular disease and Alzheimer's disease on these processes. Professor DeCarli is one of the champions of the Healthy Brain Aging Initiative, which seeks to advance novel approaches to optimize brain health from birth.

Vascular risk factors such as hypertension are common and appear in early middle life for a substantial minority of individuals. Biomarkers of brain injury due to these factors have developed slowly over the last few decades but are now proving extremely important given new therapeutic evidence of improvement in cognition with aggressive treatment. Data was presented from numerous life course studies showing the impact of vascular risk factors on brain injury, how they manifest and how they may be treated to reduce the incidence of late-life cognitive impairment and transition to dementia.

Professor Charles DeCarli & Professor Perminder Sachdev

Professor Perminder Sachdev AM, Amanda Mostyn, Richard Mostyn, Josie Mostyn, Dr Karen Mather, Professor Henry Brodaty AO

Inter-Generational Family Foundation

The Mostyn Family Foundation has funded a new CHeBA project researching the gut microbiome of centenarians, those aged 100 and over, and looking at how it is mediated by modifiable lifestyle factors including diet and physical exercise.

The Mostyn Family Foundation was founded by Bob Mostyn in 2011 with support of his sons Richard, Andrew and Robert Mostyn; a Foundation that now actively involves the grandchildren in the decision-making process of their philanthropic support for research activities.

Three generations of the Mostyn family now work collectively to provide funding support for valuable projects, while modelling social values to younger generations and raising awareness of community needs.

Board member and wife of Richard, Amanda Mostyn, says “Our decision to support CHeBA’s dementia research - particularly research looking at components of healthy ageing – came as a result of a family member being diagnosed with Alzheimer’s disease.”

It was Josie Mostyn, who is educated in nutrition, that put the proposal forward at a Board meeting where all members agreed it was critical research worthy of support.

Their contribution provides the possibility for CHeBA to commence a pilot project that will offer invaluable information on what role the microbiome might play in ageing successfully and living to and beyond 100.

The rationale for this project stems from recent observations that the gut microbiome possibly plays a major role in ageing. The human gastrointestinal tract is estimated to host about 10 trillion microorganisms, which is about 10 times the number of human somatic and germ cells in the body.

Lead researcher on the project Dr Karen Mather says that the aim is to examine the interplay of lifestyle factors, the gut microbiome and ageing by studying exceptionally long-lived individuals.

Co-Director of CHeBA, Professor Perminder Sachdev, says that centenarians offer an excellent opportunity to examine this question as they are models of successful ageing. The project will use participants from CHeBA’s long-established Sydney Centenarian Study.

Pictured L-R: Four generations of the Mostyn Family - Bob, Cam, Hendrix, Andrew, Rob and Richard Mostyn.

Public Forums

Strategies for Healthy Ageing

More than 400 community seniors attended this year's free public forum - *Strategies for Healthy Ageing* – hosted by the South Eastern Sydney Local Health District's Older Persons' Mental Health Service in partnership with CHeBA.

The event, held at The Juniors on Wednesday, 30 October 2019 showcased a series of presentations from Australia's pre-eminent academics and leaders in the field of ageing including acclaimed clinician and researcher Professor Henry Brodaty AO, who highlighted strategies for memory.

Author of *"Booming: A life-changing philosophy for ageing well"*, Marcus Riley, discussed how to age well while Consulting Adviser and Accredited Aged Care Specialist from Morgans Financial, David Codey, provided insight on financial strategies for older Australians.

This year, Alzheimer's Disease International focused its World Alzheimer Report on attitudes to dementia with the largest survey ever undertaken - and revealing a startling 50% of carers globally say their health has suffered as a result of their caring responsibilities, even whilst expressing positive sentiments about their role.

Spokesman for The Dementia Momentum, Richard Grellman AM, shared his strategies for being a carer following his wife's young onset Alzheimer's disease diagnosis when aged just 61. Suellen Grellman is very much in need of full-time high-level care and attention.

Other guests at this year's event included Uniting's Neuro Rehabilitation Specialist and Aged Care Manager, Tracey Clark, who provided insight on how to retain intimacy in later life and CEO of Dance Health Alliance, Gwen Korebrits, who led the way in promoting staying active.

Professor Brodaty said that the message of this annual forum is not only to showcase how complex ageing is but to encourage strategies to promote positive and healthy ageing.

The event was sponsored by the Juniors, South Eastern Sydney Local Health District, the Waverley Council and the Psychogeriatric Nurses Association Australia and is hosted in conjunction with CHeBA and the Dementia Centre for Research Collaboration.

Healthy Ageing Talks

Karen Allison (Study Coordinator of CogSCAN), Dr Catherine Browning (Study Coordinator of the Sydney Centenarian Study) and Dr Nicole Kochan (Project Leader of CogSCAN), presented 'Current Research on Memory and Healthy Brain Ageing' in October at the University of the Third Age at the Waverley Library.

CHeBA in the Media

Sydney Centenarian Study on ABC's *Catalyst*

Sydney Centenarian Study participant Fred Lax and his daughter Ruth Lax attending the exclusive screening of Catalyst's documentary for which Fred was interviewed.

Recently retired ABC newsreader Ian Henderson set out on a quest to find the secrets of ageing healthily and found his way to the Sydney Centenarian Study and some of our extraordinary centenarian participants! He discovered that a new understanding of how the trillions of cells in our bodies age could keep us all younger for longer. He met Australian scientists working at the cutting edge of ageing biology, including CHeBA Co-Director Professor Perminder Sachdev AM and learned that their research isn't just about making us live longer, but also about keeping us healthier into old age - improving our 'healthspan'.

View ABC Catalyst's Staying Younger for Longer: Body here: https://www.abc.net.au/catalyst/staying-younger-for-longer-body/11287578

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Destination Towels (Anthony Glick)
Dripping Wet Surf Co
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KPMG Sydney
Manly Kayak Centre
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Samsonite
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Slim Secrets
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The Bucket List
The Happy Snack Company
Think Products (Munch)
Three Blue Ducks
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- Montefiore Homes

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- Australasian Association of Gerontology (AAG)
- Australasian Society for Psychiatric Research (ASPR)
- 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
- World Health Organisation

NATIONAL

Commonwealth

- Australian Government Department of Social Services
- Australian Government Department of Health
- Commonwealth Scientific and Industrial Research Organisation (CSIRO)

Western Australia

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- Murdoch University, Perth
- The University of Western Australia

Tasmania

- University of Tasmania, Hobart

ACT

- Australian National University, Canberra

New South Wales

- NSW Health (Older People's Mental Health OPHM)
- University of Newcastle, Newcastle
- University of Wollongong, Wollongong

Sydney

- Academic Department for Old Age Psychiatry (ADFOAP), Prince of Wales Hospital
- 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
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- Macquarie University
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- University of Melbourne

Queensland

Brisbane

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

INTERNATIONAL

Africa

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

Asia-Pacific

- Beihang University, China
- Capital Medical University, China
- Chinese Academy of Sciences, China
- Fudan University, China
- Peking University, China
- Renji Hospital, China
- Shanghai Jiaotong University, China
- Tianjin Huanhu Hospital (Department of Neurolgy), China
- Tsinghua University, China
- Wenzhou University, Wenzhou, China
- Institut de Recherche pour le Développement (IRD), Tahiti, French Polynesia
- Institut Louis Malardé, Tahiti, French Polynesia
- Chinese University of Hong Kong, Hong Kong
- 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
- University of Macau, Macau
- Universiti Kebangsaan, Malaysia
- Universiti Putra Malaysia, Malaysia
- Department of Neuropsychiatry, Gyeonggi Provincial Hospital for the Elderly, Republic of Korea
- Hallym University, Republic of Korea
- Seoul National University, Republic of Korea
- Changi General Hospital, Singapore
- National Neuroscience Institute, Singapore
- National University, Singapore
- National University Health System, Singapore
- Mahidol University, Thailand
- Taipei Veterans General Hospital. No. 201, Taiwan
- St. Luke's Medical Center, Philippines

Middle East

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

Europe

- Innsbruck Medical University, Austria
- Alexandrovska University Hospital (Department of Medicine), Bulgaria
- University of Helsinki, Finland
- CHU Amiens-Picardie, France
- French National Institute of Health and Medical Research (INSERM), France
- Institut Pasteur de Lille, France
- Lille University Hospital, France
- University Aix-Marseille, France
- University of Bordeaux, France
- Forschungszentrum Juelich, Germany
- Heidelberg University, Germany
- Heinrich Heine University (Neuroscience Network Dusseldorf), Germany
- Helmholtz Association (German Center for Neurodegenerative Diseases - DZNE)
- Leiden University, Germany
- Ludwig Maximilians University Munich, Germany
- Max Planck Institute of Psychiatry, Germany
- University of Bremen, Germany
- University of Leipzig, Germany
- University of Marburg, Germany
- Harokopio University, Greece
- University of Athens, Greece
- Golgi-Cenci Foundation, Italy
- Institute of Biomembranes and Bioenergetics, Bari, Italy
- Mario Negri Institute for Pharmacological Research, Italy
- University of Pavia, Italy
- University of Trieste, Italy
- University of Udine, Italy
- Jagiellonian University, Poland
- Medical University of Silesia, Poland
- University of Porto, Portugal
- Wroclaw Medical University, Poland
- Biocruces Health Research Institute, Spain
- Universidad Miguel Hernandez de Elche, Spain
- University of Alicante, Spain
- University of Valencia, Spain
- University of Zaragoza, Spain
- Karolinska Institutet, Sweden
- Lund University, Sweden
- University of Gothenburg, Sweden
- University of Lausanne, Switzerland

- Erasmus University Rotterdaam (Erasmus University Medical Center), The Netherlands
- Leiden University, The Netherlands
- Maastricht University, The Netherlands
- Radboud University Nijmegan (Radboud University Medical Center), The Netherlands
- University of Groningen, The Netherlands
- University of Utrecht, The Netherlands
- VU University, The Netherlands
- Faroese Hospital System (Department of Occupational Medicine & Public Health), Faroe Islands, Denmakr
- Southern Denmark University, Denmark
- Jönköping University, Sweden

UK

- Cambridge University, England
- Cognitive Function & Ageing Studies, England
- King's College London, England
- Leeds-Beckett University, England
- Newcastle University, England
- Northumbria Healthcare NHS Foundation Trust, North Tyneside General Hospital, England
- The George Institute, University of Oxford, England
- University College London, England
- University of Bradford, England
- University of Central Lancashire, England
- University of Leeds, England
- University of Nottingham, England
- Royal College of Surgeons in Ireland, Ireland
- University of Aberdeen, Scotland
- University of Edinburgh, Scotland
- Swansea University, Wales

The Americas

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

CHeBA CONSORTIA COLLABORATIONS

In addition to the CHeBA-led consortia (COSMIC, ICC-Dementia, SHARED, COGNISANCE and STROKOG), 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)
- IALSA (Integrative Analysis of Longitudinal Studies on Aging and Dementia)
- IGEMS (Consortium on Interplay of Genes and Environment across Multiple Studies)

CHeBA PROJECTS

"It is our continued hope that CHeBA meets a major need in the health research environment in Australia."

-Professor Henry Brodaty AO & Professor Perminder Sachdev AM

CURRENT PROJECTS

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

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

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

Aims:

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

Findings:

- Depression incidence varied across the 8 included studies from 3.5 to 15.5 cases per 100 person years. Taking into account methodological differences between studies, an increase in the incidence of depression was observed as the time to dementia diagnosis decreased despite cross-national variability in depression rates. The results support the hypothesis that depression occurring in the pre-clinical phases of dementia is more likely to be attributable to brain changes than environmental risk factors or reverse causality. A manuscript is under revision in *Alzheimer's and Dementia*.

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

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

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

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

Aims:

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

Findings:

- Part of the literature review for this project has been published (Chinnappa-Quinn et al. *Curr Opin Psychiatry*. 2020 Mar; 33(2): 170-177. DOI: 10.1097/YCO.0000000000000565. PMID: 31652137).
- We have conducted a systematic review of peer reviewed papers investigating the effect of acute illness hospitalisation on cognition from Medline, Embase, Psycinfo and CINAHL, screening 6566 titles and abstracts. We synthesised results from 46 papers. Most papers were prone to bias as a result of have no baseline cognition data or appropriate comparison groups. However, eight studies used community cognition data and most of these showed cognitive decline associated with acute hospitalisations. Seven studies were able to be pooled statistically and the meta-analysis also supported this finding that acute hospitalisation increased cognitive decline, in particular conversion to dementia in subsequent years. This meta-analysis is currently under review for publication.
- The MAS data will be analysed using latent growth modelling to observe changes in cognitive trajectory over the 4 waves in relation to intervening hospitalisations, as well as undergoing survival analysis to assess the risk of conversion to dementia or MCI the association of this with hospitalisations at W6 from prior to W1 up to W4.

Funding: Australian Society of Anaesthetists, DCRC-ABC.

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

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

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

Aims:

- Explore covariates for correlation with Aβ levels across all cohorts. Covariates to explore include: comorbidities, therapeutic drugs, blood biochemistry, as well as lifestyle choices.

- Compare corrected Aβ levels (all cohorts) across neurodegenerative diseases: Alzheimer's disease, Parkinson's disease and Mild Cognitive Impairment (MCI)

- Identify effects of soluble Aβ levels on brain volumetric parameters, across the neurodegenerative conditions tested.

Findings:

- Plasma Aβ levels and the Aβ1−42/1-40 ratio are related to cognition and hippocampal volumes, with differential associations of Aβ1-40 and Aβ1-42 in ε4 carriers and non-carriers. Our data support the Aβ sink model of AD pathology, and suggest that plasma Aβ measures may serve as biomarkers of AD. The findings were partly the subject of an editorial (Poljak et al. *Expert Rev Neurother*. 2017 Jan; 17(1):3-5. DOI: 10.1080/14737175.2016.1217156.).

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

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

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

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

Aims:

- Examine if carriage of the Apolipoprotein E ε4 (APOE*4) allele is associated with decline of general cognitive functions and memory in late adulthood, and if this effect is dose-dependent.

- Investigate if the effect of APOE*4 on general cognitive and/or memory decline is moderated by age, sex and vascular risk factors.

- Examine if the effect of APOE*4 on general cognitive and/or memory decline differs between ethnicities, namely Asians and Whites.

Findings:

- APOE*4 carriage was related to faster general cognitive decline in women and men, and faster memory decline in men. However, carriage of two versus one APOE*4 alleles was associated with faster general cognitive and memory decline in men only. Significant effects in men were specific to the older-aged (i.e., 80-year-old) participants. Furthermore, the negative effects of carrying two versus one APOE*4 allele on general cognitive decline worsened with age in men more than women. Increasing numbers of vascular risk factors worsened the effects of APOE*4 carriage on general cognitive decline in younger-aged participants, with the effect being significant in women. In contrast, increasing numbers of vascular risk factors decreased the effects of APOE*4 carriage on general cognitive decline in older-aged participants, with the effect being significant in men. Regarding ethnoregional differences, in older-aged participants, APOE*4 had a stronger effect on memory decline in Asians versus Whites. Also, increasing numbers of vascular risk factors attenuated the effects of APOE*4 on MMSE decline in Asians, but not Whites. A manuscript has been revised and re-submitted in the Journal of Gerontology: Biological Sciences (March 20).

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

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

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

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

Aims:

- Determine if apolipoprotein changes observed in MCI and AD plasma, relative to normal controls, would be reproducible across independent cohorts of similar design.

- Identify which of the apolipoproteins change with age and/or are dysregulated in MCI and AD.

- Correlate plasma apolipoprotein changes with cognitive domain scores and brain volumetrics.

- Study the mechanisms of action, expression changes with age, and dysregulation in neurodegenerative diseases of ageing, including animal models for apolipoproteins APOA1, APOD, APOJ and APOH.

- Interactions between APOH and Aβ peptides, and binding partners of APOH in plasma and cerebrospinal fluid (CSF).

Findings:

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

- An invited book chapter detailing methods of analysis of plasma apolipoproteins has been published (Poljak A, Duncan MW, Jayasena T, Sachdev PS. Quantitative Assays of Plasma Apolipoproteins (Chapter 3). In:

Methods in Molecular Biology (MiMB): Models for Maximising Healthspan: Protocols and Methods (Ed: Guest PC). 2020; 2138:49-81. DOI: 10.1007/978-1-0716-0471-7_3.

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

Brain ageing and transcriptomics

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

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

Aim:

- 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 will be examined. Analyses are also being undertaken looking at age-related changes in brain expression from 10 brain regions using publicly available data.

Funding: NHMRC, Thomas Foundation.

Brain proteomics: Differential expression of the proteome in AD brain

CHeBA staff: Anne Poljak (adjunct), Tharusha Jayasena, Perminder Sachdev.

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

Aims:

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

Findings:

- We observed dysregulation in a variety of protein functional clusters, including antioxidant proteins, metabolic enzymes and mitochondrial proteins. These were generally downregulated in AD, whereas the expression of several proteins involved in cell cycle regulation, neuronal remodeling or structural roles, were upregulated in AD compared with controls, suggesting possible mechanisms of cellular repair or regeneration. By proteomics we observed that: Translocase of outer mitochondrial membrane (TOMM70) and Solute Carrier Family 25 Member 11 (SLC25A11) were both upregulated in AD vs control occipital lobe, possibly as a protective response to the burden of pathology. The work is ongoing, and a manuscript is in preparation.

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

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

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

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

Aims:

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

Findings:

- This work comprises a number of ongoing collaborative genetic and epigenetic projects, with a current focus on neuroimaging traits. In 2019, CHeBA researchers attended the 4th Annual BRIDGET Meeting in Edinburgh, Scotland. Analyses being undertaken include seeking to identify genetic variants associated with a composite measure of brain ageing based on MRI imaging using whole genome sequencing. The relationship between DNA methylation and cerebrovascular disease is also being examined.

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

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

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

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

Aim:

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

Findings:

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

Funding: NHMRC.

Changes in BMI predict cognitive decline in elderly women and not men: the Sydney Memory and Ageing Study

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

Other investigators: N/A

Aim:

- To examine whether the rate of change in BMI was associated with cognitive decline and dementia in elderly adults, and whether these effects differed between sexes.

Findings:

- The mean BMI at baseline was 27.1 and declined by an average 0.12 points (SE=0.16, $p<0.001$) per year. Results of latent growth curve modelling showed that in women but not men, a slower rate of BMI decline was associated with a significant reduction in the rate of decline of language abilities ($\gamma1=0.053$, SE=0.019, $p=0.005$), memory ($\gamma1=0.043$, SE=0.0.018, $p=0.014$), executive functions ($\gamma1=0.103$, SE=0.024, $p<0.001$) and global cognition ($\gamma1=0.067$, SE=0.016, $p<0.001$), and a reduced odds of dementia at the final assessment wave (OR=0.347, SE=0.325, $p=0.045$). Results for global cognition were unchanged after excluding participants who became demented at subsequent waves. Reductions in BMI over time were predictive of cognitive decline and dementia onset in women. These results highlight the importance of BMI as a marker of cognitive health and impending cognitive decline in elderly adults. A manuscript has been submitted for publication.

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

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

CHeBA staff: Lynn Chenoweth, Henry Brodaty.

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

Aim:

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

Findings:

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

staff focus groups and 20 one-on-one family interviews. There were significant improvements in FASRIT score percentages for family (p=0.001) and staff (p=0.001) post-intervention, and in staff median ratings of CARE 'safety' items (p=0.014), and family median ratings of CARE 'significance' items (p=0.020) at post-test. While existing organisational structures supported positive family/staff relationships, improvements were recommended by study participants in communication policies and procedures, care delivery information sharing and decision-making and in educating staff on how to build strong relationships with families. These findings were published in *Med Res Arch.* (Chenoweth L, Cook J, Wesson J, Brodaty H. Medical Research Archives. 2019 Aug 17; 7(7): 1-26. DOI: 10.18103/mra.v7i7.1958). The Staff and Family Relationship training program is also available at the DCRC website.

Funding: Montefiore Home.

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

CHeBA staff: Perminder Sachdev, Jessica Lo.

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

Aims:

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

Findings:

- Project proposal was approved by the RSC and data was sent to Dr Godefroy for analysis in 2018. However, Dr Godefroy found that there were missing key variables and they were not able to conduct the statistical analyses. He has decided to withdraw this project (as of Jan 2019).

Funding: Vincent Fairfax Family Foundation.

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

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

Other investigators: 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; Contributing COSMIC study leaders and associates representing cohorts from around 4 countries.

Aim:

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

Findings:

Analyses are currently underway.

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

Deprescribing guidelines for people with dementia: Cholinesterase inhibitors and Memantine

CHeBA staff: Lynn Chenoweth.

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

Aims:

- Provide recommendations regarding in what situations it might be suitable to withdraw the dementia medications cholinesterase inhibitors and Memantine.

- Provide guidance on how to conduct withdrawal, and to develop additional materials to provide information to people with dementia and their family members.

Findings:

- The guideline was produced following a systematic review using the GRADE process to assess the quality of the evidence and to convert the evidence into recommendations. The Guideline is registered on the NHMRC guideline register (https://www.clinicalguidelines.gov.au/register/evidence-based-clinical-practice-guidelinedeprescribing-cholinesterase-inhibitors-and), with recommendations only applying to individuals already taking one of the described medications (donepezil, rivastigmine, galantamine and/or memantine). The main points of this guideline are as follows:

  - There is considerable uncertainty in the benefits and harms of both prescribing and deprescribing in the individual who has used these medications for over 12 months. Cessation may have minimal,

clinically relevant negative consequences, but in some individuals discontinuation of ChEIs and/or memantine may lead to a worsening of cognitive function. In regard to quality of life and function, these outcomes may not be altered by discontinuation.

- Good communication between clinicians and people with dementia and/or carers/family on the benefits and harms of continuing versus discontinuing, in the context of their values and preferences, is necessary when discussing a potential trial of deprescribing, since individuals may feel that deprescribing is 'giving up', or a signal that they are no longer worth treating.
- The cost implications of deprescribing may include reduced medication costs, reduced costs of treating adverse drug effects, and an uncertain benefit or cost if there is a change in function that increases or decreases health service utilisation.
- These findings were also published in the Medical Journal of Australia (Reeve et al. Med J Aust. 210(4): 174-179).

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

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

CHeBA staff: Darren Lipnicki, Perminder Sachdev.

Other investigators: Eduwin Pakpahan (workgroup leader), Dame Louise Robinson, Blossom Stephan, Newcastle University Institute of Aging; Contributing COSMIC study leaders and associates: Representing cohorts from at least 4 countries. The project is also being undertaken within the NIHR funded Global Health Group on Dementia Prevention and Enhanced Care (DEPeC).

Aim:

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

Findings:

• Data being obtained from COSMIC studies.

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: Wei Wen, Jing Du, Forrest Koch, Jiyang Jiang, Perminder Sachdev.

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

Aim:

• The broad aim of this project is to design and establish a general framework for creating and computing novel diffusion weighted imaging (DWI) markers for examining the brain ageing and health.

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

Findings:

• This work started in Aug 2019. We used three independent cohorts to develop and validate our general framework. We used UK Biobank for the development of general framework. Reliability and predictive validity of our general framework and metrics arrived at using it were examined using two independent validation cohorts Sydney Memory and Ageing Study (MAS) and Renji Cerebral Small Vessel Disease Corhort Study (RCCS). A research manuscript is now in circulation and we expect to submit it in the mid 2020.

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

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

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

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

Aim:

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

Findings:

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

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

Establishing a neuroimaging working group for STROKOG

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

Other investigators: STROKOG collaborators.

Aims:

- To establish a neuroimaging working group for STROKOG.

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

Findings:

- [project in progress] The project proposal was approved by the research scientific committee at the end of 2019 and 13 studies/PI have agreed to join the workgroup. A protocol for processing MRI using CHeBA's pipeline has been established. Data is currently being requested for the WMH project and we expect some data by the end of 2020.

Funding: Vincent Fairfax Family Foundation, NHMRC.

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

CHeBA staff: Lynn Chenoweth.

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

Aims:

- Evaluate the clinical and cost-effectiveness of Dementia Care Mapping (DCM) in supporting the implementation of person-centred care training (PCCT).

- Evaluate its effectiveness as a process for improving care quality and quality outcomes for people with dementia, compared with usual dementia care.

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

Findings:

- DCM was not superior to control on any outcomes (n=675 residents: 287 control, 388 intervention). The adjusted mean CMAI score difference intervention versus control was -2.11 points) (95% CI -4.66 to 0.44, p = 0.104, adjusted ICC control=0, intervention 0.001). Sensitivity analyses supported the primary analysis. Intervention adherence was problematic. Incremental cost per unit improvement in CMAI and QALYs (intervention versus control) for baseline recruited residents (n=726, 418 intervention, 308 control) was £289 and £60,627 respectively. The main trial results and sub-study results were presented at 2018 international conferences, including the AAIC.

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

External validation of dementia risk models in stroke-survivors

CHeBA staff: Perminder Sachdev, Jessica Lo.

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

Aim:

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

Findings:

- Dementia risk prediction models developed for the general population do not perform well in individuals with stroke. Their poor performance could have been due to the need for additional and/or different predictors related to stroke and vascular risk factors or methodological differences across studies (e.g. length of follow-up, age distribution). Future work is needed to develop simple and cost-effective risk prediction models specific to post-stroke dementia.

Dr Tang has completed the project and submitted a manuscript to the journal Stroke which is currently under review.

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

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

CHeBA staff: Perminder Sachdev, Jessica Lo.

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

Aims:

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

Findings:

- [Project is on-hold] Project proposal was approved by the RSC and data was requested and sent to Marion Fahey. However, Marion left the university in 2018 and another researcher, Dr Clare Flach from the same research group will take up this project when her own project is completed ("Stroke recovery associated with cognitive impairment: A population-based study").

Funding: Vincent Fairfax Family Foundation.

Failure to identify particular odours predicts future dementia and mortality

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

Other investigators: N/A

Aim:

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

Findings:

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

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

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

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

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

Aims:

- Determine the heritability of amyloid deposition in the brain using amyloid PET imaging in the Older Australian Twins Study (OATS) cohort, as a potential endophenotype of Alzheimer's disease.

- Determine what proportion of the variance of β-amyloid burden is explained by the presence of APOE ε4 and common vascular risk factors.

- Examine the shared genetic basis between cerebral small vessel disease and β-amyloid burden.

- Investigate the relationship between amyloid burden and aspects of cognitive function.

Findings:

- OATS Wave 4 and 1P recruitment, assessment and scanning completed (n=206; 61 monozygotic and 42 dizygotic twin pairs).
- The heritability of global amyloid burden was moderate (0.41) and ranged between 0.17 and 0.54 across different brain regions.
- There were no significant genetic correlations between global amyloid burden and imaging markers of cerebral small vessel disease.
- These finding were presented by Koncz R et al. at the Alzheimer's Association International Conference in Los Angeles, USA, July 2019, as an oral presentation.
- Manuscript is currently under preparation.

Funding: NHMRC.

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

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

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

Aim:

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

Findings:

- We have established a mathematical model which summarises and analytically represents the geometry of the density, shape and flow of brain fibre tracts. The mathematical model of representing curves and trajectories, which is independent of the parametrization, was published in *Journal of the American Statistical Association* (Lafaye de Micheaux et al. 2020. DOI: 10.1080/01621459.2020.1745815). Pending on the new research students' enrolment, we will start using the model to investigate genetic influence on the spatial distribution and density of white matter fibre tracts in 2020.

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

Genetics and epigenetics of longevity

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

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

Aim:

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

Findings:

- Meta-analyses examining commonly studied genetic polymorphisms with exceptional longevity have been completed, including using data from the Sydney Centenarian Study. This work has been now been published by PhD student, Mary Revelas (Revelas et al., Mech Ageing Dev. 2018 Oct;175:24-34). Polygenic risk scores for a particular trait can be estimated using the results of previous genome-wide association studies. As expected, high polygenic risk scores for exceptional longevity were associated with longevity in our samples from the Sydney Centenarian Study. However, polygenic risk scores for cardiovascular factors and disease (e.g. low-density lipoproteins, stroke) were not significantly associated with longevity. This work has now been published in Genes (Revelas et al., Genes. 2019 Mar 18; 10(3). pii: E227). Other research currently being undertaken includes looking at the genetic factors underlying healthy longevity and using data from other sources, such as the UK Biobank.

Funding: Sachdev Foundation, NHMRC, Thomas Foundation.

Genetics of white matter hyperintensities

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

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

Aim:

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

Findings:

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

Funding: NHMRC, Thomas Foundation.

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

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

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

Aim:

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

Findings:

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

Funding: NHMRC, Thomas Foundation.

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

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

Aim:

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

Findings:

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

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

Identifying expression quantitative trait loci (eQTLS) in older adults

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

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

Aim:

- Identify genetic variants associated with gene expression.

Findings:

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

Funding: NHMRC.

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

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

Aims:

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

Findings:

- Aliquoting of MAS samples (all waves which have plasma) has been completed, Currently working on OATS samples, aliquoting all wave completed except the OATS2 (PET study). Biobanking is an ongoing project for remaining stored CHeBA blood samples, as well as new samples coming for additional waves of existing projects, or any new projects.

Funding: NHMRC and UNSW MREII 2015.

Improving clinical diagnosis of mild neurocognitive disorders using neuropsychological assessment

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

Other investigators: Ms Claudia Woolf (University of Sydney), Zara Page (UNSW Neuroscience Honours Student).

Aims:

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

Findings:

- Psychometric and normative data have been acquired for the Telephone Interview for Cognitive Status – Modified (TICS-M), a popular telephone-based cognitive screening instrument. Data were drawn from the Sydney Memory and Ageing Study from 617 participants, aged 71-91 years. The work has been published in the *Journal of the American Geriatric Society* (Bentvelzen et al. *J Am Geriatr Soc*. 2019 Oct; 67(10): 2108-2115. DOI: 10.1111/jgs.16033). An online normative data calculator is available for clinicians and researchers https://cheba.unsw.edu.au/research-groups/neuropsychology
- Our Neuroscience (Hons) student Zara Page achieved a First-Class Honours for her thesis titled Performance of older Australians from culturally and linguistically diverse backgrounds on pencil-and-paper and computerised neuropsychological assessments. The study used data from the Sydney Memory and Ageing study and observed that CALD individuals (n=164) performed more poorly than native English speakers (n=873) on neuropsychological tests in general. However, the difference was larger on pencil-and-paper tests than computerised measures, and specific language and acculturation factors strongly influenced test performance over and above demographic characteristics and health factors. Accounting for identified language and acculturation variables may improve the accuracy of neuropsychological assessments in CALD individuals. A manuscript is in preparation.

Funding: DCRC – Assessment and Better Care, UNSW.

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

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

Other investigators: STROKOG collaborators.

Aims:

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

Findings:

- [project is in progress] Data were received from collaborators in 2019 and data cleaning and harmonisation was completed by the end of 2019. A number of preliminary analyses was conducted in early 2020. We found that there was significant cognitive decline in stroke patients but it appears that the rate of decline was not much different from normal aging in the general population. We require additional normative samples to confirm this finding and such data are currently being requested.

Funding: Vincent Fairfax Family Foundation.

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

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

Other investigators: Claire Shepherd.

Aims:

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

Findings:

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

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

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

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

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

Aims:

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

Findings:

- We observed a significant age-dependent increase in the levels of D-serine, L-serine and glycine in the hippocampus of O. degus and APPsw/Tg2576 mice, along with a significant age-dependent decline in the levels of L-alanine, and L-threonine. In human plasma, concentrations of L-alanine, methylserine, glycine, D-serine and L-serine and several lipids were significantly altered in plasma from participants with dementia. Using a series of NMR based plasma metabolite measures (48 compounds identified in 30 subjects), principle components analysis showed a clear separation of dementia from normal control subjects based on features in the NMR spectra. Separation of subjects with mild cognitive impairment vs normal controls was much less pronounced and did not reach statistical significance. Five manuscripts have been published with 3 manuscripts contributing to Matthew Wong's PhD thesis. Another manuscript is currently being prepared to summarise the results of this work.

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

Maintain Your Brain

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

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

Aims:

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

Findings:

- 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.

Funding: NHMRC Dementia Team Research Grant.

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

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

Other investigators: Costas Anastasiou (workgroup leader), Nikolaos Scarmeas, Mary Yannakoulia: Greece; Contributing COSMIC study leaders and associates: Representing cohorts from around 8 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 obtained from COSMIC studies.

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

Oxidative stress in AD

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

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

Aims:

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

Findings:

- Oxidative stress to proteins can impair their function and shorten their half-life, and is a process often associated with disease. The ortho and meta isomers of tyrosine are specific products of oxidative stress and we have identified elevated levels of o- and m-tyrosine in plasma proteins of AD subjects relative to normal controls in a small cross-sectional study. Future work will also assess oxidative stress levels in MCI subjects and longitudinally in subjects progressing from normal control to MCI and AD.

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

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

CHeBA staff: Darren Lipnicki, Perminder Sachdev.

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

Aim:

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

Findings:

- Of 9,756 women dementia-free at baseline, 7,010 completed one or more follow-up assessments. The number of parities was associated with the risk of incident dementia (Hazard ratio [HR] = 1.07, 95% CI = 1.02 – 1.13). Grand multiparity increased the risk of dementia by 30% compared to 1–4 parities (HR=1.30, 95% CI=1.02–1.67). A manuscript has been submitted for publication.

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

Physical Activity and Cognitive Decline: the Sydney Memory and Ageing Study

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

Other investigators: N/A

Aim:

- To investigate whether the amount of physical activity is dose dependently associated with slowing of cognitive decline and reduction in dementia risk; whether this dose-dependent association is dependent upon physical activity intensity, and if these associations are moderated by gender.

Findings:

- Physical activity may have a dose-dependent association with attenuation of cognitive decline and reducing dementia incidence in women, and which may be specific to activities of light intensity. A manuscript is under preparation.

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

Plasma proteomics biomarkers

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

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

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).
- We performed a meta-analysis on blood and CSF proteomic biomarkers of early onset AD subtypes, including early onset familial/dominantly inherited AD and sporadic early onset AD (Kaur et al. CSF and blood protein biomarkers and APOE genotype status of early-onset Alzheimer's disease variants: A systematic review and meta-analysis. J Alzheimers Dis. 2020; 75(3):827-843. DOI: 10.3233/JAD-200052). This is one of few studies exploring factors associated with early onset sporadic AD (EOsAD) and the main observations were that (a) in a subset EOsAD cases with confirmed absence of APP, PSEN1/PSEN2 mutations, the CSF Aß42 and tau levels were higher when compared to the EOsAD group as a whole, and similar to the autosomal dominant individuals who carry mutations. This level of biomarker pattern similarity in the absence of a classical AD mutation deserves closer attention, since it implies either some as yet unknown genetic mutation, or else a potentially modifiable lifestyle/environmental factor; (b) prevalence of the APOEε4 allele was elevated in EOsAD relative to controls, and not significantly elevated in ADAD cases. However the APOEε4 enrichment in EOsAD was similar to that observed in late onset AD (LOAD), so does not explain the much earlier age of onset relative to LOAD.
- A plasma pre-analysis fractionation method has been developed which allows identification of >3000 plasma proteins. Three studies and/or manuscripts are in progress: (a) methods development and evaluation for proteomics analysis of plasma; (b) longitudinal analysis of plasma proteomic changes in MCI and AD using plasma from the Sydney MAS cohort (waves 1 and 4); (c) 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), Gelareh Mohammadi (Computer Science & Engineering, UNSW).

Aim:

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

Findings:

- To date several machine learning survival models have been developed using baseline data from the MAS study and a variety of machine learning algorithms and feature selection techniques suitable for survival analysis of high dimensional data. These models examined over 250 variables and predicted survival to dementia with a concordance index of up to 0.82. The models identified the variables that are most important in the prediction of dementia. The neuropsychological scores were the most predictive variables, but other highly predictive variables included Age, level of Education, the Brief Smell Identification Test score and other cognitive test scores. A paper has been submitted to Nature Scientific Reports on this work but is still under review. Further work is being done to improve and stabilise the results of these models. The next stage of the project will develop survival models using the longitudinal data from waves 1-4.

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 (conjoint), Mahboobeh Hosseini, Perminder Sachdev.

Other investigators: Sonia Bustamante (BMSF, UNSW).

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. We are able to detect levels of both free and bound fatty acids. Analysis of MAS wave 1 samples are currently underway and data collection is expected to be complete by July 2020.

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

Rates of conversion to dementia in diverse ageing populations, using different dementia harmonisation methods including delta

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

Other investigators: Contributing COSMIC study leaders and associates: Representing cohorts from at least 9 countries.

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 conversion 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. For studies with cognition and function (IADL) data, uniform algorithmic procedures that identify individuals impaired on both will be used. Impairment will be defined via comparisons with consensus diagnoses by expert panels, using the subset of studies with these data. For studies without suitable cognition and/or IADL data, scores on screening tests (MMSE, CDR etc) with appropriate cut-points, can tentatively be used.

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) 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 and algorithmic approaches will be examined. We will also examine how measures like delta and CFC vary with demographic characteristics and APOE e4 carrier status.

Findings:

- Data being obtained from COSMIC studies.

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

Relationship between body mass index and cognitive decline

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

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

Aim:

- Examine the association between body mass index (BMI) and the rate of prospective decline on general cognition and memory. Investigate whether this association: (a) differs between sexes; (b) is moderated by (baseline) age; (c) differs depending on carriage or non-carriage of the Apolipoprotein epsilon 4 (APOE*4); (d) is influenced by vascular risk factors; and (e) differs between ethnicities, namely Whites and Asians.

Findings:

- Specific to older-aged (i.e., 80-year old) elderly female adults, higher BMI was associated with attenuated decline of general cognition, and obese (i.e., BMI≥30 kg/m2) participants displayed a significantly slower rate of general cognitive decline compared to lower-normal participants. Between-sex comparisons indicated that both effects were significantly larger in women than men. BMI was not associated with cognitive decline in men overall. The association between BMI and decline of either general cognition or memory did not differ between APOE*4 carriers and non-carriers. The analysis of vascular risk factors indicated that the relationship between higher BMI and slower MMSE decline observed in older women was significantly weakened by the presence of vascular risk factors. Also, in this group, vascular risk factors counteracted the reduction in memory decline at higher BMI cut-points. In terms of ethnoregional differences:
  - There was a stronger association between higher BMI and attenuation of memory decline, and a larger protective effect of obesity against MMSE decline in older Asian women versus White women.
  - Although BMI was unrelated to cognitive decline in men as a whole, we found different effects of upper-normal weight (i.e., 23≤BMI<25 kg/m2) on MMSE

decline in older Asian and White men. Namely, upper-normal weight was more strongly related to MMSE decline in Asians compared to Whites.

- Overweight men (25≤BMI<30 kg/m2) also displayed a significantly slower rate of MMSE decline than lower-normal weight men among Whites, but not Asians.

• A manuscript is being revised for submission to a new journal.

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

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

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

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

Aims:

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

• Further explore the nature of this relationship, namely: (a) whether the association between education and attenuated risk of cognitive impairment is nonlinear; and (b) by treating education as categorical, to identify the maximum level of educational attainment that provides protection against cognitive impairment.

• Explore whether the protective effects of education against cognitive impairment are moderated by sex and age.

• To clarify the nature of ethnoregional differences in the relationship between education and the risk of cognitive decline.

• To determine whether education can reduce the risk of cognitive decline associated with carriage of the APOE*4 allele, and if these effects are moderated by sex, age, and ethnicity.

Findings:

• Education was associated with a reduced risk of cognitive impairment. This association, however, was non-linear, indicating that at very high levels of education, the reduction in the risk of cognitive impairment was less pronounced. Categorical analyses of education indicated that a middle level of education (i.e., about 8-11 years, typically signifying the completion of middle school or intermediate high school) significantly attenuated cognitive impairment risk relative to primary education (up to 5-7 years of education). These protective effects of middle education weakened with older age at baseline, and a trend for the effect to be larger in women than men. High school education did not provide significant additional protection against cognitive impairment risk relative to middle education.

• In terms of ethnoregional differences, compared to Whites, there was a larger protective effect of high school (versus primary) education in Asians, and a larger protective effect of middle (versus primary) education in Blacks. Middle education reduced the risk of cognitive impairment in non-APOE*4 carriers, but not among APOE*4 carriers, both overall, and in White participants specifically. In Asians, however, both high school and middle education reduced the risk of cognitive impairment in APOE*4 carriers, compared to primary education. In Blacks also, middle school reduced cognitive impairment risk among APOE*4 carriers. A manuscript being revised for re-submission to Archives of Gerontology and Geriatrics.

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

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

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

Other investigators: Kathy Samaras (UNSW).

Aim:

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

Findings:

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

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

Risk factor clustering and incident cognitive decline

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

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

Aims:

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

Findings:

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

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

Risk factors for post-stroke depression

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

Other investigators: STROKOG collaborators.

Aim:

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

Findings:

- [project in progress] The project proposal was approved by the research scientific committee at the end of 2019. Data is currently being requested.

Funding: Vincent Fairfax Family Foundation, NHMRC.

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

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

Aim:

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

Findings:

- We have processed FLAIR and T1-weighted scans from UK Biobank (~17000), all three wave of Sydney Memory and Ageing Study (~1200) and a manuscript is in circulation and we will submit it in April 2020 to a journal.

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

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

CHeBA staff: Darren Lipnicki, Perminder Sachdev.

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

Aims:

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

Findings:

- Analyses underway.

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

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

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

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

Aim:

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

Findings:

- Global cognitive function and average social network size declined across time-points.
- Younger age and more years of education predicted better cognitive function at baseline. Higher depression score was associated with smaller social network size at baseline and at year six (wave 4) follow-up. Better cognitive function at year two (wave 2) follow-up was associated with larger social network size at year four (wave 3) follow-up.
- Among participants who provided complete network data at all four waves, those who received a dementia diagnosis during the course of the study had significantly smaller networks at baseline than did those who experienced Mild Cognitive Impairment (MCI) without a dementia diagnosis and those with normal cognition.
- Just over half of the participants who provided complete data (52.9%) had smaller networks at year six follow-up compared to baseline; nearly half of participants had stable (13.7%) or larger networks (33.4%), some doubling in size (13.7%). More males (59.1%) had decreasing networks.
- Relationship quality was significantly associated with global cognitive function after controlling for age, sex, years of education, ApoE4 status, neuroticism, depression, number of medical conditions, number of mental and social activities, social network size and minutes of weekly vigorous physical exercise.
- On balance, results indicated that better perceived quality of social relationships, not the number of social relationships, was associated with better global cognitive function across six years in this study.
- Detection of causal associations may require longer study timeframes and more depth in neurocognitive and social relationship data.

Funding: Thomas Foundation.

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

CHeBA staff: Suraj Samtani (workgroup leader), Henry Brodaty, Ashley Stevens, Darren Lipnicki, Perminder Sachdev.

Other investigators: Contributing COSMIC study leaders and associates.

Aims:

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

Findings:

- Data being obtained from COSMIC studies.

Funding:

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

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

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

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

Aims:

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

Findings:

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

Funding: Self-funded.

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

CHeBA staff: Perminder Sachdev, Jessica Lo.

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

Aims:

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

Findings:

- [project is in progress] Dr Flach found that individuals who were cognitively impaired three months after stroke were at significantly increased risk of depression and disability in long-term follow-up. A manuscript draft is completed and has been circulated with collaborators in late 2019. Dr Flach is to conduct additional analyses and circulate a revised draft in early 2020.

Funding: Vincent Fairfax Family Foundation.

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

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

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

Aims:

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

Findings:

• The hydrodynamic diameter of nanoparticles, determined by dynamic light scattering (DLS) using the Malvern Zetasizer Nano Particle Characterisation System, demonstrated the stability of our nanoparticles in different biological media. Both the DMSA coated nanospheres and nanocubes showed expected changes to diameter and low polydispersity.

• The cytotoxicity of our functionalised nanoparticles was assessed in astrocytes and neurons using the lactate dehydrogenase assay and caspase-3 expression. Our nanoparticles showed no significant increases in toxicity relative to control at all concentrations up to 1mm.

• The internalisation of the nanoparticles and their localisation within the cellular organelles have been assessed using electron microscopy. After 6 hours of incubation, the nanoparticles appeared to localise on the plasma membrane and within multivesicular bodies. After 24 hours of incubation, the nanoparticles were observed to have moved into the lysosomes.

• We also demonstrated, using immunohistochemistry and electron microscopy, that these functionalised nanoparticles indeed bind to Aβ fibrils, suggesting selectivity to bind plaque deposits in AD transgenic mouse and post-mortem human probable AD brain tissue sections.

• Our nanoparticles were shown to be safe and well tolerated in AD transgenic mice (APP/PS1) and wild type mice with no changes in liver and renal function tests and no observable changes in behaviour even at repeatedly high doses of 10 ng per kg weight of mouse.

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 (conjoint), Yue Liu (MSc candidate).

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

Aims:

• Develop a greater understanding of vascular factors that contribute to the aetiology and heterogeneity of Alzheimer's and related dementias, by examining both the additive and interactive effects of cerebrovascular and Alzheimer-type pathologies in humans and animal models, using a cross-disciplinary and integrative approach.

• Establish animal models for both AD (transgenic) and cerebral vessel disease (hypoperfusion, small vessel disease, transgenic) to examine the interaction of the two pathologies, and the role of inflammation, oxidative stress, mitochondrial dysfunction, permeability of the blood-brain barrier, and stress response in the genesis of either pathology.

• Discover peripheral markers of vascular risk and/or cerebral vessel disease which alone, or in combination with markers of AD, can predict the onset of clinical symptoms and disease progression.

Findings:

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

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

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

CHeBA staff: Darren Lipnicki, Perminder Sachdev.

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

Aim:

• Our overall aim is to examine the unique and interactive effects of occupational complexity and education on late-life cognition (cognitive impairment and normal cognitive aging, including levels and rates of change). Our specific aims are to examine:

- Whether occupational complexity is associated with late-life cognition over and above the effect of education. High occupational complexity is associated with lower likelihood of developing cognitive impairment. High occupational complexity is also associated with higher levels of cognition and slower rates of cognitive decline at earlier stages of cognitive aging.
- Whether occupational complexity is the mechanism though which early-life education is associated with late-life cognition. The association between education and cognitive impairment is mediated by occupational complexity. The association between education and cognitive aging (i.e., levels, rates of change) is mediated by occupational complexity.

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

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

Findings: Analyses currently underway.

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

The effects of intravenous NAD+ on Ageing and Metabolic Syndrome

CHeBA staff: Nady Braidy.

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

Aims:

- Investigate the safety and tolerability of intravenous NAD+ as well as its efficacy in elevating NAD+ levels in healthy elderly people between the ages of 70 and 80.

- Determine whether intravenous NAD+ will significantly increase cellular concentrations of NAD+, improve the NAD+/NADH ratio, favourably change metabolic biomarkers, and upregulate expression of anti-ageing genes in elderly individuals.

Findings:

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

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

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

The organisation of the elderly connectome

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

Aims:

- Examine the core features of both structural and functional networks in the brain of the oldest of the old (centenarian) and how this compares to the brain of the young-old (e.g. 70 - 75) and previously published data.

- Examine whether changes in both structural and functional connectivity is predictive of cognitive performance in the elderly, especially the centenarians.

- Examine whether age-related changes in cognition can be predicted by changes in structural and functional connectivity.

- Our focus is now in the longitudinal changes of the elderly brain network using multiple time-points scans.

- Another new focus is the centenarian brain.

Findings:

- We examined functional default mode network of 57 centenarian brains using independent component analysis implemented in FSL. Results showed that centenarians without diagnosis of dementia had more synchronised activation of bilateral parietofrontal control networks compared to young-old participants. Stronger functional connectivity between bilateral parietofrontal control networks was associated with better performance in visuospatial ability in centenarians. The paper is in revision at Neuroimage.

Funding: NHMRC.

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

CHeBA staff: Louise Mewton, Darren Lipnicki, Perminder Sachdev, Rachel Haris.

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 underway.

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

The relationship between blood pressure and risk of cognitive decline

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

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

Aims:

• To examine the effect of BP and antihypertensives on cognitive function in late life. Specifically:

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

Findings: Data being obtained from COSMIC studies.

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

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

CHeBA staff: Anne Poljak (adjunct), Fatemeh Khorshidi (UPA 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. A manuscript based on this work is currently under review.

• Experimental work to establish dose response curves and proteomics analysis using ethanol and close to completion. Dose response for resveratrol and nicotinamide are yet to be performed.

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

The role of plasma fatty acids in ageing and age-related cognitive change and disorders

CHeBA staff: Anne Poljak (adjunct), Tharusha Jayasena, Perminder Sachdev, Maboobeh Hosseini.

Other investigators: Sonia Bustamante.

Aims:

• Explore the possibility that plasma fatty acids are correlated with brain volumetric and cognitive changes.

• Compare plasma fatty acid profiles across dementia subtypes (AD, vascular dementia) and stroke.

• Compare fatty acid levels in control vs AD, using plasma from MAS and OATS subjects.

Findings:

• We 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. *Ageing Res Rev*. 2020 Jul; 60:101043. DOI: 10.1016/j.arr.2020.101043).

• A book chapter reviewing the role of lipids was published (Sachdev PS, Poljak A. Lipidomics for Biomarkers and Biomechanisms in Brain Ageing and Dementia (Chapter 12). In: *Neuroscience of Dementia* (Eds: Martin CR, Preedy VR). Elsevier BV: 2020.

• Dr Tharusha Jayasena has completed plasma fatty acids analysis on most of MAS W1, using electron capture-negative ionisation gas chromatography/mass spectrometry, analysing 30 plasma fatty acids.

Funding: NHMRC, Rebecca Cooper Foundation.

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

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

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

Aim:

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

Findings:

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

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, Adam Theobald (until April 2019), Catherine Browning, Kristan Kang, Fleur Harrison, Julia Riches, Yvonne Leung (until July 2019), 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:

• Levels of psychological distress and degree of life satisfaction in SCS participants were compared to a younger CHeBA cohort to examine the psychological health of centenarians and near-centenarians. Protective factors for maintaining good psychological health as people reach very advanced ages were also explored. The study found that centenarians and near-centenarians were more satisfied with their overall life than a younger CHeBA cohort, despite showing higher levels of psychological distress. Furthermore, in Sydney Centenarian participants, more psychotropic medications and having fewer relatives and friends were associated with higher psychological distress. Lower cognitive performance and having fewer relatives and friends were associated with lower life satisfaction. This study shows that despite showing higher levels of distress over the previous 4 weeks compared to the younger group, centenarians and near-centenarians remained highly satisfied with their overall life. This study was published in the *Australia & New Zealand Journal of Psychiatry* (Cheng et al. *Aust N Z J Psychiatry*. 2019 Oct; 53(10):976-988. DOI: 10.1177/0004867419848831).

• Genetic studies have linked cardiovascular health with longevity. This study compared the genetic profiles of centenarians and near-centenarians from the Sydney Centenarian Study (95+ years) to those of a younger cohort from the Hunter Community Study (55-65 years). As expected, higher genetic risk for longevity was associated with living to an exceptional age. Although genetic risk for cardiovascular health (e.g. heart disease) was nominally associated with longevity, a larger sample size is needed to explore this further. These findings were published in *Genes* (Revelas et al. *Genes*. 2019 Mar 18;10(3). pii: E227. DOI: 10.3390/genes10030227).

• Near-centenarians and centenarians without a diagnosis of dementia form a model of successful cognitive ageing. CHeBA researchers have previously identified brain structural profile in near-centenarians and centenarians by using data from the Sydney Centenarians Study. However, functional characteristics of extremely old brains have not been documented. Resting-state functional MRI (rs-fMRI) offers an unprecedented opportunity to study human brain function and neural activity. This study was the world-first published rs-fMRI paper to depict characteristics of neural activity in near-centenarians and centenarians. Findings suggested that, compared to young-old controls,

centenarians showed more synchronized activation of left and right fronto-parietal control networks. In near-centenarians and centenarians, this coupled activation of bilateral fronto-parietal control networks contributed to a better performance in visuospatial tasks. These findings emphasized the important role of fronto-parietal control network in cognitive reserve capacity. Future studies will investigate the underlying mechanisms for this cognitive reserve and develop potential therapeutic strategies against age-related decline (Jiang et al. *NeuroImage*. 2020 Apr 14:116855. DOI: 10.1016/j.neuroimage.2020.116855).

• Cognitive reserve can influence the likelihood of maintaining good cognitive function in later life. Evidence suggests that cognitive reserve built throughout a person's lifetime can reduce the risk of dementia. However, given that dementia risk increases with age it was not known whether cognitive reserve remains protective in centenarians. This study examined the relationships between cognitive reserve and cognitive performance and rates of dementia in SCS participants. Education, occupational attainment, engagement in mental activities through life, and reading vocabulary were used as proxy measures of cognitive reserve. It was found that almost all cognitive reserve measures were associated with cognitive scores, except for years of education. This is interesting as education in other studies was protective of cognition. This may be an older-birth cohort effect since these participants experienced the Great Depression during the years that they might have otherwise attended university. The study also found that mental activities and reading vocabulary combined were more strongly associated with cognitive performance than occupation and education combined. The implication of this finding is encouraging since it suggests that cognitive reserve predictors built throughout life like mental activities and literacy showed stronger protective effects on late-life cognition in near Centenarians and Centenarians. That is, it demonstrates continuing effects of cognitive reserve on cognitive performance at the end of the age spectrum. A manuscript is currently under preparation for submission.

Funding: NHMRC.

The Sydney Memory and Ageing Study (MAS)

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

Other staff: Josephine Bigland (UNSW).

Aims:

• Examine the clinical characteristics, incidence and prevalence of Mild Cognitive Impairment (MCI) and related syndromes, including Alzheimer's disease and other dementias.

• Determine the rate of change in cognitive function over time in community dwelling older Australians.

• Investigate risk factors for, and protective factors against, cognitive decline and dementia.

• Develop and refine measures for early diagnosis, prognosis and biomarkers of MCI and dementia.

Highlights from 2019:

• Data from MAS made headlines this year as the most comprehensive analysis of cognition in older statin users to date was published. Findings from over 1,000 MAS participants, followed-up over six years, found no links between cholesterol-lowering statin medication and cognitive decline, presenting new advice amidst consumer concerns that statins may have a negative impact on cognitive health. Up to half the individuals prescribed statin therapy do not fill their prescription largely due to this concern, which carries a significant impact on public health. In fact, the authors found that statin use might even be protective against cognitive decline. This study provides reassurance older adults to feel more confident about their statin prescription (Samaras et al., *J Am Coll Cardiol*. 2019; Nov 26; 74(21): 2554-68. DOI: 10.1016/j.jacc.2019.09.041).

• Perivascular spaces surround small blood vessels as they penetrate brain tissue and are a common MRI finding in older adults. Using data from MAS participants with MRI data, a CHeBA researcher has developed a new rating scale to understand the relationship between perivascular spaces and dementia. The new rating scale is easy to use, quick, has good psychometric properties and performs better than existing. Accurate identification and quantification of perivascular spaces will help with understanding the relationship between small vessel disease and dementia, as well as assist with diagnosis and prognosis of dementia (Paradise et al., *J Neurol Sci*. 2020; 409: 116621. DOI: 10.1016/j.jns.2019.116621).

• MAS contributes important data to several large, ongoing, consortia projects. One such consortia project, comprised of over 48,000 individuals from around the world, found education, smoking, physical activity, diabetes, and stroke all have strong associations with late life cognitive decline. Importantly, these are all modifiable lifestyle factors that can be targeted for early prevention strategies. Different effects between Asian and white cohorts were found for smoking and diabetes, suggesting that any global strategy may need to consider ethno-regional differences (Lipnicki et al., *PLoS Med*. 2019 Jul; 16(7): e1002853. DOI: 10.1371/journal.pmed.1002853.).

• Early-life stress (ELS) has previously been identified as a risk factor for cognitive decline, mainly in clinical groups. A recent study using MAS data found no relationship between global cognitive function and overall experiences of ELS. However, those who have had experienced physical neglect were found to have poorer global cognition compared to those who had not. This suggests that the relationship between ELS and cognition in older age may be dependent on the nature of the trauma experienced (Grainger et al., *Int Psychogeriatr*. 2019; Oct 29:1-5. DOI: 10.1017/s1041610219001583.).

• Telephone-based cognitive screens, such as the Modified Telephone Interview for Cognitive Status (TICS-M), have great potential for increasing older adults' access to cognitive screening. This seminal study found that cognitive data gathered from telephone interviews correlated well with established face-face cognitive

screens and neuropsychological tests. Cut-off scores produced from this data also reliably distinguished between those with and without a dementia diagnosis. This study will help improve the accessibility and cost-effectiveness of cognitive testing for older adults (Bentvelzen et al., J Am Geriatr Soc. 2019; Jul 9; 67(10):2108-15. DOI: 10.1111/jgs.16033).

• Dementia is a known risk factor for falls and injury-related hospitalisations, but it is not clear whether individuals with mild cognitive impairment (MCI) have elevated falls risk. This study compared injury-related hospitalisation rates for older adults with normal cognition, MCI, and dementia in Australians. People with MCI had higher injury rates than people with normal cognition and lower injury rates than people with dementia. For individuals with MCI and dementia, the most common fall-associated injuries were non-fracture head injuries. These findings suggest falls-risk screening and prevention initiatives may be useful for older people with MCI (Harvey et al., *Arch Gerontol Geriatr*. 2019; Jul-Aug; 83:155-60. DOI: 10.1016/j.archger.2019.03.028).

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

Towards understanding the role of gene expression in ageing

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

Other investigators: Bernhard Baune (University of Adelaide), Liliana Ciobanu (University of Adelaide), Nicola Armstrong (Murdoch University) (CHeBA Hon. Research Fellow), John Kwok (University of Sydney; UNSW), 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 twins from the Older Australian Twins Study has been undertaken and is being written up for publication.

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

Upregulation of NAD+ Anabolism to Promote Lifespan

CHeBA staff: Nady Braidy.

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

Aims:

• Determine the effect of SIRT2 transgene on lifespan and underlying age-related degeneration in chow and high fat diet fed aged Wistar rats.

• Examine whether SIRT2 over-expression alters NAD+ levels and improves cognition in chow and high fat diet fed aged Wistar rats.

• Measure the changes in intracellular NAD+ levels and SIRT2 expression in physiologically aged Wistar rats treated with the natural polyphenols: resveratrol (increases NAD+ synthesis) and apigenin (an inhibitor of the NAD+ degrading enzyme CD38).

• Assess whether treatment with the apigenin and resveratrol, can extend lifespan, delay age-related degeneration, and delay/postpone cognitive decline in aged Wistar rats.

Findings:

• We tested whether restoration of NAD+ levels in the brain of obese mice can improve brain function. Increasing NAD+ levels enhanced insulin secretion in a SIRT1-dependent manner, and reduced brain oxidative stress and neuroinflammation. We also identified a novel compound oxaloacetate as a 'new' precursor for the promotion of NAD+ anabolism. Two manuscripts are currently under preparation for this project.

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

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

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

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

Aims:

• Determine if vitamin binding protein levels are different in MCI and AD plasma relative to normal controls, and whether observations would be reproducible across independent cohorts of similar design.

• Identify which of the vitamin binding proteins change with age and/or are dysregulated in MCI and AD.

• Correlate plasma vitamin binding protein levels with cognitive domain scores and brain volumetrics.

Assay plasma levels using ELISA quantification. Afamin (vitamin E binding) and VDBP are of specific interest, based on our preliminary discovery proteomics data.

Findings:

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

- Plasma afamin levels have been assayed by ELISA assay, in the laboratory of Prof Hans Dieplinger (Austria), and a publication is in preparation. We identified lower afamin levels in AD samples, and a trend toward lower levels in MCI, but not so marked as in AD. This data validates our previous proteomics results, and supports other published findings.

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

COMPLETED PROJECTS

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

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

Other investigators: Wanlin Zhu (Beijing Normal University), (Beihang University, China) (CHeBA Hon. Research Fellow).

Aim:

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

Findings:

- We created a new module called TOPMAL (TOolbox for Probabilistic MApping of Lesions) to expend our pipeline's (UBO Detector, see https://cheba.unsw.edu.au/research-groups/neuroimaging/pipeline) functionalities. TOPMAL can be used for mapping white matter WMH burdens to strategic WM tracts. Together with UBO Detector, this new module is open-source and open to all for downloading.

- This new module has been tested with a community-based cohort of 466 older individuals. We examined the associations of WMH loadings on strategic WM tracts with cognitive domains and diagnostic classifications (mild cognitive impairment vs. cognitively normal), and compared them with the relationships of total WMH, GM and WM volumes with cognition. We found that regional (fibre tract specific) WMH burdens were independently associated with poorer performance in processing speed (e.g. cingulum, inferior fronto-occipital fasciculus, and uncinate fasciculus), and executive function (inferior fronto-occipital fasciculus, uncinate fasciculus, anterior thalamic radiation, superior longitudinal fasciculus). The findings emphasize the association of regional WM deficit with cognitive decline, and the importance of studying the distribution of structural lesions in ageing and neuropathology.

Funding: NHMRC, John Holden Family Foundation.

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

CHeBA staff: Darren Lipnicki, John Crawford, Steve Makkar, Anbupalam Thalamuthu, Nicole Kochan, Henry Brodaty, Katya Numbers, Julian Trollor, Yvonne Leung, Jessica Lo, Perminder Sachdev.

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

Aims:

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

Findings:

- The overall sample comprised 48,522 individuals (58.4% women) aged 54–105 (mean = 72.7) years at baseline. We analysed two cognitive outcomes: scores for the Mini-Mental state Examination, and global cognition scores derived from tests of memory, language, attention, and executive functioning. For at least one cognitive outcome, age, APOE*4 carriage, depression, diabetes, current smoking, and stroke history were independently associated with poorer cognitive performance, and higher levels of education and more physical activity were associated with better performance. Age, APOE*4 carriage and diabetes were independently associated with faster cognitive decline. Some different effects between Asians and Whites were observed, including stronger associations for Asians between ever smoking and poorer cognition, and between diabetes and cognitive decline. These findings were published in *PLoS Medicine* (Lipnicki et al. *PLoS Med*. 2019 Jul 23; 16(7): e1002853. DOI: 10.1371/journal.pmed.1002853. PMID: 31335910).

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

Genetic and epigenetic markers of late-life depression

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

Other investigators: Dr Simone Reppermund (UNSW Medicine) (CHeBA Hon. Research Fellow), Professor David Ames (National Ageing Research Institute, Royal Melbourne Hospital), Dr Nicola Armstrong (Murdoch University) (CHeBA Hon. Research Fellow), Associate Professor John Kwok (NeuRA, UNSW), Professor Peter

Schofield (NeuRA, UNSW), Professor Naomi Wray (Queensland Brain Institute, University of Queensland), Associate Professor Margaret J. Wright (QIMR Berghofer Institute, Brisbane, Australia).

Aim:

- Estimate heritability for late-life depression and depressive symptoms.
- Calculate bivariate genetic correlations between measures for depression and related phenotypes, such as anxiety.
- Identify differentially methylated regions of the genome associated with depression in late life.

Findings:

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

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

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

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

Aim:

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

Findings:

- Adequate CBF is necessary to maintain brain metabolism and function. ASL is an emerging MRI technique offering a non-invasive and reliable quantification of CBF. The genetic basis of CBF has not been well documented, and one approach to investigate this is to examine its heritability. Our project aimed to examine the heritability of CBF using ASL data from a cohort of community-dwelling older twins (including both monozygotic and dizygotic twin pairs; aged between 65-93 years). We have found:
- The cerebral cortex had higher CBF than subcortical grey matter (GM) regions, and CBF in the GM regions of the anterior cerebral artery (ACA) territory was lower than that of the middle (MCA) and posterior (PCA) cerebral arteries.
- After accounting for the effects of age, sex and scanner, moderate heritability was identified for global CBF, as well as for cortical and subcortical GM and the GM in the major arterial territories.
- Strong genetic correlations were found between CBF in subcortical and cortical GM regions, as well as among the three arterial territories (ACA, MCA, PCA), suggesting a largely convergent genetic control for the CBF in brain GM.
- The moderate heritability of CBF warrants future investigations to uncover the genetic variants and genes that regulate CBF.
- These findings have been summarised in *Frontiers in Aging Neuroscience* (Jiang J et al. *Front Aging Neurosci*. 2019 Jul 2; 11:169. DOI: 10.3389/fnagi.2019.00169).

Funding: John Holden Family Foundation

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

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

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

Aim:

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

Findings:

- Genetic variants located in a locus on chromosome 19, containing the GDF-15 gene, were significantly associated with GDF-15 blood concentration in Sydney MAS and three other international cohorts.

Funding: NHMRC, Thomas Foundation.

Inflammatory markers and brain structure

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

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

Aims:

- Explore the relationships of brain structural indices with the circulating levels of a spectrum of inflammatory markers available in the Sydney Memory and Ageing

Study (MAS), including interleukin (IL)-1β, IL-6, IL-8, IL-10, IL12p70, serum vascular cell adhesion molecule-1 (sVCAM-1), plasminogen activator inhibitor-1 (PAI-1), serum amyloid A (SAA), tumour necrosis factor α (TNFα), C-reactive protein (CRP), and macrophage inhibitory cytokine-1 (MIC-1/GDF15). The aim is to find a robust circulating biomarker of brain structural measures in non-demented older individuals.

- Examine the relationship of MIC-1/GDF15 serum levels with human brain structural measures using multimodal MRI data, in a community-dwelling sample aged 70-90 years over two years.

- Conduct a genome-wide meta-analysis to identify genetic variants of MIC-1/GDF15 serum levels in population-based cohorts, and to test whether these variants influence brain structures and cognitive performance in MAS.

Findings:

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

Funding: NHMRC, John Holden Family Foundation.

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

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

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

Aim:

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

Findings:

- Across the five population cohorts examined, no negative association between total undifferentiated sedentary time and global cognition was found, cross-sectionally nor longitudinally. There is reason to believe that specific types of sedentary behaviour may differentially influence cognition depending on what a person is doing while sitting. These findings were published in *Sports Medicine* (Maasakkers et al. *Sports Med*. 2020 Feb; 50(2):403-413. DOI: 10.1007/s40279-019-01186-7. PMID: 31529300).

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

Parity and the risk of dementia across geographic regions: a COSMIC study

CHeBA staff: Darren Lipnicki, Perminder Sachdev.

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

Aim:

- To expand upon an earlier COSMIC project to determine the association between number of childbirths and risk of dementia for women across various geographic regions.

Findings:

- Across all cohorts, grand multiparous (5 or more childbirths) women had a 47% greater risk of dementia than primiparous (1 childbirth) women, while nulliparous (no childbirth) women and women with 2 to 4 childbirths showed a comparable risk of dementia to primiparous women. However, there were differences associated with geographic region and dementia subtype. Compared to women with 1 to 4 childbirths, grand multiparous women showed a higher risk of dementia in European and Latin America cohorts, while nulliparous women showed a higher risk of dementia in Asian cohorts. Grand multiparity was associated with 6.9-fold higher risk of vascular dementia in European cohorts, whereas nulliparity was associated with a higher risk of nonvascular dementia in Asian cohorts (1.9-fold risk of Alzheimer's disease and 3.5-fold risk of non-Alzheimer, non-vascular dementia). A manuscript has been completed for submission and currently under review.

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

Personality and Total Health (PATH) Through Life project

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

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

Aim:

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

Findings:

- On brain MRI, cortical sulci were examined in detail. On average, sulci were wider in old age participants compared to middle age participants. Differences in sulcal width were generally higher in males than females. Differences in the width of the superior frontal and central sulci were significantly associated with differences in the volume of adjacent local gyri, while age-related differences in the width of lateral and superior temporal sulci were associated with differences in whole brain cortical volume. These findings suggest that sulcal characteristics provide unique information about changes in local and global brain structure in aging (Jin et al, Front Aging Neurosci).

- The relationship between diabetes, BMI and bran volume was examined. Diabetes was most strongly associated with brain volumes. We found evidence of protective reserve from higher brain volumes and that a combination of high BMI and higher blood glucose was particularly concerning for individuals with lower brain volumes (Walsh et al, Eur J Neurol).

- Diabetes and brain structure and function: Type 2 diabetes is associated with smaller right putamen volume and lower Purdue Pegboard scores after controlling for age, sex and intracranial volume. These findings add to the evidence suggesting that higher blood glucose levels, especially type 2 diabetes, may impair brain structure and function.

- Myelin content of the brain's white matte and neuropsychological function: We found that estimated myelin content of the bilateral anterior limb of the internal capsule and left splenium of the corpus callosum were significant predictors of processing speed, even after controlling for socio-demographic, health and genetic variables and correcting for multiple comparisons. We also found significant differences in estimated myelin content between middle-age and older participants in all six white matter tracts. The present results indicate that myelin content, estimated in vivo using a neuroimaging approach in healthy older adults, is sufficiently precise to predict variability in processing speed in behavioural measures (Chopra et al, Neuroimage).

Funding: NHMRC (administered by ANU).

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

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

Other investigators: STROKOG collaborators.

Aims:

- Harmonise shared data from STROKOG studies.

- Perform joint analyses using combined, harmonised data to estimate prevalence of post-stroke cognitive impairment.

- Compare prevalence estimates and profile of post-stroke cognitive impairment across geographical regions and ethnic groups.

- Perform individual participant data (IPD) meta-analysis on harmonised data to investigate the relationship between putative risk factors and cognitive function with greater statistical power.

Findings:

- From our combined sample of 11 hospital-based studies from Africa, Asia, Australia, Europe and USA, overall 45% of post-stroke or TIA participants were impaired in global cognition, and 30 to 35% in different cognitive domains, at 2-6 months after stroke or TIA.

- The degree of impairment was similar in the five cognitive domains (attention & processing speed, memory, language, perceptual motor and frontal executive function).

- The prevalence of impairment in global cognition was similar amongst Whites, Koreans, and Black Americans, and slightly lower in Singaporean Chinese and Black Nigerians; however, the difference was not statistically significant. Additional studies in non-White groups are required to further explore ethno-racial differences in cognitive impairment.

- Diabetes and a history of past-stroke had strong negative effects on cognitive function in all domains; these effects were independent of stroke, age and gender. Hypertension, atrial fibrillation, and smoking had less strong or domain specific negative associations.

- The paper has been published in the journal *Neurology* (Lo et al. *Neurology*. 2019 Dec 10;93(24): e2257-e2271. doi: 10.1212/WNL.0000000000008612. PMID: 31712368 / PMC6937495).

Funding: Vincent Fairfax Family Foundation.

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

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

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

Aim:

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

Findings:

- We have completed analyses on pre- and post-treatment fMRI data for 20 participants. These results showed no statistical differences between the 2 groups using conservative correction for multiple comparisons for regions of interest (ROIs) for the task related and resting state data.

Funding: Alzheimer's Australia Dementia Research Foundation.

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

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

Other investigators: STROKOG collaborators.

Aim:

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

Findings:

- Diabetes, but not prediabetes, is associated with poorer cognitive performance in patients 3-6 months after stroke. A manuscript has been accepted by the journal Stroke. We expect the paper to be published in early 2020.

Funding: Vincent Fairfax Family Foundation.

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

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

Other investigators: Marc Wilkins (Ramaciottti Centre for Genomics, UNSW), Susan Corley (Ramaciottti Centre for Genomics, UNSW)

Aims:

- Undertake a discovery driven RNA sequencing (RNAseq) study to examine age-associated changes in the gene expression profiles of two distinct human brain regions, the dorsolateral prefrontal cortex (DLPFC), and the posterior cingulate cortex (PCC).

- Identify changes in cortical gene expression that may drive changes in neocortical plasticity, as well the excitation-inhibition imbalance known to occur in the ageing human brain.

- Investigate changes in gene expression for candidate biological pathways important in brain ageing including neuroinflammation, neurotransmission and synaptic function.

Findings: Post mortem tissue acquired From 67 control individuals for the two brain regions of interest (DLPFC and PCC). RNA extraction and next generation sequencing were completed in 2019 and preliminary data analyses are being conducted. Further analyses are planned for 2020 with preparation of manuscripts for publication to commence at the end of the year.

Funding: NHMRC.

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

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

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

Aim:

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

Findings:

• Sixty-eight participants (45 females) completed the trial with thirty three participants receiving the active tDCS and cognitive training intervention. Although at the 3 month follow-up, both groups showed large sized memory improvements compared to pre-treatment, CT + Active tDCS did not produce greater memory improvement compared to CT + Sham tDCS. Our study findings raise the possibility that both active and sham tDCS may have enhanced the effects of CT. Based on the observed treatment effects, further study of this combined intervention for improving memory in aMCI is warranted. This manuscript has published in the *Journal of Alzheimer's Disease* (Martin DM, et al. J Alzheimers Dis. 2019 Aug 12; 71(2):503-512. DOI: 10.3233/JAD-190306. PMID: 31424410).

Funding: Thomas Foundation, DCRC-ABC.

White matter hyperintensity extraction pipeline development

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

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

Aim:

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

Findings:

• A fully automated WMH detection and quantification pipeline has been created and it is now online for general neuroimaging research community to download at: https://cheba.unsw.edu.au/research-groups/neuroimaging/pipeline. By April 2020, the pipeline has been downloaded 93 times by 75 institutions.

Funding: NHMRC, John Holden Family Foundation.

APPENDICES

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

-Professor Henry Brodaty AO & Professor Perminder Sachdev AM

APPENDIX A: STAFF LIST

LEADERSHIP

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

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

Angela (Angie) Russell
Centre Manager

ACADEMIC STAFF

Nady Braidy
Research Fellow, Leader Brain Ageing Research Laboratory

Catherine Browning
Postdoctoral Fellow, Sydney Centenarian Study (SCS) Co-ordinator

Anne-Nicole Casey
Postdoctoral Fellow

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

Lynn Chenoweth
Professor of Nursing

Debjani Das
Postdoctoral Fellow, Social Cognitive Change in Late Adulthood (SOCCOG) Study (until 22 February 2019)

Meredith Gresham
Research Fellow, COGNISANCE Project Co-ordinator

Megan Heffernan
Postdoctoral Fellow, Maintain Your Brain Project Coordinator

Tharusha Jayasena
Postdoctoral Fellow, Proteomics Group

Jiyang Jiang
Postdoctoral Fellow, Neuroimaging Group

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

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

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

Yvonne Leung
Postdoctoral Fellow, ICC-Dementia Consortium Co-ordinator (until 28 June 2019)

Darren Lipnicki
Postdoctoral Fellow, COSMIC Consortium Co-ordinator

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

Steve Makkar
Postdoctoral Fellow, CHeBA Consortia (until 30 October 2019)

Karen Mather
Senior Research Fellow, Leader Genetics & Epigenomics Group

Louise Mewton
Senior Research Fellow, UNSW Scientia Program of Research

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

Suraj Samtani
Postdoctoral Fellow, SHARED Project Co-ordinator

Anbupalam (Anbu) Thalamuthu
Postdoctoral Research Fellow

Stephanie Ward
Senior Research Fellow, Clinical Leader, ADNet Registry Project

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

PROFESSIONAL & TECHNICAL STAFF - RESEARCH

Karen Allison
Research Officer, CogSCAN Study Co-ordinator

Suzanne (Suzi) Artiss
Data Manager

Adam Bentvelzen
Research Assistant, Memory and Ageing Study (MAS)

Josephine (Josie) Bigland
Research Assistant (Casual), CHeBA Longitudinal Studies

Russell Chander
Research Assistant (Casual), CHeBA Longitudinal Studies

Tiffany Chau
Research Assistant, Maintain Your Brain Project

Rhiagh Cleary
Research Assistant, Social Cognitive Change in Late Adulthood (SocCog) Study Co-ordinator

John Crawford
Senior Statistician

Karen Croot
Research Officer, CogSCAN Study

Jing Du
Student Assistant (Casual), Neuroimaging Group

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

Elizabeth Haris
Research Assistant, Alcohol Use and Cognition Study

Fleur Harrison
Research Assistant, Sydney Centenarian Study (SCS)

Mahboobeh (Mabi) Hosseini
Research Assistant, CHeBA Biobank

Sri Chandana Kanchibotla
Research Assistant, Genetics & Epigenomics Group

Kristan Kang
Research Manager

Lauren King
Research Assistant, COGNISANCE Project

Forrest Koch
Research Assistant (Casual), Neuroimaging Group

Rebecca Koncz
Research Assistant (Casual), NSW Memory Clinic Network Project (until 26 April 2019)

Yue Liu
Student Assistant (Casual), Neuroimaging Group

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

Naga Sowjanya Mutyala
Research Officer (Casual), Genetics & Epigenomics Group

Min Yee Ong
Research Assistant, CogSCAN Study

Julia Riches
Research Assistant, Sydney Centenarian Study (SCS)

Matilda Rossie
Research Assistant, CogSCAN Study

Juan Carlo San Jose
Health Informatics Specialist
Research Data Management Officer, Maintain Your Brain Project (until 30 November 2019)

Adam Theobald
Research Officer, Sydney Centenarian Study (SCS) Coordinator (until 9 April 2019)

Virginia (Ginny) Winter
Research Assistant, Memory and Ageing Study (MAS)

PROFESSIONAL & TECHNICAL STAFF - SUPPORT

Kim Babbage
Event & Engagement Officer

Alexandra (Alex) Bentley
Administrative Assistant

Sophia Dean
Administrative Officer

Heidi Douglass
Marketing, Communications & Project Officer

Celia Falato
Administrative Assistant

Suzanne (Suzi) Forrester
Administrative Assistant, OATS

Michelle Savignano
Web Coordinator

CONJOINT & ADJUNCT STAFF

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

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

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

Charlene Levitan
Adjunct Associate Lecturer (2015-2019)

Anne Poljak
Lecturer, Protein Chemist, Leader Proteomics Group

Julian Trollor
Professor, Leader Neuroinflammation Group

VISITING ACADEMICS

Bernhard Baune
Visiting Professorial Fellow (January 2013 - present)

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

CHeBA HONARARY RESEARCH FELLOWS

Nicola Armstrong

Simone Reppermund

Haobo Zhang

APPENDIX B: EXTERNAL APPOINTMENTS

Dr Nady Braidy

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

Professor Henry Brodaty

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

Dr Anne-Nicole Casey

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

Dr Vibeke Catts

Member, Behavior Genetics Association and Australian Society for Medical Research

Professor Lynn Chenoweth

- Adjunct Professor, School of Nursing, Faculty of Medicine, The University of Notre Dame Australia, 2017-2019, continuing
- Adjunct Professor, School of Nursing, Faculty of Health, Macau University, Macau, 2015-2019, continuing.
- Editorial board for Older People Nursing, International Journal of Older People Nursing, Worldviews on Evidence-based Nursing, Annals of Alzheimer's and Parkinson's Disease, Neurodegenerative Disease Management
- Board membership: AMAN Pty Ltd. (Australian Multicultural Aged Nursing) Lebanese Muslim Association, Sydney; The Notre Dame University Australia, Sydney. Nursing Board.

- Expert group membership:
  - Optimising an evidence-based intervention to improve care for Ambulatory Care Sensitive conditions in nursing homes. CIA Downs M (Bradford University, UK).
  - Clinical Guidelines for evidence-based deprescribing for acetylcholinesterase inhibitors and memantine in people with dementia. CIA Hilmer S (University of Sydney), CIB Rockwood K (Dalhousie University).
  - Mapping the journey in residential aged care for residents with dementia. CIA Scherer S (NARI/Royal Freemasons, Victoria).
  - Non-drug care pathway (for behaviours in dementia). CIA Vickers J (Wicking Dementia Research Centre Tasmania), in collaboration with Care Visions China.
  - Dementia Clinical Quality Indicators Registry Project. CIA McNeill J (School of Public Health and Preventive Medicine, Monash University).
  - The Notre Dame University Australia, Sydney. Primary Health Care Curriculum Committee.

Dr Nicole Kochan

- Honorary Associate, Department of Psychology, Macquarie University (2007-present)
- Australian Psychological Society Approved Supervisor (College of Clinical Neuropsychologists)
- Member, APS College of Clinical Neuropsychologists (CCN)
- Member, American Association for the Advancement of Science (AAAS)
- Member, International Society to Advance Alzheimer Research and Treatment (ISTAART)
- Member, Women in Research Network, UNSW

Dr Rebecca Koncz

- Senior Lecturer, Concord Clinical School, Sydney Medical Program, University of Sydney (2018-present)
- Neuropsychiatrist, Sydney Local Health District (2017-present)
- Conjoint Associate Lecturer, School of Psychiatry, UNSW Sydney (2015-present)
- Fellow, Royal Australian and New Zealand College of Psychiatrists (RANZCP) (2017-present)
- Member, “Motivation” taskforce, The Human Affectome Project (2017-present)
- Member, Physical Health in Mental Health expert group, NSW Ministry of Health (2019-ongoing)

Dr Mari Kondo

- Visiting Fellow at the Australian National University (2018-present)
- Member of Australasian Neuroscience Society (2019-present)

Dr Teresa Lee

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

Dr Matthew Lennon

- Member, Australian and New Zealand Association of Neurologists
- Member, Australian Medical Association
- Conjoint associate lecturer, University of New South Wales
- Editorial Board, Journal of Alzhiemer's Disease

Dr Yvonne Leung

- Adjunct associate lecturer (July 2019-present)

Dr Karen Mather

- Visiting Senior Research Officer, Neuroscience Research Australia (NeuRA)
- Member, Australian Association Gerontology
- Member, ISTAART (Alzheimer’s Association of the International Society to Advance Alzheimer Research & Treatment)

Dr Louise Mewton

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

Dr Adith Mohan

- Consultant Neuropsychiatrist, Neuropsychiatric Institute, Prince of Wales Hospital
- Senior Lecturer, School of Psychiatry, UNSW Sydney

- Fellow, Royal Australian and New Zealand College of Psychiatrists (RANZCP)
- Committee member, Section of Neuropsychiatry, RANZCP

Dr Katya Numbers

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

Dr Matthew Paradise

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

Dr Anne Poljak

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

Professor Perminder Sachdev

- Scientia Professor, Neuropsychiatry (previously Professor of Neuropsychiatry, 1999-2009), School of Psychiatry, UNSW (2009- present)
- Clinical Director, Neuropsychiatric Institute, Prince of Wales Hospital, Sydney (1987-present)
- Visiting Fellow, Australian National University (2009-present)
- Visiting Professor, National University of Korea, Seoul (2014-2018)
- Visiting Professor, Jiao Tong University, Shanghai (2018-present)
- Committee Member of the WHO's Expert Advisory Committee for the Global Dementia Observatory (GDO)
- Executive Member of the International Society of Vascular Behavioural and Cognitive Disorders (VASCOG) (2012-present)
- Member, Scientific Program Committee, Alzheimer's Association International Conference
- Member, Expert Advisory Panel, NHMRC National Institute for Dementia Research
- Founding Executive Committee Member of the Tourette Syndrome Association of Australia (1989-present)
- Chair, Medical Advisory Committee of the Tourette Syndrome Association of Australia (1996-present)
- Fellow of the Australian Academy of Health & Medical Sciences (2015-present)
- Fellow of the NHMRC Academy 2011 (2011-present)
- Member of the NHMRC Assigner's Academy (2012-present)
- Invited Member, Task Force of the International League Against Epilepsy (ILAE) Neuropsychobiology Commission (2011-present)
- Editorial board for the following journals: Neuropsychiatric Disorders and Treatment, Acta Neuropsychiatrica, Current Opinion in Psychiatry, Middle Eastern Journal of Ageing, Middle Eastern Journal of Psychiatry & Alzheimer's, Brain and Mind Matters, The Open Neuroimaging Journal, American Journal of Geriatric Psychiatry, International Psychogeriatrics
- Deputy Director, Alzheimer's Disease Network (ADNeT)
- Committee Member, Ageing Futures Institute, UNSW Sydney
- Convenor of the XXIV World Congress of Neurology (WCN2019). 27-31 Oct 2019; Dubai, UAE

Professor Julian Trollor

- Chair, Intellectual Disability Mental Health, School of Psychiatry, UNSW Sydney (2009-present)
- Senior Medical Practitioner (Academic): Professor in Neuropsychiatry and Intellectual Disability, South Eastern Sydney Local Health District, Sydney (2009-present)
- Appointed to NSW Institute of Psychiatry Board (2012-present)
- Unconditional Registration, the New South Wales Medical Board, currently Australian Health Practitioner Regulation Agency
- Fellow, the Royal Australian and New Zealand College of Psychiatrists (RANZCP)
- Founder, Neuropsychiatry Section, RANZCP
- Co-Founder & Executive Member, Section of Psychiatry of Intellectual and Developmental Disability, RANZCP
- Executive Committee Member, NSW Health Agency for Clinical Innovation, Intellectual Disability Health Network
- Expert consultant for ASD Health Pathways Development
- Member, Research and Development Committee, NSW Health Agency for Clinical Innovation, Intellectual Disability Health Network
- Executive Member, NSW Ministry of Health; Department of Family and Community Services, Joint Committee Intellectual Disability Mental Health
- NSW Ombudsman Panel of Expert Advisers
- Visiting Senior Research Fellow, Neuroscience Research Australia

- Executive Member & past Secretary & Treasurer, International Neuropsychiatric Association
- International Member, Neuroleptic Malignant Syndrome Information Service
- Member in the following organisations: Australasian Society for the Study of Intellectual Disability; Faculty of Psychiatry of Old Age & Faculty of Adult Psychiatry, RANZCP; National Association for the Dually Diagnosed; Joint Mental Health and Disability Committee, NSW Health and Ageing Disability and Home Care, NSW Government Family and Community Services; NSW Council for Intellectual Disability; Society for the Study of Behavioural Phenotypes; Australian Medical Association; Australian Salaried Medical Officers Federation; International Association for the Scientific Study of Intellectual Disability; Intellectual Disability Advisory Committee; Health Education and Training Institute Higher Education Governing Council HETI
- Vice President & Member, Australian Association of Developmental Disability Medicine
- Neurocognitive Disorder Working Group, Diagnostic Manual for Intellectual Disability
- Committee Member, RANZCP, New National Guideline for the Assessment and Diagnosis of Autism Spectrum Disorders in Australia
- Past & Current Reviewer for the following journals: Acta Neuropsychiatrica, Alzheimer Disease & Associated Disorders, Archives of General Psychiatry, Australasian Psychiatry, Australian and New Zealand Journal of Psychiatry, BMC Psychiatry, BMJ Open, Brain, British Journal of Developmental Disabilities, British Journal of Psychiatry, Comprehensive Psychiatry, Current Psychiatry Reviews, European Journal of Neurology, International Journal of Geriatric Psychiatry, International Psychogeriatrics, JARED, Journal of Attention Disorders, Journal of Geriatric Psychiatry and Neurology, Journal of Intellectual Disability Research, Neurology, Neuro-Psychopharmacology & Biological Psychiatry, Psychiatry Research – Neuroimaging, The Journal of Psychosomatic Research, The Medical Journal of Australia, Therapeutic Advances in Chronic Disease
- Associate Editor for Journal Intellectual & Developmental Disability
- Editorial Board of Advances in Mental Health and Intellectual Disabilities Journal
- Reviewer for the following funding bodies: NHMRC, Australia Research Council, Alzheimer's Australia, Alzheimer's USA, Welcome Trust, Neuroscience Research Grants, Pfizer, Rotary Health Foundation, The Dunhill Medical Trust
- Reviewer & Contributor for the following bodies policy documents: NSW Health; NSW Health, The NSW Strategic Framework and Workforce Plan for Mental Health 2018-2022; NSW Agency for Clinical Innovation; Clinical Care of People who might be Suicidal Education and Training Initiative (COPSETI); Podcasts 2017; Health Education and Training Institute (HETI)
- Expert Consultant for Mental Health Regulation 2019
- Expert Consultant on the Royal Commission into Violence, Abuse, Neglect and Exploitation of People with Disability

APPENDIX C: POSTGRADUATE STUDENTS

CURRENT

Andrew Affleck

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

Abdullah Alqarni

- Sex differences in white matter hyperintensities
- PhD student
- School of Psychiatry, Faculty of Medicine, UNSW
- Supervisors: Associate Professor Wei Wen, Dr Jiyang Jiang, Professor Perminder Sachdev

Russell Chander

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

Xi (Sophie) Chen

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

Jing Du

- Investigation of cerebrovascular burden using neuroimaging
- PhD Student
- School of Psychiatry, Faculty of Medicine, UNSW
- Supervisors: Professor Wei Wen, Dr Jiyang Jiang

Lucia (Premilla) Chinnappa-Quinn

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

Heidi Foo

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

Fleur Harrison

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

Rene Jezewski

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

Fatemeh Khorshidi

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

Rebecca Koncz

- The relative genetic and environmental contributions to amyloid deposition in the brains of older adults: amyloid imaging using the twin design
- PhD student
- School of Psychiatry, Faculty of Medicine, UNSW
- Supervisors: Professor Perminder Sachdev, Professor Christopher Rowe (Austin Health, Melbourne), A/Prof Wei Wen, Dr Anbupalam Thalamuthu

Jessica Lazarus

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

Matthew Lennon

- Risk and preventive factors in Dementia – An international harmonization of longitudinal studies
- Masters by Research student
- School of Psychiatry and St Vincents Clinical School, Faculty of Medicine, UNSW
- Supervisors: Professor Perminder Sachdev, Dr John Crawford, Dr Ben Lam

Yue Liu

- Contribution of cerebrovascular and Alzheimer-type pathology in the aetiology of neurocognitive disorders
- PhD student
- School of Psychiatry, Faculty of Medicine, UNSW
- Supervisors: Professor Perminder Sachdev, Dr Nady Braidy, Dr Anne Poljak, Associate Professor Wei Wen

Janet Mitchell

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

Adith Mohan

- Influence of ageing on the human brain transcriptome
- PhD student
- School of Psychiatry, Faculty of Medicine, UNSW
- Supervisors: Professor Perminder Sachdev, Dr Karen Mather, Dr Anbupalam Thalamuthu

Matthew Paradise

- Neuroimaging of cerebrovascular disease
- PhD student

- School of Psychiatry, Faculty of Medicine, UNSW
- Supervisors: Professor Perminder Sachdev, Associate Professor Wei Wen

Mary Revelas (nee Gianniosis)

- The genetics of exceptional longevity and successful ageing
- PhD student
- School of Psychiatry, Faculty of Medicine, UNSW
- Supervisors: Dr Karen Mather, Professor Perminder Sachdev, Dr Anbupalam Thalamuthu

Upul Senanayake

- Computer aided early identification system for Individuals at risk of dementia
- PhD student
- School of Computer Science and Engineering, Faculty of Engineering, UNSW
- Supervisors: Professor Arcot Sowmya, Dr Laughlin Dawes, Professor Perminder Sachdev and A/ Professor Wei Wen

Annette Spooner

- Early Detection of Alzheimer's Disease using Machine Learning
- PhD student
- School of Computer Science and Engineering, Faculty of Engineering, UNSW
- Supervisors: Professor Arcot Sowmya, Professor Perminder Sachdev, Associate Professor Gelareh Mohammadi

Marina Ulanova

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

Gurjeet Kaur Virk

- Development of blood biomarkers for early onset Alzheimer's disease using discovery proteomics
- Scientia PhD student
- School of Psychiatry, Faculty of Medicine, UNSW
- Supervisors: Professor Perminder Sachdev, Dr Anne Poljak, Dr Nady Braidy

Jacqueline Wesson

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

Mark Yates

- Does the dementia care in hospitals program reduce the incidence of hospital acquired adverse events in patients with cognitive impairment?
- PhD student
- School of Psychiatry, Faculty of Medicine, UNSW
- Supervisors: Professor Henry Brodaty

COMPLETED

Matthew Wong

- Natural variation in the human plasma lipidome signature using mass spectrometry: relevance to healthy ageing
- PhD student
- School of Psychiatry, Faculty of Medicine, UNSW
- Supervisors: Dr Nady Braidy, Professor Perminder Sachdev, Dr Anne Poljak
- Thesis finalised in Dec 2019

Helen Wu

- The role of peripheral blood microRNAs as biomarkers of early Alzheimer's disease
- PhD student
- School of Psychiatry, Faculty of Medicine, UNSW
- Supervisors: Dr Karen Mather, Professor Perminder Sachdev, Professor Henry Brodaty, Dr Anbupalam Thalamuthu
- PhD conferred 2019

APPENDIX D: AWARDS & PROMOTIONS

Dr Nady Braidy

Formally appointed as Senior Research Fellow at UNSW Sydney.

Dr Catherine Browning

Promoted as the Sydney Centenarian Study Coordinator and Postdoctoral Fellow.

Dr Vibeke Catts

Awarded a travel grant from the Twin Registry Australia (TRA) to attend the IGEMS Consortia Meeting and the BGA Annual Conference (June 2019; Stockholm Sweden). The travel grant also enabled further training in statistics for one week at the TRA (Oct 2019; Melbourne, Australia).

Mr Russell Chander

Awarded a $5000 grant (Dec 2019–Dec 2020) at the Society for Mental Health Research Conference 2019. This award was for a project pitch competition ("Improving our science communication about neuroimaging" with Professor Dan Hermens (University of the Sunshine Coast) as the lead investigator).

Dr Michael Connors

Received the New Investigator Award for the study of neuropsychiatric symptoms in neurodegenerative disease, International Society to Advance Alzheimer's Research and Treatment (ISTAART) Neuropsychiatric Syndromes (NPS) Professional Interest Area (PIA), 2019.

Ms Fleur Harrison

Awarded in Dec 2019 – joint recipient of the 2020 Josh Woolfson Memorial Scholarship ($10,000/year), which supports research looking at the modifiable risk factors of Alzheimer's disease as well as developing intervention strategies for risk reduction.

Dr Rebecca Koncz

Formally appointed as a Clinical Academic, Sydney Local Health District.

Dr Matthew Lennon

Awarded the Sir John Monash Foundation Scholarship to go and complete a Masters of Neuroscience in Oxford (Oct 2020–Oct 2021). Dr Lennon will be taking a year off his PhD to complete this.

Dr Yvonne Leung

Awarded the Mostyn Family Foundation Grant ($17,000) for the project "Diet, gut microbiome and exceptional ageing".

Dr Louise Mewton

Awarded the UNSW-USyd collaborative seed-funding grant.

Dr Matthew Paradise

Awarded the Josh Woolfson Memorial Scholarship, UNSW ($10,000/year 2018–ongoing).

Dr Annette Spooner

Finalist in the 2019 UNSW 3MT Competition: won the School of Computer Science and Engineering heat, runner up in the Faculty of Engineering heat and progressed to the University final.

Professor Julian Trollor

Awarded RANZCP Senior Research Award 2019.

APPENDIX E: RESEARCH GRANTS & FUNDING

GRANTS

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: RG19162

Investigator/s: Prof Claudia Cooper, Prof Helen Kales, Prof Henry Brodaty**, Dr Penny Rapaport, Dr Miguel Rio, Prof Anne Matie Minihane, Prof Irene Petersen, Dr Julie Barber, Dr Iain Lang, Ms Rachael Hunter, Dr Zuzana Walker, Dr Nicholas Bass, Dr Natalie Marchant, Dr Jonathan Huntley, Dr Jennifer Wenborn, Dr Joanne Rodda, Prof Paul Higgs, Dr Kate Walers, Dr Sarah Morgan-Trimmer, Dr Elisa Aguirre, Prof Karen Ritchie, Ms Alexandra Burton

Duration: 5 years: 2019-2023

Total Funds: £3,884,409 (**AUD12,603)

UNSW Scientia Fellowship Research Support Program

Funding Source: UNSW Sydney

Project ID: PS416170-A

Investigator/s: Dr Louise Mewton

Duration: 4 years: January 2019-January 2023

Total funds: $160,000

Innovative approaches to the application of nanotechnology for specific diagnosis and treatment of the dementias

Funding Source: Dementia Australia Research Foundation (DARF) – Yulgilbar Innovation Grant

Project ID: RG181392

Investigator/s: Prof Perminder Sachdev, Prof Richard Tilley, Scientia Prof Justin J Gooding, Dr Andre Bongers, Prof Ashley Bush, Laureate Prof Frank Caruso, Dr Nady Braidy, Dr Lucy Gloag, Dr Karen Mather, Dr Anne Poljak, A/Prof Wei Wen

Duration: 3 years: 1 March 2019-1 March 2022

Total Funds: $1,000,000

Understanding cognitive disorders in relation to cerebrovascular disease in an international collaborative effort: The Stroke and Cognition (STROKOG) Consortium

Funding Source: NHMRC

Project ID: RG180366

Investigator/s Prof Perminder Sachdev, A/Prof Wei Wen, Dr John Crawford

Duration: 3 years: 2019-2021

Total Funds: $649,205

CO-desiGning demeNtia dIagnoSis ANd post-diagnostic CarE (COGNISANCE)

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

Project ID: RG181644

Investigator/s: Prof Henry Brodaty, A/Prof Lee-Fay Low, Prof Perminder Sachdev, Prof Yun-Hee Jeon, Dr Lyn Phillipson

Duration: 3 years: 2019-2021

Total Funds: $742,041

Social Health And REserve in the Dementia patient (SHARED)

Funding Source: NHMRC

Project ID: RG181672

Investigator/s: Prof Henry Brodaty, Prof Perminder Sachdev

Duration: 3 years: 2019-2021

Total Funds: $724,254

Lipids in brain ageing and cognitive disorders

Funding Source: Rebecca Cooper Foundation

Project ID: RG182333

Investigator/s: Dr Anne Poljak, Prof Perminder Sachdev

Duration: 2 years: 2019-2020

Total Funds: $100,000

Online Alcohol Prevention

Funding Source: University of Sydney/UNSW Sydney Mental Health and Wellbeing - Early Intervention and Prevention (Older People) Seed Funding Scheme

Project ID: RG192547

Investigator/s: Dr Louise Mewton, Dr Matthew Sunderland, A/Prof Nicola Newton, A/Prof Cath Chapman, Dr Kirsten Morley,

Prof Andrew Baillie, Prof Maree Teesson, Prof Perminder Sachdev, Prof Paul Haber, Dr Alison Mahoney

Duration: 1 year: 2019

Total Funds: $20,000

The Brain Ageing Research Laboratory (BARL) for collaborative research

Funding Source: UNSW / Research Infrastructure Scheme (RIS)

Project ID: RG182773

Investigator/s: Prof Perminder Sachdev, Prof Henry Brodaty, Dr Nady Braidy, Dr Anne Poljak, Dr Karen Mather, … Prof Julian Trollor, A/Prof Wei Wen, …, Dr Adith Mohan, Dr Lucy Gloag, Dr Tharusha Jayasena, et al

Duration: 1 year: 2019

Total Funds: $179,167

A novel cellular approach for early detection of Alzheimer's disease, modelling and developing diagnostics

Funding Source: UNSW Medicine Neuroscience, Mental Health and Addiction Theme and SPHERE Clinical Academic Group Funding (Mindgardens Seed Funding Grant)

Project ID: PS50645

Investigator/s: Dr Nady Braidy, A/Prof Kuldip Sidhu, Prof Perminder Sachdev

Duration: 1 year: 2019

Total Funds: $20,000

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

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

Mapping alcohol consumption from adolescence to old age: an integrated analysis of Australian longitudinal cohort data

Funding Source: Society for Mental Health Research (SMHR)/Early Career Research Fellowship

Project ID: RG180987

Investigator/s: Dr Louise Mewton

Duration: 1 year: 2019

Total Funds: $20,000

High value data collections publishing scheme

Funding Source: UNSW Sydney / High Value Data Collections Publishing Scheme

Project ID: RG192941-A

Investigator/s: Dr Kristan Kang, A/Prof Wei Wen

Duration: 1 year: 2019

Total Funds: $14,000

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 Brants

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

The Australian Dementia Network (ADNet): Bringing together Australia's dementia stakeholders

Funding Source: NHMRC

Project ID: RG181548 / RG191015

Investigator/s: Prof Christopher Rowe, Prof Perminder Sachdev**, Prof Sharon Naismith, Prof Michael Breakspear, Prof Henry Brodaty, Prof Kaarin Anstey, Prof Ralph Martins, Dr

Stephanie Ward, Prof James Vickers, Prof Colin Masters

Duration: 5 years: 1 July 2018-30 June 2023

Total Funds: $18,000,000 (**$732,439 / $183,109 – total $915,548)

Clarify risk and protective factors for dementia with the Interplay of Genes and Environment in Multiple Studies (IGEMS) Consortium

Funding Source: National Institute on Aging

Project ID: RG182556

Investigator/s: Prof Nancy Pedersen, Dr Margaret Gatz, Dr Vibeke Catts, Prof Perminder Sachdev

Duration: 5 years: July 2018-June 2021

Total Funds: USD40,534.34

BRAIN-MEND: biological resource analysis to identify new mechanism and phenotypes in neurodegenerative diseases

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

Project ID: RG173345

Investigator/s: Prof Naomi Wray, Dr Nicola Armstrong, A/Prof Ian Blair, A/Prof John Kwok, A/Prof Simon Laws, Dr Karen Mather**, Dr Allan McRae, Prof George Mellick, Prof Perminder Sachdev

Duration: 3 years: 2018-2020

Total Funds: $849,967 (**$42,154)

Maintain Your Brain

Funding Source: NHMRC

Project ID: RG142234

Investigator/s: Prof Henry Brodaty**, A/Prof Michael Valenzuela, Prof Perminder Sachdev, Prof John McNeil, Prof Anthony Maeder, Prof Nicola Lautenschlarger, Prof Louisa Jorm, Prof Maria Fiatarone Singh, Prof Kaarin Anstey, Prof Gavin Andrews

Duration: 3 years: 2018-2020

Total Funds: $12,818,309 (**$4,272,769)

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

Funding Source: Australian Rotary Health

Project ID: RG180380

Investigator/s: Dr Louise Mewton, A/Prof Tim Slade, Prof Maree Teesson, A/Prof Nicola Newton, Dr Cath Chapman, Dr Louise Birrell

Duration: 3 years: 2018-2020

Total Funds: $209,829

Ageing and Cognition Clinics: A state-wide harmonised approach

Funding Source: UNSW Medicine Neuroscience, Mental Health and Addiction Theme and SPHERE Clinical Academic Group Funding (Mindgardens Seed Funding Grant)

Project ID: PS45977

Investigator/s: Prof Perminder Sachdev, Prof Henry Brodaty, Prof Sharon Naismith, A/Prof Peter Gonski, Dr Danielle Lasschuit, Dr Rowena Mobbs

Duration: 1 year: April 2018-April 2019

Total Funds: $20,000

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

Funding Source: National Institute on Aging (NIA) | National Institutes of Health (NIH)

Project ID: RG172507

Investigator/s: Prof Perminder Sachdev, Prof M Ganguli, Prof Karen Ritchie, Prof Ki Woong Kim, Prof Richard Lipton, Prof Ron Petersen

Duration: 5 years: 15 September 2017-30 June 2022

Total Funds: USD2,573,572

Cross-comparison, validation and performance of computerised neuropsychological assessment devices in the evaluation of mild cognitive impairment and dementia (CogSCAN)

Funding Source: NHMRC

Project ID: RG163145

Investigator/s: Dr Nicole Kochan

Duration: 3 years: 2017-2020

Total Funds: $700,482

Social cognitive change in late adulthood (SoCOG)

Funding Source: Australian Research Council (ARC)

Project ID: RG170732

Investigator/s: Prof Julie Henry, Prof Perminder Sachdev, Dr Karen Mather

Duration: 4 years: 2017-2020

Total Funds: $323,250

Infrastructure Support for the Centre for Healthy Brain Ageing (CHeBA)z3031

Funding Source: Black Dog Institute/NSW Health Medical Research Support Program

Project ID: RG170787

Investigator/s: Prof Perminder Sachdev, Prof Henry Brodaty

Duration: 3 years: July 2017-June 2020

Total Funds: $377,086

Modulation of SIRT2 through upregulation of NAD+ anabolism to promote lifespan

Funding Source: ARC - DECRA

Project ID: RG161166A | RG161166

Investigator/s: Dr Nady Braidy

Duration: 3 years: 2017-2019

Total Funds: $372,000

Involvement of SIRT3 and related energy metabolite changes in the Alzheimer brain

Funding Source: Alzheimer's Australia Dementia Research Foundation Dementia (AADRF)/Dementia Grants Program

Project ID: RG170876

Investigator/s: Dr Tharusha Jayasena, Prof Perminder Sachdev, Dr Anne Poljak, Dr Naidy Braidy

Duration: 2 years: 2017-2019

Total funds: $50,000

Slowing progression of Alzheimer's disease by modulating the kynurenine pathway

Funding Source: NHMRC

Project ID: RG171146-A

Investigator/s: Dr Nady Braidy**, Dr Arne Ittner

Duration: 3 years: 2017-2019

Total Funds: $211,384 (**$10,000)

Risk factors, early diagnosis and effective interventions for neurocognitive disorders

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

Project ID: RG141685

Investigator/s: Prof Perminder Sachdev, Prof Henry Brodaty, Prof Gavin Andrews

Duration: 5 years: 2016-2020

Total Funds: $6,782,730

Understanding the molecular control of human neurogenesis in health and in schizophrenia

Funding Source: UNSW Sydney Vice-Chancellor's Postdoctoral Fellowship – Research Support

Project ID: RG152485

Investigator/s: Dr Mari Kondo

Duration: 3 years: 2016-2018*

Total Funds: $30,000

*Extended to 22 October 2021

BRIDGET: Brain imaging, cognition, Dementia and next generation GEnomics: a Transdisciplinary approach to search for risk and protective factors of neurodegenerative disease

Funding Source: NHMRC NIDR-EU JPND Co-funded Project Grant

Project ID: RG152067

Investigators: Prof Perminder Sachdev, Dr Karen Mather, Dr Anbupalam Thalamuthu, A/ Prof Wei Wen, Dr Nicola Armstrong

Duration: 3 years: 2016-2018*

Total Funds: $1,081,489

*Extend to 31 December 2020

A European DNA bank for deciphering the missing heritability of Alzheimer's disease (EADB)

Funding Source: NHMRC NIDR-EU JPND Co-funded Project Grant

Project ID: RG152100

Investigators: Prof Perminder Sachdev, Dr Karen Mather, Dr Anbupalam Thalamuthu, Dr Nicola Armstrong, Prof Henry Brodaty

Duration: 3 years: 2016-2018

Total Funds: $1,556,995*

*Extended to 31 December 2020

Apathy in older community-dwelling persons: assessment, investigation, differentiation

Funding Source: Alzheimer's Australia Dementia Research Fund (AADRF)/DCRC Early Diagnosis and Prevention Shared Grant – PhD Scholarship for Ms Fleur Harrison

Project ID: RG161424
Investigator/s: Prof Henry Brodaty (Supervisor), Ms Fleur Harrison
Duration: 4 years: 2016-2019*
Total Funds: $60,000*
*Extended to 31 December 2023

Evaluating the effectiveness and cost effectiveness of Dementia Care Mapping (DCM) to enable person-centred care for people with dementia and their carers: a UK cluster randomised controlled trial in care homes (DCM EPIC trial)

Funding Source: Leeds Beckett University
Project ID: RG172452
Investigator/s: Prof Lynn Chenoweth
Duration: 2 years: 2016-2018*
Total Funds: $9,716
*Extended to 2019

CRE in cognitive health: evidence, intervention and population modelling

Funding Source: NHMRC
Project ID: RG173231-A** / RG173231
Investigator/s: Prof Kaarin Anstey, Prof Nicola Lautenschlager, Prof Perminder Sachdev**, Prof Ester Cerin, A/Prof Jonathan Shaw, A/Prof Nicholas Cherbuin, Dr Kathryn Ellis, Dr Ian McRae, Prof Linda Clare
Duration: 5 years: 2015-2020
Total Funds: $2,499,871 (**$147,322 – 2017-18*)
*Extended to 31 December 2019

PHILANTHROPIC

Mapping Neuropathology in Centenarians with Dementia

Funding Source: Sachdev Foundation
Project ID: PS55062_PS55172
Awardee/s: Prof Perminder Sachdev
Duration: 1 year: 2019-2020
Total Funds: $45,000

New therapeutic strategies for the treatment of Alzheimer's disease

Funding Source: Biospecialties Australia Pty Ltd
Project ID: PS44710_PS44672
Awardee/s: Dr Naidy Braidy
Duration: 2 years: 2017-2018*
Total Funds: $25,000
*Extended to 31 Dec 2019

The Montefiore Chair of Healthy Brain Ageing at UNSW

Funding Source: Montefiore
Project ID: PS34587_PS34590
Awardee/s: Prof Henry Brodaty
Prof Perminder Sachdev
Duration: 5 years: 2017-2021
Total Funds: $529,183

The CHeBA Cerebral Small Vessel Disease (SVD) Fund

Funding Source: John Holden Family Foundation
Project ID: PS41604_PS41625
Awardee/s: Prof Perminder Sachdev
Duration: 6 years: 2016-2020
Total Funds: $600,000

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

Funding Source: Henroth Investments Pty Ltd
Project ID: PS38235_PS38252
Awardee/s: Prof Perminder Sachdev
Prof Henry Brodaty
Duration: 5 years: 2016-2020
Total Funds: $90,000
Funding Source: Sachdev Foundation
Project ID: PS38235_PS38252
Awardee/s: Prof Perminder Sachdev
Prof Henry Brodaty
Duration: 3 years: 2016/17-2018/19
Total Funds: $124,000
Funding Source: Vincent Fairfax Family Foundation
Project ID: PS42069_PS42704
Awardee/s: Prof Perminder Sachdev
Prof Henry Brodaty
Duration: 5 years: July 2015- June 2019
Total Funds: $500,000
Funding Source: The Yulgilbar Foundation
Project ID: PS38235_PS38252
Awardee/s: Prof Perminder Sachdev
Prof Henry Brodaty
Duration: 5 years: July 2015-June 2019
Total Funds: $250,000

The Thomas Foundation Grant

Funding Source: The Thomas Foundation
Project ID: PS34586_PS34589
Awardee/s: Prof Henry Brodaty
Prof Perminder Sachdev
Duration: 5 years: 2011-2015*
Total Funds: $1,000,000
*Extended to 31 December 2019

OTHER

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: $426,257*
*As at 31 December 2019

Centre for Healthy Brain Ageing Event & Sponsorship Fund

Funding Source: Miscellaneous
Project ID: PS33379_PS33397
Awardees: Prof Henry Brodaty
Prof Perminder Sachdev
Duration: Ongoing
Total Funds: $3,436*
*As at 31 December 2019

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: $97,299*
*As at 31 December 2019

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: $139,665*
*As at 31 December 2019

APPENDIX F: STATEMENT OF IN-KIND CONTRIBUTIONS

Aria Restaurant Sydney

Anthony Glick Photography Destination Towels

Aoyuan International

Austin Ware Surf Coaching

Australian Healthy Food Guide, Next Media

Bates Smart

Bistecca

Bounce Australia

Brain Snacks

Carman's Fine Foods

Chiosco by Ormeggio

Dripping Wet Surf Co

FDC Construction & Fitout

Fine Fettle Foods

Hurley

KPMG Sydney

Manly Kayak Centre

Monster Health Foods

Prevention Australia, Next Media

Photoscenic

Queenscliff Surf Lifesaving Club (QSLSC)

Samsonite

Slim Secrets

Sprout Daily

Surfyogis

The Bucket List

The Happy Snack Company

Think Products (Munch)

Three Blue Ducks

Thunder Jet Boat Sydney

APPENDIX G: STATEMENT OF FINANCIAL PERFORMANCE

STATEMENT OF FINANCIAL PERFORMANCE FOR THE YEAR ENDED 31 DECEMBER 2019

	Notes	2019 $	2018 $
Funds			
Research Revenue		4,713,144	3,592,567
Donations		684,568	922,881
Fees		-	-
Faculty Funds	3	-	-
UNSW Contribution - Competitive	1	388,199	40,164
UNSW Contribution - Strategic	2	-	-
Sundry Other Revenue		13,012	59,980
Total Funds		5,798,923	4,615,591
Costs			
People Costs		4,375,008	3,318,824
Scholarship Stipends		56,717	92,921
Contract & Consulting Services		159,927	1,124,527
Repairs and Maintenance		-	9
Consumables		130,607	116,534
Travel		87,583	83,889
Equipment		165,446	50,064
Entertainment		*3,571*	*2,023*
Marketing		*3,644*	*5,791*
Overheads		*1,805*	*1,334*
Other Expenses		*361,924*	*45,270*
Interest Expense		-	-
Other Expenses		370,944	54,418
Internal Expense		208,211	141,669
Total Costs		5,554,442	4,982,854
Total Costs - Report Variance			
Operating result		244,481	(367,263)
Opening Balance		3,018,453	3,385,716
Closing Balance		3,262,934	3,018,453

Notes to the Statement of Financial Performance

1. UNSW Contribution - Competitive relates to funding awarded to CHEBA from UNSW through various competitive schemes supporting research activities and infrastructure.
2. UNSW Contribution - Strategic relates to funding provided to CHEBA from UNSW as a strategic investment in the centre's research activities.
3. Faculty Funds - Operating funds provided by the faculty are budget allocations, with no revenue transferred to CHEBA.

APPENDIX H: PUBLICATIONS

Book Chapters

Braidy N, Poljak A, Sachdev PS. Nicotinamide adenine dinucleotide (NAD+) in ageing. In: Gu D, Dupre ME (Eds) Encyclopedia of Gerontology and Population Aging. Springer International Publishing: Cham, Switzerland. 2019; 1-10. ISBN: 978-3-030-22009-9. DOI: 10.1007/978-3-319-69892-2_1035-1.

Chenoweth L, Williams A. Situating Nursing, Contexts of Care: Working in the aged care sector. In: Crisp J, Douglas C, Rebeiro G, Waters D (Eds) Potter & Perry's Fundamentals of Nursing. 2019; In press.

Cvejic RC, Trollor JN, Hocking DR. Fragile X-associated tremor ataxia syndrome In: Hocking DR, Bradshaw JL, Fielding J (Eds) Degenerative Disorders of the Brain, 1st edition. 2019: pp.143-162. Routledge: London, UK. ISBN: 9781351208918. DOI: 10.4324/9781351208918

Chenoweth L, Lapkin, S. Building nursing practice, Fundamentals of Care Framework: Working with older people. In: Crisp J, Douglas C, Rebeiro G, Waters D (Eds) Potter & Perry's Fundamentals of Nursing. 2019; In press.

Journal Articles

Aerts L, Cations M, Harrison F, Jessop T, Shell A, Chenoweth L, Brodaty H. Why deprescribing antipsychotics in older people with dementia in long-term care is not always successful: insights from the HALT study. Int J Geriatr Psychiatry. 2019 Nov; 34(11): 1572-1581. DOI: 10.1002/gps.5167. PMID: 31276255 [Epub 2019 Jul 15].

Arancibia D, Lira M, Cruz Y, Barrera DP, Montenegro-Venegas C, Godoy JA, Garner CC, Inestrosa NC, Gundelfinger ED, Zamorano P, Torres VI. Serine-arginine protein kinase SRPK2 modulates the assembly of the active zone scaffolding protein CAST1/ERC2. Cells. 2019 Oct 29; 8(11): 1333. DOI: 10.3390/cells8111333. PMID: 31671734 [Epub 2019 Nov 2].

Bastias-Candia S, Martinez M, Zolezzi JM, Inestrosa NC. Wnt signaling upregulates teneurin-3 expression via canonical and non-canonical wnt pathway crosstalk. Front Neurosci. 2019; 13: 505. DOI: 10.3389/fnins.2019.00505. PMID: 31156379 [Epub 2019 June 4].

Beghi E, Giussani G, Abd-Allah F, Abdela J, Abdelalim A, Abraha HN, …, Sachdev PS, et al. Global, regional, and national burden of epilepsy, 1990–2016: a systematic analysis for the Global Burden of Disease Study 2016. Lancet Neurol. 2019 Apr; 18(4): 357-375. DOI: 10.1016/S1474-4422(18)30454-X. PMID: 30773428 [Epub 2019 Feb 14].

Bentvelzen AC, Crawford JD, Theobald A, Maston K, Slavin MJ, Reppermund S, Kang K, Numbers K, Brodaty H, Sachdev P, Kochan NA. Validation and normative data for the modified telephone interview for cognitive status: The Sydney Memory and Ageing Study. J Am Geriatr Soc. 2019 Jul 9; 67(10): 2108-2115. DOI: 10.1111/jgs.16033. PMID: 31290146 [Epub 2019 July 11].

Braidy N, Zarka M, Jugder B-E, Welch J, Jayasena T, Chan DKY, Sachdev P, Bridge W. The precursor to glutathione (GSH), γ-glutamylcysteine (GGC), can ameliorate oxidative damage and neuroinflammation induced by amyloid-beta oligomers in primary adult human brain cells. Front Aging Neurosci. 2019; Aug 8; 11: 177. DOI: 10.3389/fnagi.2019.00177. PMID: 31440155.

Cearns M, Opel N, Clark S, Kaehler C, Thalamuthu A, Heindel W, Winter T, Teismann H, Minnerup H, Dannlowski U, Berger K, Baune BT. Predicting rehospitalization within 2 years of initial patient admission for a major depressive episode: a multimodal machine learning approach. Transl Psychiatry. 2019 Nov 11; 9(1): 285. DOI: 10.1038/s41398-019-0615-2. PMID: 31712550 [Epub 2019 Nov 13].

Chauhan G, Adams HHH, Satizabal CL, Bis JC, Teumer A, Sargurupremraj M, …, Brodaty H, …, Wen W, Thalamuthu A, …, Mather KA, Sachdev PS, et al. Genetic and lifestyle risk factors for MRI-defined brain infarcts in a population-based setting. Neurology. 2019 Jan 29; 92(5): e486-e503. DOI: 10.1212/wnl.0000000000006851. PMID: 30651383 / PMCID: PMC6369905 [Epub 2019 Jan 16].

Chen Z, Jiang R, Chen M, Zheng J, Chen M, Braidy N, Liu S, Liu G, Maimaitiming Z, Shen T, Dunaief JL, Vulpe CD, Anderson GJ, Chen H. Multi-copper ferroxidase deficiency leads to iron accumulation and oxidative damage in astrocytes and oligodendrocytes. Sci Rep. 2019 Jul 1; 9(1): 9437. DOI: 10.1038/s41598-019-46019-9. PMID: 31263155 [Epub 2019 July 3].

1Cheng A, Leung Y, Crawford JD, Harrison F, Sachdev P, Brodaty H. The psychological health of 207 near-centenarians (95–99) and centenarians from the Sydney Centenarian Study. Aust N Z J Psychiatry. 2019 Oct; 53(10): 976-988. DOI: 10.1177/0004867419848831. PMID: 31096761 [Epub 2019 May 17].

Chenoweth L, Cook J, Wesson J, Brodaty H. Evaluating an education program promoting positive family and staff relationships and collaboration in aged care services: Pre/post/follow-up pilot study. Medical Research Archives. 2019 Aug 17; 7(7): 1-26. DOI: 10.18103/mra.v7i7.1958.

Chenoweth L, Stein-Parbury J, Lapkin S, Wang A, Liu Z, Williams A. Effects of person-centered care at the organisational-level for people with dementia. A systematic review. PLoS One. 2019; 14(2): e0212686. DOI: 10.1371/journal.pone.0212686. PMID: 30794651. [Epub 2019 Feb 23].

Cherbuin N, Shaw ME, Walsh E, Sachdev P, Anstey KJ. Validated Alzheimer's Disease Risk Index (ANU-ADRI) is associated with smaller volumes in the default mode network in the early 60s. Brain Imaging Behav. 2019 Feb; 13(1): 65-74. DOI: 10.1007/s11682-017-9789-5. PMID: 29243120 [Epub 2017 Dec 16].

Cisternas P, Martinez M, Ahima RS, William Wong G, Inestrosa NC. Modulation of glucose metabolism in hippocampal neurons by adiponectin and resistin. Mol Neurobiol. 2019 Apr; 56(4): 3024-3037. DOI: 10.1007/s12035-018-1271-x. PMID: 30076527 [Epub 2018 Aug 5].

Cisternas P, Oliva CA, Torres VI, Barrera DP, Inestrosa NC. Presymptomatic treatment with andrographolide improves brain metabolic markers and cognitive behavior in a model of early-onset Alzheimer's disease. Front Cell Neurosci. 2019; 13: 295. DOI: 10.3389/fncel.2019.00295. PMID: 31379502 [Epub 2019 Aug 6].

Cisternas P, Zolezzi JM, Martinez M, Torres VI, Wong GW, Inestrosa NC. Wnt-induced activation of glucose metabolism mediates the in vivo neuroprotective roles of Wnt signaling in Alzheimer disease. J Neurochem. 2019 Apr; 149(1): 54-72. DOI: 10.1111/jnc.14608. PMID: 30300917 [Epub 2018 Oct 10].

Clement J, Wong M, Poljak A, Sachdev P, Braidy N. The plasma NAD+ metabolome is dysregulated in "normal" aging. Rejuvenation Res. 2019 Apr; 22(2): 121-130. DOI: 10.1089/rej.2018.2077. PMID: 30124109 [Epub 2018 Aug 21].

Connors MH, Seeher K, Teixeira-Pinto A, Woodward M, Ames D, Brodaty H. Mild cognitive impairment and caregiver burden: a 3-year-longitudinal study. Am J Geriatr Psychiatry. 2019 Nov; 27(11): 1206-1215. DOI: 10.1016/j.jagp.2019.05.012. PMID: 31230914 [Epub 2019 May 17].

Cooper C, Aguirre E, Barber JA, Bass N, Brodaty H, Burton A, Higgs P, Hunter R, Huntley J, Lang I, Kales HC, Marchant NL, Minihane AM, Ritchie K, Morgan-Trimmer S, Walker Z, Walters K, Wenborn J, Rapaport P. APPLE-Tree (Active Prevention in People at risk of dementia: Lifestyle, bEhaviour change and Technology to REducE cognitive and functional decline) programme: Protocol. Int J Geriatr Psychiatry. 2019 Dec 13. DOI: 10.1002/gps.5249. PMID: 31833588 [Epub 2019 Dec 14].

Croot K, Raiser T, Taylor-Rubin C, Ruggero L, Ackl N, Wlasich E, Danek A, Scharfenberg A, Foxe D, Hodges JR, Piguet O, Kochan NA, Nickels L. Lexical retrieval treatment in primary progressive aphasia: an investigation of treatment duration in a heterogeneous case series. Cortex. 2019 June; 115: 133-158. DOI: 10.1016/j.cortex.2019.01.009. PMID: 30822613 [Epub 2019 Jan 30].

Cvejic RC, Hocking DR, Wen W, Georgiou-Karistianis N, Cornish KM, Godler DE, Rogers C, Trollor JN. Reduced caudate volume and cognitive slowing in men at risk of fragile X-associated tremor ataxia syndrome. Brain Imaging Behav. 2019 Aug; 13(4):1128-1134. DOI: 10.1007/s11682-018-9928-7. PMID: 30046972 [Epub 2018 Jul 27].

Davies G, Lam M, Harris SE, Trampush JW, Luciano M, Hill WD, …, Thalamuthu A, …, Armstrong NJ, Assareh AA, …, Brodaty H, …, Kochan NA, …, Lee T, …, Reppermund S, …, Sachdev PS, …, Trollor JN, et al. Author Correction: Study of 300,486 individuals identifies 148 independent genetic loci influencing general cognitive function. Nat Commun. 2019 May 1; 10(1): 2068. DOI: 10.1038/s41467-019-10160-w. PMID: 31043617 [Epub 2019 May 3].

Dehhaghi M, Tan V, Heng B, Braidy N, Mohammadipanah F, Guillemin GJ. Neuroprotective effect of myxobacterial extracts on quinolinic acid-induced toxicity in primary human neurons. Neurotox Res. 2019 Feb; 35(2): 281-290. DOI: 10.1007/s12640-018-9945-8. PMID: 30267267 [Epub 2018 Sep 30].

Dong Y, Ling MTY, Ng KET, Wang A, Wan EYS, Merchant RA, Venketasubramanian N, Chen CL, Mahendran R, Collinson SL. The Clinical Utility of the TYM and RBANS in a One-Stop Memory Clinic in Singapore:

A Pilot Study. J Geriatr Psychiatry Neurol. 2019 Jan 10:891988718824034. DOI: 10.1177/0891988718824034. PMID: 30630388 [Epub 2019 Jan 12].

Du J, Wang Y, Zhi N, Geng J, Cao W, Yu L, Mi J, Zhou Y, Xu Q, Wen W, Sachdev P. Structural brain network measures are superior to vascular burden scores in predicting early cognitive impairment in post stroke patients with small vessel disease. NeuroImage Clin. 2019; 22: 101712. DOI: 10.1016/j.nicl.2019.101712. PMID: 30772684 / PMCID: PMC6378318 [Epub 2019 Feb 5].

Feigin VL, Nichols E, Alam T, Bannick MS, Beghi E, Blake N, Culpepper WJ, …, Sachdev PS, et al. Global, regional, and national burden of neurological disorders, 1990–2016: a systematic analysis for the Global Burden of Disease Study 2016. Lancet Neurol. 2019 May; 18(5): 459-480. DOI: 10.1016/S1474-4422(18)30499-X. PMID: 30879893 [Epub 2019 Mar 14].

Ertilav K, Naziroglu M, Ataizi ZS, Braidy N. Selenium enhances the apoptotic efficacy of docetaxel through activation of TRPM2 channel in DBTRG glioblastoma cells. Neurotox Res. 2019; 35(4): 797-808. DOI: 10.1007/s12640-019-0009-5. PMID: 30796690 [Epub 2019 Feb 24].

Goltermann J, Redlich R, Dohm K, Zaremba D, Repple J, Kaehler C, Grotegerd D, Forster K, Meinert S, Enneking V, Schlaghecken E, Fleischer L, Hahn T, Kugel H, Jansen A, Krug A, Brosch K, Nenadic I, Schmitt S, Stein F, Meller T, Yuksel D, Fischer E, Rietschel M, Witt SH, Forstner AJ, Nothen MM, Kircher T, Thalamuthu A, Baune BT, Dannlowski U, Opel N. Apolipoprotein E Homozygous epsilon4 Allele Status: A deteriorating effect on visuospatial working memory and global brain structure. Front Neurol. 2019; 10: 552. DOI: 10.3389/fneur.2019.00552. PMID: 31191441 [Epub 2019 June 14].

Grainger SA, Crawford JD, Kochan NA, Mather KA, Chander RJ, Draper B, Brodaty H, Sachdev PS, Henry JD. An investigation into early-life stress and cognitive function in older age. Int Psychogeriatr. 2019 Oct 29: 1-5. DOI: 10.1017/s1041610219001583. PMID: 31658915 [Epub 2019 Oct 30].

Griffiths AW, Surr CA, Creese B, Garrod L, Chenoweth L. The development and use of the assessment of dementia awareness and person-centred care training tool in long-term care. Dementia. 2019 Jan 1; 18(7-8): 3059-3070. DOI: 10.1177/1471301218768165. PMID: 29631493 [Epub 2018 Apr 9].

Harvey LA, Toson B, Brodaty H, Draper B, Kochan N, Sachdev P, Mitchell R, Close JCT. Injury-related hospitalisation in community-dwelling older people across the cognitive spectrum: a population based study. Arch Gerontol Geriatr. 2019 Jul-Aug; 83: 155-160. DOI: 10.1016/j.archger.2019.03.028. PMID: 31035034 [Epub 2019 Apr 1].

Heffernan M, Andrews G, Fiatarone Singh MA, Valenzuela M, Anstey KJ, Maeder A, McNeil J, Jorm L, Lautenschlager N, Sachdev P, Ginige A, Hobbs M, Boulamatsis C, Chau T, Cobiac L, Cox K, Daniel K, Flood VM, Guerrero Y, Gunn J, Jain N, Kochan NA, Lampit A, Mavros Y, Meiklejohn J, Noble Y, O'Leary F, Radd-Vagenas S, Walton C, Brodaty H. Maintain Your Brain: Protocol of a 3-year randomized controlled trial of a personalized multi-modal digital health intervention to prevent cognitive decline among community dwelling 55 to 77 year olds. J Alzheimers Dis. 2019. 70(S1): S221-S237. DOI: 10.3233/jad-180572. PMID: 30475762 [Epub 2018 Nov 27].

Inskip M, Mavros Y, Sachdev PS, Fiatarone Singh MA. PRomoting Independence in Lewy Body Dementia through Exercise (PRIDE) Study: Protocol for a Pilot Study. Contemp Clin Trials Commun. 2019; 16: 100466. DOI: 10.1016/j.conctc.2019.100466. PMID: 31701040 / PMCID: PMC6831670 [Epub 2019 Oct 12].

Jain RK, Vakil D, Cunningham C, Sidhu K. Human mesenchymal stem cells conditioned media promotes the wound healing process - an in vitro study. J Stem Cell Ther Transplant. 2019; 3: 028-030. DOI: 10.29328/journal.jsctt.1001016.

Jeon YH, Krein L, Simpson JM, Szanton SL, Clemson L, Naismith SL, Low LF, Mowszowski L, Gonski P, Norman R, Gitlin LN, Brodaty H. Feasibility and potential effects of interdisciplinary home-based reablement program (I-HARP) for people with cognitive and functional decline: a pilot trial. Aging Ment Health. 2019 Jul 26; 1-10. DOI: 10.1080/13607863.2019.1642298. PMID: 31345051 [Epub 2019 July 28].

Jeon Y-H, Simpson JM, Low L-F, Woods R, Norman R, Mowszowski L, Clemson L, Naismith SL, Brodaty H, Hilmer S, Amberber AM, Gitlin LN, Szanton S. A pragmatic randomised controlled trial (RCT) and realist evaluation of the interdisciplinary home-bAsed Reablement program (I-HARP) for improving functional independence of community dwelling older people with dementia: an effectiveness-implementation hybrid design. BMC Geriatrics. 2019 Jul 29; 19(1): 199. DOI: 10.1186/s12877-019-1216-x. PMID: 31357949 / PMCID: PMC6664757.

Jia T, Chu C, Liu Y, van Dongen J, Papastergios E, Armstrong NJ, Bastin ME, …, Brodaty H, …, Jiang J, …, Mather KA, …, Thalamuthu A, Trollor J, …, Wen W, Whelan R, …, Sachdev PS, et al. Epigenome-wide meta-analysis of blood DNA methylation and its association with subcortical volumes: findings from the ENIGMA Epigenetics Working Group. Mol Psychiatry. 2019 Dec 6. DOI: 10.1038/s41380-019-0605-z. PMID: 31811260 [Epub 2019 Dec 8].

Jiang J, Thalamuthu A, Koch FC, Liu T, Xu Q, Trollor JN, Ames D, Wright MJ, Catts V, Sachdev PS, Wen W. Cerebral blood flow in community-based older twins is moderately heritable: an arterial spin labeling perfusion imaging study. Front Aging Neurosci. 2019; 11: 169. DOI: 10.3389/fnagi.2019.00169 [Epub 2019 July 2].

Lipnicki DM, Makkar SR, Crawford JD, Thalamuthu A, Kochan NA, Lima-Costa MF, Castro-Costa E, Ferri CP, Brayne C, Stephan B, Llibre-Rodriguez JJ, Llibre-Guerra JJ, Valhuerdi-Cepero AJ, Lipton RB, Katz MJ, Derby CA, Ritchie K, Ancelin ML, Carriere I, Scarmeas N, Yannakoulia M, Hadjigeorgiou GM, Lam L, Chan WC, Fung A, Guaita A, Vaccaro R, Davin A, Kim KW, Han JW, Suh SW, Riedel-Heller SG, Roehr S, Pabst A, van Boxtel M, Kohler S, Deckers K, Ganguli M, Jacobsen EP, Hughes TF, Anstey KJ, Cherbuin N, Haan MN, Aiello AE, Dang K, Kumagai S, Chen T, Narazaki K, Ng TP, Gao Q, Nyunt MSZ, Scazufca M, Brodaty H, Numbers K, Trollor JN, Meguro K, Yamaguchi S, Ishii H, Lobo A, Lopez-Anton R, Santabarbara J, Leung Y, Lo JW, Popovic G, Sachdev PS. Determinants of cognitive performance and decline in 20 diverse ethno-regional groups: a COSMIC collaboration. PLoS Med. 2019; 2019 Jul 23; 16(7): e1002853. DOI: 10.1371/journal.pmed.1002853. PMID: 31335910 / PMCID: PMC6650056.

Lira M, Arancibia D, Orrego PR, Montenegro-Venegas C, Cruz Y, Garcia J, Leal-Ortiz S, Godoy JA, Gundelfinger ED, Inestrosa NC, Garner CC, Zamorano P, Torres VI. The Exocyst Component Exo70 Modulates Dendrite Arbor Formation, Synapse Density, and Spine Maturation in Primary Hippocampal Neurons. Mol Neurobiol. 2019 Jul; 56(7): 4620-4638. DOI: 10.1007/s12035-018-1378-0. PMID: 30374940 [Epub 2018 Oct 31].

Lo JW, Crawford JD, Desmond DW, Godefroy O, Jokinen H, Mahinrad S, Bae HJ, Lim JS, Kohler S, Douven E, Staals J, Chen C, Xu X, Chong EJ, Akinyemi RO, Kalaria RN, Ogunniyi A, Barbay M, Roussel M, Lee BC, Srikanth VK, Moran C, Kandiah N, Chander RJ, Sabayan B, Jukema JW, Melkas S, Erkinjuntti T, Brodaty H, Bordet R, Bombois S, Henon H, Lipnicki DM, Kochan NA, Sachdev PS. Profile of and risk factors for poststroke cognitive impairment in diverse ethno-regional groups. Neurology. 2019 Dec 10; 93(24): e2257-e2271. DOI: 10.1212/wnl.0000000000008612. PMID: 31712368 [Epub 2019 Nov 11].

Low A, Ng KP, Chander RJ, Wong B, Kandiah N. Association of asymmetrical white matter hyperintensities and apolipoprotein E4 on cognitive impairment. J Alzheimers Dis. 2019; 70(3): 953-964. DOI: 10.3233/jad-190159. PMID: 31306121 [Epub 2019 July 16].

Low LF, McGrath M, Swaffer K, Brodaty H. Communicating a diagnosis of dementia: A systematic mixed studies review of attitudes and practices of health practitioners. Dementia (London). 2019 Oct-Nov; 18(7-8): 2856-2905. DOI: 10.1177/1471301218761911. PMID: 29544345 [Epub 2018 Mar 15].

Luckett T, Luscombe G, Phillips J, Beattie E, Chenoweth L, Davidson PM, Goodall S, Pond D, Mitchell G, Agar M. Australian long-term care personnel's knowledge and attitudes regarding palliative care for people with advanced dementia. Dementia. 2019 Nov 10:1471301219886768. DOI: 10.1177/1471301219886768. PMID: 31707844 [Epub 2019 Nov 12].

Martin DM, Mohan A, Alonzo A, Gates N, Gbadeyan O, Meinzer M, Sachdev P, Brodaty H, Loo C. A pilot double-blind randomized controlled trial of cognitive training combined with transcranial direct current stimulation for amnestic mild cognitive impairment. J Alzheimers Dis. 2019 Aug 12; 71(2):503-512. DOI: 10.3233/JAD-190306 [Epub 2019 Aug 12].

Mitchell R, Draper B, Close J, Harvey L, Brodaty H, Do V, Driscoll TR, Braithwaite J. Future hospital service utilisation in older adults living in long-term residential aged care or the community hospitalised with a fall-related injury. Osteoporos Int. 2019 Oct; 30(10): 1995-2008. DOI: 10.1007/s00198-019-05096-2. PMID: 31342137 [Epub 2019 July 24].

Mitchell R, Draper B, Harvey L, Wadolowski M, Brodaty H, Close J. Comparison of hospitalised trends, treatment cost and health outcomes of fall-related hip fracture for people aged >/= 65 years living in residential aged care and the community. Osteoporos Int. 2019 Feb; 30(2): 311-321. DOI: 10.1007/s00198-018-4800-6. PMID: 30569228 [Epub 2018 Dec 19].

Mitchell R, Fajardo Pulido D, Ryder T, Norton G, Brodaty H, Draper B, Close J, Rapport F, Lystad R, Harris I, Harvey L, Sherrington C, Cameron ID, Braithwaite J. Access to rehabilitation services for older adults living with dementia or in a residential aged care

facility following a hip fracture: healthcare professionals' views. Disabil Rehabil. 2019 Jul 23. DOI: 10.1080/09638288.2019.1643418. PMID: 31335212 [Epub 2019 July 25].

Mohan A, Bayes A, Sachdev PS, Parker G, Mitchell PB. Junior clinical academic psychiatrists in Australia: The University of New South Wales initiative. Australas Psychiatry. 2019 Jun; 27(3): 241-4. DOI: 10.1177/1039856218819135. PMID: 30570347. [Epub 2018/12/21].

Nabavi SF, Sureda A, Sanches-Silva A, Pandima Devi K, Ahmed T, Shahid M, Sobarzo-Sanchez E, Dacrema M, Daglia M, Braidy N, Vacca RA, Berindan-Neagoe I, Gulei D, Barreca D, Banach M, Nabavi SM, Dehpour AR, Shirooie S. Novel therapeutic strategies for stroke: The role of autophagy. Crit Rev Clin Lab Sci. 2019; 56(3): 182-199. DOI: 10.1080/10408363.2019.1575333. PMID: 30821184 [Epub 2019 Mar 2].

Naghav M, on behalf of the Global Burden of Disease Self-Harm Collaborators. Global, regional, and national burden of suicide mortality 1990 to 2016: systematic analysis for the Global Burden of Disease Study 2016. Br Med J. 2019; 364: 194. DOI: 10.1136/bmj.l94. PMID: 31339847 [Epub 2019 Feb 14]. ***Sachdev PS as a collaborator***

Nichols E, Szoeke CEI, Vollset SE, Abbasi N, Abd-Allah F, Abdela J, …, Sachdev PS, et al. Global, regional, and national burden of Alzheimer's disease and other dementias, 1990-2016: a systematic analysis for the Global Burden of Disease Study 2016. Lancet Neurol. 2019 Jan; 18(1): 88-106. DOI: 10.1016/s1474-4422(18)30403-4. PMID: 30497964 PMCID: PMC6291454 [Epub 2018 Dec 1].

O'Connor CM, Clemson L, Brodaty H, Low LF, Jeon YH, Gitlin LN, Piguet O, Mioshi E. The tailored activity program (TAP) to address behavioral disturbances in frontotemporal dementia: a feasibility and pilot study. Disabil Rehabil. 2019 Feb; 41(3): 299-310. DOI: 10.1080/09638288.2017.1387614. PMID: 29034719 [Epub 2017 Oct 15].

Opel N, Redlich R, Repple J, Kaehler C, Grotegerd D, Dohm K, Zaremba D, Goltermann J, Steinmann LM, Krughofer R, Leehr EJ, Bohnlein J, Forster K, Burger C, Meinert S, Enneking V, Emden D, Leenings R, Winter N, Heindel W, Kugel H, Thalamuthu A, Hahn T, Arolt V, Baune BT, Dannlowski U. Childhood maltreatment moderates the influence of genetic load for obesity on reward related brain structure and function in major depression. Psychoneuroendocrinology. 2019; Feb; 100: 18-26. DOI: 10.1016/j.psyneuen.2018.09.027. PMID: 30268003. [Epub 2018 Sep 30].

Ozturk Y, Gunaydin C, Yalcin F, Naziroglu M, Braidy N. Resveratrol enhances apoptotic and oxidant effects of paclitaxel through trpm2 channel activation in DBTRG glioblastoma cells. Oxid Med Cell Longev. 2019; 2019: 4619865. DOI: 10.1155/2019/4619865. PMID: 30984336 [Epub 2019 Apr 16].

Paradise M, Seruga A, Crawford JD, Chaganti J, Thalamuthu A, Kochan NA, Brodaty H, Wen W, Sachdev PS. The relationship of cerebral microbleeds to cognition and incident dementia in non-demented older individuals. Brain Imaging Behav. 2019 Jun; 13(3): 750-761. DOI: 10.1007/s11682-018-9883-3. PMID: 29802601 [Epub 2018 May 25].

Pardo E, Barake F, Godoy JA, Oyanadel C, Espinoza S, Metz C, Retamal C, Massardo L, Tapia-Rojas C, Inestrosa NC, Soza A, Gonzalez A. GALECTIN-8 Is a Neuroprotective Factor in the Brain that Can Be Neutralized by Human Autoantibodies. Mol Neurobiol. 2019 Nov; 56(11): 7774-7788. DOI: 10.1007/s12035-019-1621-3. PMID: 31119556 [Epub 2019 May 22].

Pedersen NL, Gatz M, Finch BK, Finkel D, Butler DA, Dahl Aslan A, Franz CE, Kaprio J, Lapham S, McGue M, Mosing MA, Neiderhiser J, Nygaard M, Panizzon M, Prescott CA, Reynolds CA, Sachdev P, Whitfield KE. IGEMS: The Consortium on Interplay of Genes and Environment Across Multiple Studies - An Update. Twin Res Hum Genet. 2019 Sep 23: 1-8. DOI: 10.1017/thg.2019.76. PMID: 31544729 [Epub 2019 Sep 24].

Ramos-Fernandez E, Tapia-Rojas C, Ramirez VT, Inestrosa NC. Wnt-7a stimulates dendritic spine morphogenesis and PSD-95 expression through canonical signalling. Mol Neurobiol. 2019 Mar; 56(3): 1870-1882. DOI: 10.1007/s12035-018-1162-1. PMID: 29967987 [Epub 2018 July 4].

Rashedi V, Foroughan M, Nazari H, Seeher K, Brodaty H. Validity and reliability of the Persian version of general practitioner assessment of cognition (P-GPCOG). Aging Ment Health. 2019 Aug; 23(8): 961-965. DOI: 10.1080/13607863.2018.1473840. PMID: 29781711 [Epub 2018 May 21].

Reeve E, Farrell B, Thompson W, Herrmann N, Sketris I, Magin PJ, Chenoweth L, Gorman M, Quirke L, Bethune G, Hilmer SN. Deprescribing cholinesterase inhibitors and memantine in dementia: guideline summary. Med J Aust. 2019; Mar; 210(4): 174-179. DOI: 10.5694/mja2.50015. PMID: 30771226. [Epub 2019 Feb 17].

Reppermund S, Heintze T, Srasuebkul P, Reeve R, Dean K, Smith M, Emerson E, Snoyman P, Baldry E, Dowse L, Szanto T, Sara G, Florio T, Johnson A, Clements M, McKenzie K, Trollor J. Health and wellbeing of people with intellectual disability in New South Wales, Australia: a data linkage cohort. BMJ Open. 2019 Sep 30; 9(9): e031624. DOI: 10.1136/bmjopen-2019-031624. PMID: 31575581 [Epub 2019 Oct 3].

Reppermund S, Srasuebkul P, Dean K, Trollor JN. Factors associated with death in people with intellectual disability. J Appl Res Intellect Disabil. 2019 Dec 1. DOI: 10.1111/jar.12684. PMID: 31786826 [Epub 2019 Dec 2].

Revelas M, Thalamuthu A, Oldmeadow C, Evans TJ, Armstrong NJ, Riveros C, Kwok JB, Schofield PR, Brodaty H, Scott RJ, Attia JR, Sachdev PS, Mather KA. Exceptional longevity and polygenic risk for cardiovascular health. Genes. 2019 Mar; 10(3): 227. DOI: 10.3390/genes10030227. PMID: 30889929 [Epub 2019 Mar 18].

Sachdev PS, Lipnicki DM, Crawford JD, Brodaty H. The Vascular Behavioral and Cognitive Disorders criteria for vascular cognitive disorders: a validation study. Eur J Neurol. 2019 Sep; 26(9): 1161-1167. DOI: 10.1111/ene.13960. PMID: 30927497 [Epub 2019 Mar 17].

Salazar P, Cisternas P, Martinez M, Inestrosa NC. Hypothyroidism and cognitive disorders during development and adulthood: implications in the central nervous system. Mol Neurobiol. 2019 Apr; 56(4): 2952-2963. DOI: 10.1007/s12035-018-1270-y. PMID: 30073507 [Epub 2018 Aug 4].

Salech F, Varela-Nallar L, Arredondo SB, Bustamante DB, Andaur GA, Cisneros R, Ponce DP, Ayala P, Inestrosa NC, Valdes JL, M IB, Couve A. Local Klotho Enhances Neuronal Progenitor Proliferation in the Adult Hippocampus. J Gerontol A Biol Sci Med Sci. 2019 Jun 18; 74(7): 1043-1051. DOI: 10.1093/gerona/glx248. PMID: 29300914 [Epub 2018 Jan 5].

Samaras K, Makkar SR, Crawford JD, Kochan NA, Slavin MJ, Wen W, Trollor JN, Brodaty H, Sachdev PS. Effects of statins on memory, cognition, and brain volume in the elderly. J Am Coll Cardiol. 2019; 74(21): 2554-2568. DOI: 10.1016/j.jacc.2019.09.041. PMID: 31753200 [Epub 2019 Nov 26].

Satizabal C, Adams H, Hibar D, White C, Knol M, Stein J, …, Assareh A, …, Brodaty H, …, Reppermund S, …, Thalamuthu A, …, Wen W, … Sachdev PS, …, Mather KA, …, et al. Genetic architecture of subcortical brain structures in 38,851 Individuals. Nat Genet. 2019 Nov; 51(11): 1624-1636. DOI: 10.1038/s41588-019-0511-y. PMID: 31636452 [Epub 2019 Oct 21].

Santabarbara J, Lipnicki DM, Villagrasa B, Lobo E, Lopez-Anton R. Anxiety and risk of dementia: Systematic review and meta-analysis of prospective cohort studies. Maturitas. 2019 Jan; 119: 14-20. DOI: 10.1016/j.maturitas.2018.10.014. PMID: 30502746 [Epub 2018 Dec 7].

Slot RER, Sikkes SAM, Berkhof J, Brodaty H, Buckley R, Cavedo E, Dardiotis E, Guillo-Benarous F, Hampel H, Kochan NA, Lista S, Luck T, Maruff P, Molinuevo JL, Kornhuber J, Reisberg B, Riedel-Heller SG, Risacher SL, Roehr S, Sachdev PS, Scarmeas N, Scheltens P, Shulman MB, Saykin AJ, Verfaillie SCJ, Visser PJ, Vos SJB, Wagner M, Wolfsgruber S, Jessen F, The Alzheimer's Disease Neuroimaging Initiative, The DESCRIPA working group, The INSIGHT-preAD study group, on behalf of the SCD-I Working Group, van der Flier WM. Subjective cognitive decline and rates of incident Alzheimer's disease and non-Alzheimer's disease dementia. Alzheimers Dement. 2019 Mar; 15(3): 465-476. DOI: 10.1016/j.jalz.2018.10.003. PMID: 30555032 [Epub 2018 Dec 18].

Smith EE, Biessels GJ, De Guio F, de Leeuw FE, Duchesne S, Düring M, … Sachdev PS, et al. Harmonizing brain magnetic resonance imaging methods for vascular contributions to neurodegeneration. Alzheimers Dement. 2019 Feb 26; 11: 191-204. DOI: 10.1016/j.dadm.2019.01.002. PMID: 30859119.

Sopina E, Chenoweth L, Luckett T, Agar M, Luscombe GM, Davidson PM, Pond CD, Phillips J, Goodall S. Health-related quality of life in people with advanced dementia: a comparison of EQ-5D-5L and QUALID instruments. Qual Life Res. 2019 Jan; 28(1): 121-129. DOI: 10.1007/s11136-018-1987-0. PMID: 30187395 [Epub 2018 Sep 7].

Surr CA, Griffiths AW, Kelley R, Holloway I, Walwyn REA, Martin A, McDermid J, Chenoweth L, Farrin AJ. The implementation of dementia care mapping in a randomized controlled trial in long-term care: results of a process evaluation. Am J Alzheimers Dis Other Demen. 2019 Sep; 34(6): 390-398. DOI: 10.1177/1533317519845725. PMID: 31056923 [Epub 2019 May 5].

Surr C, Woodward-Carlton B, Griffiths AW, the DCM-EPIC team. Does DCM Improve Care in Care Homes? The EPIC trial. Journal of Dementia Care. 2019; 27(5): 24-27. *Chenoweth L is part of the DCM-EPIC team*

Sweeney MD, Montagne A, Sagare AP, Nation DA, Schneider LS, Chui HC, …, Sachdev P, et al. Vascular dysfunction-The disregarded partner of Alzheimer's disease. Alzheimers Dement. 2019 Jan; 15(1): 158-167. DOI: 10.1016/j.jalz.2018.07.222. PMID: 30642436 [Epub 2019 Jan 16].

Tarrada A, Hingray C, Sachdev P, Le Thien M-A, Kanemoto K, de Toffol B. Epileptic psychoses are underrecognized by French neurologists and psychiatrists. Epilepsy Behav. 2019 Nov; 100(Pt A): 106528. DOI: 10.1016/j.yebeh.2019.106528. PMID: 31654941 [Epub 2019 Oct 22].

Taylor ME, Boripuntakul S, Toson B, Close JCT, Lord SR, Kochan NA, Sachdev PS, Brodaty H, Delbaere K. The role of cognitive function and physical activity in physical decline in older adults across the cognitive spectrum. Aging Ment Health. 2019 Jul; 23(7): 863-871. DOI: 10.1080/13607863.2018.1474446. PMID: 29798680 [Epub 2018 May 25].

Taylor ME, Lord SR, Delbaere K, Wen W, Jiang J, Brodaty H, Kurrle SE, Stefanie Mikolaizak A, Close JCT. White matter hyperintensities are associated with falls in older people with dementia. Brain Imaging Behav. 2019 Oct; 13(5): 1265-1272. DOI: 10.1007/s11682-018-9943-8. PMID: 30145714.

Walsh EI, Shaw M, Sachdev P, Anstey KJ, Cherbuin N. The impact of type 2 diabetes and body mass index on cerebral structure is modulated by brain reserve. Eur J Neurol. 2019 Jan; 26(1): 121-127. DOI: 10.1111/ene.13780. PMID: 30133070 [Epub 2018 Aug 23].

Walton E, Hibar D, Yilmaz Z, Jahanshad N, Cheung J, Batury VL, Seitz J, Bulik CM, PGC-ED, ENIGMA Genetics Working Group, Thompson PM, Ehrlich S. Exploration of shared genetic architecture between subcortical brain volumes and anorexia nervosa. Mol Neurobiol. 2019 Jul; 56(7): 5146-5156. DOI: 10.1007/s12035-018-1439-4. PMID: 30519816 [Epub 2018 Dec 7]. ***Sachdev P is part of the ENIGMA Genetics Working Group.

Walton CC, Lampit A, Boulamatsis C, Hallock H, Barr P, Ginige JA, Brodaty H, Chau T, Heffernan M, Sachdev PS, Fiatarone Singh MA, Valenzuela M. Design and development of the brain training system for the digital maintain your brain dementia prevention trial. JMIR Aging. 2019 Jan-Jun; 2(1): e13135. DOI: 10.2196/13135. PMID: 31518277 / PMCID: PMC6647452 [Epub 2019 Feb 27].

Weaver NA, Zhao L, Biesbroek JM, Kuijf HJ, Aben HP, Bae HJ, Caballero MAA, Chappell FM, Chen C, Dichgans M, Duering M, Georgakis MK, van der Giessen RS, Gyanwali B, Hamilton OKL, Hilal S, Vom Hofe EM, de Kort PLM, Koudstaal PJ, Lam BYK, Lim JS, Makin SDJ, Mok VCT, Shi L, Valdes Hernandez MC, Venketasubramanian N, Wardlaw JM, Wollenweber FA, Wong A, Xin X, Biessels GJ. The Meta VCI Map consortium for meta-analyses on strategic lesion locations for vascular cognitive impairment using lesion-symptom mapping: Design and multicenter pilot study. Alzheimers Dement. 2019 Dec; 11: 310-326. DOI: 10.1016/j.dadm.2019.02.007. PMID: 31011619 / PMCID: PMC6465616 [Epub 2019 Apr 24] ***Sachdev P is a collaborator***

Viaje S, Crombez G, Lord SR, Close JCT, Sachdev P, Brodaty H, Delbaere K. The role of concern about falling on stepping performance during complex activities. BMC Geriatr. 2019 Nov 27; 19(1): 333. DOI: 10.1186/s12877-019-1356-z. PMID: 31775634 [Epub 2019 Nov 30].

Wadhwa R, Wen W, Frankland A, Leung V, Sinbandhit C, Stuart A, Dawes L, Hadzi-Pavlovic D, Levy F, Lenrootl R, Mitchell PB, Roberts G. White matter hyperintensities in young individuals with bipolar disorder or at high genetic risk. J Affect Disord. 2019 Feb 15; 245: 228-236. DOI: 10.1016/j.jad.2018.10.368. PMID: 30412775 [Epub 2018 Nov 10].

Wand APF, Draper B, Brodaty H, Peisah C. Self-harm in the very old one year later: has anything changed? Int Psychogeriatr. 2019 Nov; 31(11): 1559-1568. DOI: 10.1017/s1041610219000632. PMID: 31244448 [Epub 2019 June 27].

Wand APF, Peisah C, Draper B, Brodaty H. Corrigendum to 'Why Do the Very Old Self-Harm? A Qualitative Study' [American Journal of Geriatric Psychiatry 26 (2018) 862-871]. Am J Geriatr Psychiatry. 2019 Feb; 27(2): 211. DOI: 10.1016/j.jagp.2018.11.005. PMID: 30528898 [Epub 2018 Dec 12].

Wand APF, Peisah C, Draper B, Brodaty H. Carer insights into self-harm in the very old: A qualitative study. Int J Geriatr Psychiatry. 2019 Apr; 34(4): 594-600. DOI: 10.1002/gps.5057. PMID: 30592092 [Epub 2018 Dec 29].

Ward SA, Pase MP. Advances in pathophysiology and neuroimaging: Implications for sleep and dementia. Respirology. 2019 Nov 14. DOI: 10.1111/resp.13728. PMID: 31726479 [Epub 2019 Nov 15].

Weaver NA, Zhao L, Biesbroek JM, Kuijf HJ, Aben HP, Bae HJ, Caballero MAA, Chappell FM, Chen C, Dichgans M, Duering M, Georgakis MK, van der Giessen RS, Gyanwali B, Hamilton OKL, Hilal S, Vom Hofe EM, de Kort PLM, Koudstaal PJ, Lam BYK, Lim JS, Makin SDJ, Mok VCT, Shi L, Valdes Hernandez MC, Venketasubramanian N, Wardlaw JM, Wollenweber FA, Wong A, Xin X, Biessels GJ. The Meta VCI Map consortium for meta-analyses on strategic lesion locations for vascular cognitive impairment using lesion-symptom mapping: Design and multicenter pilot study. Alzheimers Dement. 2019 Dec; 11: 310-326. DOI: 10.1016/j.dadm.2019.02.007. PMID: 31011619 [Epub 2019 Apr 24] ***Brodaty H is a collaborator***

Williamson A, Makkar SR, Redman S. How was research engaged with and used in the development of 131 policy documents? Findings and measurement implications from a mixed methods study. Implement Sci. 2019 Apr 30; 14(1): 44. DOI: 10.1186/s13012-019-0886-2. PMID: 31039811 [Epub 2019 May 2].

Wong M, Braidy N, Pickford R, Sachdev P, Poljak A. Comparison of single phase and biphasic extraction protocols for lipidomic studies using human plasma. Front Neurol. 2019; Aug 21; 10(879): 1-11. DOI: 10.3389/fneur.2019.00879. PMID: 31496985 / PMCID: PMC6712511.

Wong MWK, Braidy N, Pickford R, Vafaee F, Crawford J, Muenchhoff J, Schofield P, Attia J, Brodaty H, Sachdev P, Poljak A. Plasma lipidome variation during the second half of the human lifespan is associated with age and sex but minimally with BMI. PLoS One. 2019; 14(3): e0214141. DOI: 10.1371/journal.pone.0214141. PMID: 30893377 [Epub 2019 Mar 20].

Wong MWK, Braidy N, Crawford J, Pickford R, Song F, Mather KA, Attia J, Brodaty H, Sachdev P, Poljak A. APOE genotype differentially modulates plasma lipids in healthy older individuals, with relevance to brain health. J Alzheimers Dis. 2019; 72(3): 703-716. DOI: 10.3233/jad-190524. PMID: 31640095 [Epub 2019 Oct 24].

Zamanzadeh V, Pakpour V, Rahmani A, Chenoweth L, Mohammadi E. Dissatisfaction: Iranian Older People's Experiences of Living in Aged Care Homes. Journal of Transcultural Nursing. 2019; 31(112):56-66.

Review Articles

Bastias-Candia S, Zolezzi JM, Inestrosa NC. Revisiting the Paraquat-Induced Sporadic Parkinson's Disease-Like Model. Mol Neurobiol. 2019 Feb; 56(2): 1044-1055. DOI: 10.1007/s12035-018-1148-z. PMID: 29862459 [Epub 2018 June 5].

Braidy N, Berg J, Clement J, Khorshidi F, Poljak A, Jayasena T, Grant R, Sachdev P. Role of nicotinamide adenine dinucleotide and related precursors as therapeutic targets for age-related degenerative diseases: rationale, biochemistry, pharmacokinetics, and outcomes. Antioxidants & Redox Signaling. 2019 Jan 10; 30(2): 251-294. DOI: 10.1089/ars.2017.7269. PMID: 29634344 [Epub 2018 May 11].

Chen X, Maguire B, Brodaty H, O'Leary F. Dietary patterns and cognitive health in older adults: a systematic review. J Alzheimers Dis. 2019; 67(2): 583-619. DOI: 10.3233/jad-180468. PMID: 30689586 [Epub 2019 Jan 29].

Cheng A, Leung Y, Harrison F, Brodaty H. The prevalence and predictors of anxiety and depression in near-centenarians and centenarians: a systematic review. Int Psychogeriatr. 2019 Nov; 31(11): 1539-1558. DOI: 10.1017/s1041610219000802. PMID: 31354113 [Epub 2019 July 29].

Chenoweth L, Stein-Parbury J, Lapkin S, Wang YA. Effects of person-centered care at the organisational-level for people with dementia. A systematic review. PLOS One. 2019 Feb 22; 14(2): e0212686. DOI: 10.1371/journal.pone.0212686. PMID: 30794651 / PMCID: PMC6386385.

Connors MH, Quinto L, Brodaty H. Longitudinal outcomes of patients with pseudodementia: A systematic review. Psychol Med. 2019; 49(5): 727-737. DOI: 10.1017/S0033291718002829. PMID: 30319082 [Epub 2018 Oct 15).

Farzaei MH, Bahramsoltani R, Abbasabadi Z, Braidy N, Nabavi SM. Role of green tea catechins in prevention of age-related cognitive decline: Pharmacological targets and clinical perspective. J Cell Physiol. 2019 Mar; 234(3): 2447-2459. DOI: 10.1002/jcp.27289. PMID: 30187490 [Epub 2018 Sep 7].

Foo H, Mather KA, Thalamuthu A, Sachdev PS. The many ages of man: diverse approaches to assessing ageing-related biological and psychological measures and their relationship to chronological age. Curr Opin Psychiatry. 2019 Mar; 32(2): 130-137. DOI: 10.1097/yco.0000000000000473. PMID: 30461440. [Epub 2018 Nov 22].

Gates NJ, Vernooij RW, Di Nisio M, Karim S, March E, Martinez G, Rutjes AW. Computerised cognitive training for preventing dementia in people with mild cognitive impairment. Cochrane Database Syst Rev. 2019 Mar 13; 3: Cd012279. DOI: 10.1002/14651858.CD012279.pub2. PMID: 30864747 [Epub 2019 Mar 14].

Gates NJ, Rutjes AW, Di Nisio M, Karim S, Chong LY, March E, Martinez G, Vernooij RW. Computerised cognitive training for maintaining cognitive function in cognitively healthy people in midlife. Cochrane Database Syst Rev. 2019 Mar 13; 3: Cd012278. DOI: 10.1002/14651858.CD012278.pub2. PMID: 30864746 [Epub 2019 Mar 14].

Gates NJ, Rutjes AW, Di Nisio M, Karim S, Chong LY, March E, Martinez G, Vernooij RW. Computerised cognitive training for maintaining cognitive function in cognitively healthy people in late life. Cochrane Database Syst Rev. 2019 Mar 13; 3: Cd012277. DOI: 10.1002/14651858.CD012277.pub2. PMID: 30864187 [Epub 2019 Mar 14].

Gladman JT, Corriveau RA, Debette S, Dichgans M, Greenberg SM, Sachdev PS, Wardlaw JM, Biessels GJ. Vascular contributions to cognitive impairment and dementia: Research consortia that focus on etiology and treatable targets to lessen the burden of dementia worldwide. Alzheimers Dement. 2019 Nov 19; 5: 789-796. DOI: 10.1016/j.trci.2019.09.017. PMID: 31921967.

Harrison SL, Cations M, Jessop T, Hilmer SN, Sawan M, Brodaty H. Approaches to deprescribing psychotropic medications for changed behaviours in long-term care residents living with dementia. Drugs Aging. 2019 Feb; 36(2): 125-136. DOI: 10.1007/s40266-018-0623-6. PMID: 30535930 [Epub 2018 Dec 12].

Kua ZJ, Valenzuela M, Dong Y. Can computerized cognitive training improve cognition in patients with heart failure? A review. J Cardiovasc Nurs. 2019 Mar/Apr; 34(2): E19-E27. DOI: 10.1097/jcn.0000000000000558. PMID: 30585868 [Epub 2018 Dec 27].

Lees B, Mewton L, Stapinski LA, Squeglia LM, Rae CD, Teesson M. Neurobiological and cognitive profile of young binge drinkers: a systematic review and meta-analysis. Neuropsychol Rev. 2019 Sep; 29(3): 357-385. DOI: 10.1007/s11065-019-09411-w. PMID: 31512192 [Epub 2019 Sep 11].

Lennon MJ, Makkar SR, Crawford JD, Sachdev PS. Midlife hypertension and Alzheimer's disease: a systematic review and meta-analysis. J Alzheimers Disease. 2019 Sep 3; 71(1): 307-316. DOI: 10.3233/jad-190474. PMID: 31381518 [Epub 2019 Jul 29]

Nangle MR, Riches J, Grainger SA, Manchery N, Sachdev PS, Henry JD. Oral health and cognitive function in older adults: a systematic review. Gerontology. 2019; 65(6): 659-672. DOI: 10.1159/000496730. PMID: 30904915 [Epub 2019 Mar 22].

Paradise MB, Sachdev PS. Vascular Cognitive Disorder. Semin Neurol. 2019 Apr; 39(2): 241-250. DOI: 10.1055/s-0039-1678582. PMID: 30925616 [Epub 2019 Mar 30].

Vacca RA, Bawari S, Valenti D, Tewari D, Fazel Nabavi S, Shirooie S, Sah AN, Volpicella M, Braidy N, Nabavi SM. Down syndrome: neurobiological alterations and therapeutic targets. Neurosci Biobehav Rev. 2019 Jan 4; 98: 234-255. DOI: 10.1016/j.neubiorev.2019.01.001. PMID: 30615933 [Epub 2019 Jan 8].

Editorials

Cunningham C, Macfarlane S, Brodaty H. Language paradigms when behaviour changes with dementia: #BanBPSD. Int J Geriatr Psychiatry. 2019 Aug; 34(8): 1109-1113. DOI: 10.1002/gps.5122. PMID: 30993781 [Epub 2019 Apr 18].

Letters to the Editor, Author Replies, Other

Armstrong NJ, Mather KA, Sargurupremraj M, Knol MJ, Malik R, Satizabal CL, …, Wen W, …, Brodaty H, …, Thalamuthu A, …, Trollor J, …, Sachdev PS, et al. Common genetic variation indicates separate etiologies for periventricular and deep white matter hyperintensities. bioRxiv. 2019; 683367. DOI: 10.1101/683367 [Epub 2019 June 27] ***Preprint/not peer-reviewed***

Surr CA, Holloway I, Walwyn REA, Griffiths AW, Meads D, Kelley R, Martin A, McLellan V, Ballard C, Fossey J, Burnley N, Chenoweth L. Dementia Care Mapping (DCM™) to reduce agitation in care home residents with dementia: The DCM™ EPIC cluster RCT. Monograph. National Institute for Health Research - Health Technology Assessment (NIHR-HTA) Repository. 2019; UK.

Hawkins TC, Samuel R, Fiatarone Singh MA, Gates N, Wilson GC, Jain N, Meiklejohn J, Brodaty H, Wen W, Singh N, Baune BT, Suo C, Baker MK, Foroughi N, Wang Y, Sachdev PS, Valenzuela MJ, Hausdorff JM, Mavros Y. Impairment of dual-task gait dynamics in older adults with mild cognitive impairment: Relationships to neuropsychological status, fitness and brain morphology. medRxiv. 2019; 19005249. DOI: 10.1101/19005249 [Epub 2019 Aug 23] ***Preprint/not peer-reviewed***

Paradise M. Commentary on: Mechanisms Linking White Matter Lesions, Tract Integrity and Depression in Alzheimer's Disease. Am J Geriatr Psychiatry. 2019 Sep; 27(9): 960-962. DOI: 10.1016/j.jagp.2019.05.010. PMID: 31201001 [Epub 2019 June 16].

Peisah C, Jessop T, Brodaty H. Nursing home "no returns" policy, when residents are discharged to the emergency department at 4 am: what does the law say? Med J Aust. 2019 May; 210(8): 381-381.e1. DOI: 10.5694/mja2.50134. PMID: 30968425 [Epub 2019 Apr 9].

Shin J, Ma S, Hofer E, Patel Y, Roshchupkin GV, Sousa AM, …, Mather KA, …, Jiang J, …, Thalamuthu A, …, Trollor JN, …, Brodaty H, Wen W, Sachdev PS, …, et al. Planar cell polarity pathway and development of the human visual cortex. bioRxiv. 2019: 404558. DOI: 10.1101/404558 ***Preprint/not peer-reviewed***

Published Abstracts

Brodaty H, Heffernan M, Fiatarone Singh MA, Valenzuela M, Andrews G, Chau T, San Jose JC, Sachdev PS, Anstey KJ, Jorm L, Lautenschlager NT, McNeil J, Maeder A, Ginige JA. How many people aged 55-77 years are eligible for lifestyle interventions to prevent cognitive decline? [Poster Abstract P3-598]. Alzheimer's Association International Conference (AAIC) 2019. 14-18 July 2019; Los Angeles, CA, USA. Alzheimers Dement. 2019; 15(7, Suppl): P1205. DOI: 10.1016/j.jalz.2019.06.3635.

Casey A-NS, Kochan NA, Sachdev P, Brodaty H. Shrinking and growing social networks in the Sydney Memory and Ageing Study. GSA 2019 Annual Scientific Meeting. 13-17 Nov 2019; Austin, TX, USA. Innovation in Aging. 2019; 3(Suppl. 1): S41-S42. DOI: 10.1093/geroni/igz038.161.

Casey A-NS, Liu Z, Kochan NA, Sachdev PS, Brodaty H. Cross-lagged modelling of global cognition and core social network size in the Sydney Memory and Ageing Study [Poster Abstract P4-656]. Alzheimer's Association International Conference (AAIC) 2019. 14-16 July 2019; Los Angeles, CA, USA. Alzheimer's & Dementia. 2019; 15(7 Suppl): P1582. DOI: 10.1016/j.jalz.2019.09.022.

Harvey L, Taylor M, Delbaere K, Lord S, Brodaty H, Kochan N, Sachdev P, Mitchell R, Close J. 57 The Use of the Physiological Profile Assessment to Improve Prediction of Fragility Fractures in Community-Dwelling Older People [Abstract 57]. 1st World Congress on Falls and Postural Stability. 4-7 Dec 2019; Kuala Lumpur, Malaysia. Age and Ageing. 2019; 48(Suppl. 4): iv13-iv17. DOI: 10.1093/ageing/afz164.57.

Kochan NA, Croot K, Allison KC, Brodaty H, Crawford JD, Lee T, Henry JD, Draper B, Close J, Ong MY, Rossie M, Bunce D, Sachdev PS. A cross-comparison and validation of four computer-administered neuropsychological assessment batteries in community-living older adults, and patients with mild cognitive impairment and mild dementia: study protocol of CogSCAN [Poster Abstract TD-P-12]. Alzheimer's Association International Conference (AAIC) 2019. 14-18 July 2019; Los Angeles, CA, USA. Alzheimers Dement. 2019; 15(7 Suppl): P157-P158. DOI: 10.1016/j.jalz.2019.06.4323.

Kochan NA, Croot K, Allison KC, Brodaty H, Crawford JD, Lee T, Henry JD, Draper B, Close J, Ong MY, Rossie M, Bunce D, Sachdev PS. A cross-comparison and validation of four computer-administered neuropsychological assessment batteries in community-living older adults, and patients with mild cognitive impairment and mild dementia: study protocol of CogSCAN [Poster Abstract P1-445]. Alzheimer's Association International Conference (AAIC) 2019. 14-16 July 2019; Los Angeles, CA, USA. Alzheimer's & Dementia. 2019; 15(7 Suppl): P441-P442. DOI: 10.1016/j.jalz.2019.06.1060.

Koncz R, Thalamuthu A, Wen W, Catts VS, Rowe CC, Sachdev PS. The heritability of amyloid deposition and its shared genetic basis with small vessel disease in the brains of older people [Abstract O5-07-06]. Alzheimer's Association International Conference (AAIC) 2019. 14-16 July 2019; Los Angeles, CA, USA. Alzheimer's & Dementia. 2019; 15(7, Supplement): P1633-P1634. DOI: 10.1016/j.jalz.2019.06.4875.

Lipnicki DM, Trollor JN, Kochan NA, Numbers K, Kang K, Crawford JD, Brodaty H, Sachdev PS. Failure to identify particular odours predicts future dementia and mortality [Abstract O1-02-04]. Alzheimer's Association International Conference (AAIC) 2019. 14-18 July 2019; Los Angeles, CA, USA. Alzheimers Dement. 2019; 15(7, Suppl): P195-P196. DOI: 10.1016/j.jalz.2019.06.4526.

Lo JW, Crawford JD, Desmond DW, Godefroy O, Jokinen H, Mahinrad S, Bae H-J, Lim J-S, Koehler S, Douven E, Staals J, Chen C, Xu X, Chong E, Akinyemi RO, Kalaria RN, Ogunniyi A, Barbay M, Roussel M, Lee B-C, Srikanth VK, Moran C, Kandiah N, Chander RJ, Sabayan B, Jukema W, Melkas S, Erkinjuntti T, Brodaty H, Bordet R, Bombois S, Hénon H, Lipnicki DM, Kochan NA, Sachdev PS. Profile of and risk factors for post-stroke cognitive impairment in diverse ethno-regional groups [Abstract O4-03-04]. Alzheimer's Association International Conference (AAIC) 2019. 14-16 July 2019; Los Angeles, CA, USA. Alzheimers Dement. 2019; 15(7 Suppl): P1236. DOI: 10.1016/j.jalz.2019.06.4755.

Martin D, Mohan A, Alonzo A, Sachdev P, Brodaty H, Loo C. tDCS combined with cognitive training for improving memory in people with amnestic mild cognitive impairment (aMCI) [Abstract 302]. 3rd International Brain Stimulation Conference. 24-27 Feb 2019; Vancouver, Canada. Brain Stimulation. 2019 Mar-Apr; 12(2): 441. DOI: 10.1016/j.brs.2018.12.429.

Makkar SR, Lipnicki DM, Crawford JD, Kochan NA, Brodaty H, Sachdev PS. Changes in BMI predict cognitive decline in elderly women but not men: results from the Sydney Memory and Ageing Study (MAS) [Poster Abstract P3-556]. Alzheimer's Association International Conference (AAIC) 2019; 14-18 July 2019; Los Angeles, CA, USA. Alzheimers Dement. 2019; 15(7 Suppl): P1187-P1188.

Makkar SR, Lipnicki DM, Kochan NA, Crawford JD, Brodaty H, Sachdev PS, Costa E, Brayne C, Llibre Rodriguez JJ, Lipton RB, Katz MJ, Ritchie K, Ancelin M-L, Scarmeas N, Lam LCW, Guaita A, Kim KW, Riedel-Heller SG, van Boxtel MPJ, Koehler S, Ganguli M, Anstey KJ, Haan M, Kumagai S, Ng TP, Scazufca M, Meguro K, Lobo A. Relationship between education, apolipoprotein epsilon 4 (APOE*4) and cognitive impairment in diverse ethno-regional groups: the COSMIC collaboration [Poster Abstract P2-544]. Alzheimer's Association International Conference (AAIC) 2019. 14-18 July 2019; Los Angeles, CA, USA. Alzheimers Dement. 2019; 15(7, Suppl): P828-P829. DOI: 10.1016/j.jalz.2019.06.2952.

Mohan A, Thalamuthu A, Mather K, Catts VS, Sachdev PS. Differential expression of neuroinflammatory, neurotransmission-related and synaptic genes across 10 regions of the aging human brain: a microarray study [Poster Abstract P3-141]. Alzheimer's Association International Conference (AAIC) 2019. 14-18 July 2019; Los Angeles, CA, USA. Alzheimers Dement. 2019; 15(7 Suppl): P985-P986. DOI: 10.1016/j.jalz.2019.06.3169.

Paradise MB, Wen W, Sachdev PS. Perivascular spaces are associated with longitudinal cognitive decline and incident dementia in a healthy older cohort [Poster Abstract P3-311]. Alzheimer's Association International Conference (AAIC) 2019. 14-16 July 2019; Los Angeles, CA, USA. Alzheimer's & Dementia. 2019; 15(7 Suppl): P1410-P1411. DOI: 10.1016/j.jalz.2019.06.3981.

Peters R, Kiely KM, Lipnicki DM, Ancelin M-L, Anstey KJ, Brodaty H, Costa E, Guaita A, Haan M, Katz MJ, Kim KW, Lipton RB, Llibre Rodriguez JJ, Ritchie K, Scarmeas N, Sachdev PS. Lifestyle and cardiovascular risk factor clusters and cognitive decline [Poster Abstract P4-414]. Alzheimer's Association International Conference (AAIC) 2019. 14-18 July 2019; Los Angeles, CA, USA. Alzheimers Dement. 2019; 15(7, Suppl): P1461-P1462. DOI: 10.1016/j.jalz.2019.06.4086.

Reppermund S, Cohen-Woods S, Brodaty H, Christensen H, Trollor J, Mather K, Sachdev P. AGEDEP: Building an International Consortium on Geriatric Depression [Poster Abstract p14].19th IPA International Congress. 31 Aug–3 Sep 2019; Santiago, Spain. Int Psychogeriatr. 2019; 31(S1): 92-92. DOI: 10.1017/S1041610219001339.

Roehr S, Pabst A, Riedel-Heller SG, Ancelin M-L, Anstey KJ, Brayne C, Brodaty H, Ganguli M, Guerchet M, Guaita A, Katz MJ, Kim KW, Koehler S, Kumagai S, Lipton RB, Lobo A, Ng TP, Preux P-M, Ritchie K, Shahar S, Turana Y, van Boxtel MPJ, Lipnicki DM, Sachdev PS. Subjective cognitive decline in and across international cohort studies of ageing: the COSMIC collaboration [Abstract O3-11-06]. Alzheimer's Association International Conference (AAIC) 2019. 14-18 July 2019; Los Angeles, CA, USA. Alzheimers Dement. 2019; 15(7, Suppl): P913-P914. DOI: 10.1016/j.jalz.2019.06.4689.

Sachdev P. Cerebrovascular disease, dementia and depression- where is the nexus? [Abstract WCN19-1780]. XXIV World Congress of Neurology (WCN 2019). 27-31 Oct 2019; Dubai, UAE. J Neurol Sci. 2019; 405(Suppl): 38. DOI: 10.1016/j.jns.2019.10.102.

Sachdev P. Research diagnostic criteria for neurocognitive disorders using the biomarker approach [Abstract WCN19-1781]. XXIV Word Congress of Neurology (WCN 2019). 27-31 Oct 2019; Dubai, UAE. J Neurol Sci. 2019; 405(Suppl): 58-59. DOI: 10.1016/j.jns.2019.10.165.

Sachdev P, Lipnicki D, Makkar S, Crawford J, Thalamuthu A, Kochan NA, Brodaty H. Determinants of cognitive performance and decline in diverse ethno-regional groups: the COSMIC collaboration [Abstract]. 19th IPA International Congress. 31 Aug – 3 Sep 2019; Santiago, Spain. Int Psychogeriatr. 2019; 31(S1): 78-79. DOI: 10.1017/S1041610219001339.

Virk GK, Poljak A, Braidy N, Sachdev PS. Method development and proteomic analysis of depleted plasma for biomarker discovery in neurodegenerative diseases [Poster Abstract P2-219]. Alzheimer's Association International Conference (AAIC) 2019. 14-18 July 2019; Los Angeles, CA, USA. Alzheimers Dement. 2019; 15(7, Suppl): P661. DOI: 10.1016/j.jalz.2019.06.2626.

Ward SA, Brodaty H, Ahern S, Sachdev PS, Rowe C. The Australian Dementia Network (ADNET) clinical quality registry [Abstract S4-01-04]. Alzheimer's Association International Conference (AAIC) 2019. 14-18 July 2019; Los Angeles, CA, USA. Alzheimers Dement. 2019; 15(7, Suppl): P1215-P1216. DOI: 10.1016/j.jalz.2019.06.4712.

APPENDIX I: CONFERENCE PRESENTATIONS

Affleck AJ, Sachdev PS, Halliday GH. Heterogeneous antihypertensive medication usage is associated with Alzheimer disease neuropathologic scores. 11th ForeFront Scientific Meeting. 31 Oct – 1 Nov 2019; Sydney, Australia [Oral Presentation].

Bourke C, Chenoweth L, Williams A, Georgesopoulos E. An End of Life Care Assessment Tool for people living with dementia: a mixed method study. Australian Association of Gerontology Annual Conference. Oct 2019; Freemantle, WA, Australia [Oral Presentation].

Brodaty H. Post-Diagnostic Support for People with Dementia and their Care Partners, 29th Alzheimer Europe Conference. 23-25 Oct 2019; The Hague, Netherlands.

Brodaty H. ABCD: The Role of Psychogeriatrics in Assessment and Better Care for Dementia. Alzheimer's Association International Conference (AAIC) Satellite Symposium. 27 Sep 2019; Sydney, Australia.

Brodaty H. Preventing Dementia. 21st Asia-Pacific Regional Conference of Alzheimer's Disease International. 17 Aug 2019; Kuala Lumpur, Malaysia.

Catts V, Thalamuthu A, Lee T, Crawford J, Sachdev P. Heritability of subjective cognitive decline in Older Australian Twins. 49th Behavior Genetics Annual Meeting. 26-29 June 2019, Stockholm, Sweden [Poster Presentation].

Casey A-N, Kochan NA, Sachdev P, Brodaty H. Shrinking and growing social networks in the Sydney Memory and Ageing Study. 2019 Gerontological Society of America (GSA) 71st Annual Scientific Meeting. 13 Nov 2019; Austin, TX, USA [Oral Presentation].

Casey A-N, Kochan NA, Sachdev P, Brodaty H. Baseline self-reported social network size and incident dementia in the Sydney Memory and Ageing Study. Alzheimer's Association International Conference (AAIC) Satellite Symposium 2019. 25 Sep 2019; Sydney, Australia [Poster Presentation].

Casey A-N, Liu Z, Kochan NA, Sachdev P, Brodaty H. Cross-lagged modelling of global cognition and core social network size in the Sydney Memory and Ageing Study. Alzheimer's Association International Conference (AAIC) 2019. 14-18 July 2019; Los Angeles, USA [Poster Presentation].

Chenoweth L, Jessop T, Harrison F, Cations M, Brodaty H. Supporting antipsychotic deprescribing in people with dementia with a person-centred care intervention. 7th World Congress on Nursing & Healthcare. 17-18 June 2019; London, UK [Invited Keynote Speaker].

Chander RJ, Mather K, Cleary R, Grainger SA, Kochan NA, Henry JD, Sachdev PS. Influence of oxytocin receptor (OXTR) rs53576 polymorphism on cognitive and affective empathy in healthy adults: A meta-analysis [Poster #14]. 14th GeneMappers Conference. 20-22 Nov 2019; Manly, Sydney, Australia. DOI: 10.13140/RG.2.2.22913.61282 [Poster Presentation].

Chander RJ, Mather K, Cleary R, Grainger SA, Kochan NA, Henry JD, Sachdev PS. Influence of oxytocin receptor (OXTR) rs53576 polymorphism on cognitive and affective empathy in healthy adults: A meta-analysis [Lightning Talk]. 14th GeneMappers Conference. 20-22 Nov 2019; Manly, Sydney, Australia [Oral Presentation].

Cleary R, Numbers K, Chander R, Crawford J, Kochan N, Sachdev P, Brodaty H, Draper B. The relationship between severity of childhood trauma and cognitive decline in older adults. 20th Australasian Conference on Traumatic Stress. 12-14 Sep 2019; Sydney, Australia [Poster Presentation].

Jayasena T. Energy metabolite changes in the Alzheimer's disease brain. Dementia Australia. 18 Feb 2019; Kings Cross Rotary, Sydney [Invited Speaker].

Jiang J, Sachdev PS, Liu T, Theobald A, Brodaty H, Wen W, 2019. Altered functional connectivity of precuneus and PCC in the ninth decade of life and beyond. 2019 Organization for Human Brain Mapping Annual Meeting. 9-13 June 2019; Italy [Poster Presentation].

Kochan NA, Croot K, Allison K, Brodaty H, Crawford J, Lee T, Henry J, Draper B, Close J, Ong MY, Rossie M, Bunce D, Sachdev PS. Cross-comparison and validation of four computer-administered neuropsychological assessment batteries in community-living older adults, and patients with MCI and mild dementia – CogSCAN Study Protocol. Alzheimer's Association International Conference (AAIC) 2019. 14-18 July 2019; Los Angeles, USA [Oral and Poster Presentation].

Kochan NA, Croot K, Allison K, Brodaty H, Crawford J, Lee T, Henry J, Draper B, Close J, Ong MY, Rossie M, Bunce D, Sachdev PS. Cross-comparison and validation of four computer-administered neuropsychological batteries in older adults. The CogSCAN Study Protocol. Australian Psychological Society College of Clinical Neuropsychologists (APS CCN) 2019 Conference. 7-9 Nov 2019; Barossa Valley, South Australia [Oral Research Paper].

Koncx R, Thalamuthu A, Wen W, Catts VS, Rowe CC, Sachdev PS. The heritability of amyloid deposition and its shared genetic basis with small vessel disease in the brains of older people. Alzheimer's Association International Conference (AAIC) 2019. 14-18 July 2019; Los Angeles, USA [Oral Presentation].

Lennon MJ, Makkar SR, Crawford J, Sachdev P. Midlife Hypertension and Alzheimer's Disease: A meta-analysis and literature review. The Australian Dementia Forum. 17-19 June; Hobart, TAS [Oral Presentation].

Lipnicki DM, Makkar SR, Crawford JD, Thalamuthu A, Kochan NA, Sachdev PS, for Cohort Studies of Memory in an International Consortium (COSMIC). Late-life risk factors for cognitive performance and decline around the globe: the COSMIC collaboration. Alzheimer's Association International Conference (AAIC) Satellite Symposium. 27 Sep 2019; Sydney, Australia [Invited Speaker].

Lipnicki D, Trollor T, Kochan N, Numbers K, Kang K, Crawford JD, Brodaty H, Sachdev P. Failure to identify particular odours predicts future dementia and mortality. Alzheimer's Association International Conference (AAIC) 2019. 14-18 July 2019; Los Angeles, USA [Oral Presentation].

Lo JW, Crawford JD, Desmond DW, Godefroy O, Jokinen H, Mahinrad S, Bae HJ, Lim JS, Koehler S, Douven E, Staals J, Chen C, Xu X, Chong E, Akinyemi RO, Kalaria RN, Ogunniyi A, Barbay M, Roussel M, Lee BC, Srikanth VK, Moran C, Kandiah N, Chander RJ, Sabayan B, Jukema W, Melkas S, Erkinjuntti T, Brodaty H, Bordet R, Bombios S, Hénon, Lipnicki DM, Kochan NA, Sachdev PS. Profile of and risk factors for post-stroke cognitive impairment in diverse ethno-regional groups. Alzheimer's Association International Conference (AAIC) 2019. 14-18 July 2019; Los Angeles, USA [Poster Presentation].

Low A, Ng KP, Chander RJ, Wong B, Kandiah N. Association of symmetrical white matter hyperintensities and apolipoprotein e4 on cognitive impairment. Alzheimer's Association International Conference (AAIC) 2019. 14-18 July 2019; Los Angeles, USA [Poster Presentation].

Mather KA. Protein polygenic risk scores and genetic determinants of exceptional longevity. International Centenarian Consortium. 28 May 2019; Lausanne, Switzerland [Oral Presentation].

Mather KA. Genetics of deep and periventricular white matter hyperintensities. BRIDGET Consortium Meeting. June 2019; University of Edinburgh, Scotland.

Mather KA. Measuring computer attitudes and experience in an older Australian adult sample in the CogSCAN Study. 4th Annual NHMRC National Institute for Dementia Research (NNIDR) Australian Dementia Forum. 13-14 June 2019; Hobart, Australia [Poster Presentation].

Mather KA. CogSCAN: Study of Computer-Administered Neuropsychological Tests in Seniors. 18th National Conference of Emerging Researchers in Ageing (ERA) Conference. Working with Diverse Populations in Ageing Research Workshop. 5 Nov 2019; Sydney, Australia [Oral Presentation].

Mather KA. Measuring computer experience and attitudes to inform performance on computerised cognitive testing. Australian Psychological Society College of Clinical Neuropsychologists (APS CCN) 2019 Conference. 7-9 Nov 2019; Barossa Valley, South Australia [Oral Research Paper].

Mewton L. The Brain Games Study: Cognitive training for the prevention of psychopathology in at-risk youth. Society for Mental Health Research. 29 Nov 2019; Melbourne, Australia [Invited Speaker].

Mewton L. Inhibitory training does not reduce alcohol consumption when compared with appropriate control conditions. College on Problems of Drug Dependence. 15 June 2019; San Antonio, Texas, USA [Oral Presentation].

Mitchell J, Brodaty H, Chenoweth L. Person-centred care: how is it practiced today? 34th International Conference of Alzheimer's Disease International. 2019; Singapore [Oral Presentation].

Mitchell J, Chenoweth L, Braithwaite J, Long J, Brodaty H. Person-centred care: how is it practiced today in Sydney aged care homes? Alzheimer's Association International Conference (AAIC) Satellite Symposium. 25-27 Sep 2019; Sydney, Australia.

Ong MY, Numbers K, Croot K, Alllison K, Crawford JD, Brodaty H, Lee T, Henry J, Draper B, Close J, Rossie M, Sachdev P, Kochan N. Validating a multi-domain subjective cognitive index: relationship with objective cognitive performance. Australian Psychological Society College of Clinical Neuropsychologists (APS CCN) 2019 Conference. 7-9 Nov 2019; Barossa Valley, SA, Australia [Oral Presentation].

Page Z. Research in Action: Examples of Ageing Research with Diverse Populations. Three Minute Thesis and Q&A. 18th National Conference of Emerging Researchers in Ageing (ERA) Conference. Working with Diverse Populations in Ageing Research Workshop. 5 Nov 2019; Sydney, Australia [Oral Presentation].

Paradise MB, Wen W, Sachdev PS. Perivascular spaces are associated with longitudinal cognitive decline and incident dementia in a healthy older cohort [Poster Abstract P3-311]. Alzheimer's Association International Conference (AAIC) 2019. 14-16 July 2019; Los Angeles, CA, USA. Alzheimer's & Dementia. 2019; 15(7 Suppl): P1410-P1411. DOI: 10.1016/j.jalz.2019.06.3981 [Poster Presentation].

Reppermund S, Cohen-Woods S, Brodaty H, Christensen H, Trollor J, Mather K, Sachdev P. AGEDEP: Building an International Consortium on Geriatric Depression [Poster Abstract P14]. 2019. 19th IPA International Congress. 31 Aug – 3 Sep 2019; Santiago, Spain. Int Psychogeriatr. 2019; 31(S1): 92. DOI: 10.1017/S1041610219001339 [Poster Presentation].

Sachdev P. Can we aspire to live to 150? 19th IPA International Congress. 31 aug – 3 Sep 2019; Santiago, Spain [Plenary Speaker].

Sachdev P, Lipnicki D, Makkar S, Crawford J, Thalamuthu A, Kochan NA, Brodaty H. Determinants of cognitive performance and decline in diverse ethno-regional groups: the COSMIC collaboration. 19th IPA International Congress. 31 Aug – 3 Sep 2019; Santiago, Spain. Int Psychogeriatr. 2019; 31(S1):78-79. DOI: 10.1017/S1041610219001339.

Sachdev P. Talk title TBC. AFPA 7th World Congress of Asian Psychiatry (WCAP2019). 21-24 Feb 2019; Sydney, Australia.

Sachdev P. A classification of neurodegenerative disorders based on biomarkers - is this the future? 19th World Congress of Psychiatry. 21-24 August 2019; Lisbon, Portugal [Invited Speaker].

Sachdev P. Risk Reduction/Vascular Contributions. Alzheimer's Association International Conference (AAIC) Satellite Symposium. 25-27 Sep 2019; Sydney, Australia [Invited Panel Participant].

Sachdev P. Data from the STROKOG consortium. Alzheimer's Association International Conference (AAIC) Satellite Symposium. 25-27 Sep 2019; Sydney, Australia [Invited Speaker].

Sachdev P. Talk title TBC. IFA Copenhagen Summit on Cognitive Reserve. 24-25 Oct 2019; Copenhagen, Denmark [Invited Speaker].

Sachdev P. Invited Moderator for the Plenary Panel – Laying the Foundation: The Evidence and Science of Cognitive Reserve. IFA Copenhagen Summit on Cognitive Reserve. 24-25 Oct 2019; Copenhagen, Denmark.

Spooner A. Dementia: The Devil is in the Data. Survival Analysis of High-Dimensional Clinical Data. UNSW Faculty of Engineering Postgraduate Research Symposium. 9 Dec 2019; UNSw Sydney [Poster Presentation].

Trollor J. Dying for Change Roundtable. World Congress of the International Association for the Scientific Study of Intellectual and Developmental Disabilities (IASSIDDD). 6-9 Aug 2019; Glasgow, UK [Oral Presentation].

Trollor J, Srasuebkul P, Reppermund S, Heintze T. Translating findings from population health data, qualitative research and policy analysis into clinical benefit for people with intellectual disability. World Congress of the International Association for the Scientific Study of Intellectual and Developmental Disabilities (IASSIDDD). 6-9 Aug 2019; Glasgow, UK [Oral Presentation].

Trollor J. Health and wellbeing of autistic adults and their carers. 30th Annual National PANDDA Conference 2019. 22 Oct 2019; The Novotel Hotel, Parramatta, Sydney [Keynote Speaker].

Trollor J. Health needs of people with intellectual disability in NSW prisons. Corrective Services NSW 2019 Psychology Conference. 27 Aug 2019; Ryde-Eastwood Leagues Club, Sydney [Keynote Speaker].

Trollor J. Improving the mental health and wellbeing of people with intellectual or developmental disability. RANZCP Congress 2019; 16 May 2019; Cairns, Qld, Australia [Keynote Speaker].

Numbers K, Crawford J, Kochan N, Brodaty H. Subjective cognitive complaints, cognitive decline and clinical conversion in the Sydney Memory and Ageing Study. 4th Annual Australia Dementia Forum (ADF) 2019 Meeting. June 2019; Hobart, Australia [Oral Presentation].

Wong MWK, Braidy N, Crawford J, Pickford R, Song F, Mather KA, Attia J, Brodaty H, Sachdev P, Poljak A. APOE genotype shapes the normal ageing plasma lipidome and reveals possible mechanisms for AD risk. The International Research Network for Dementia Prevention (IRNDP) 2019. 14-15 Oct 2019; NeuRA, Sydney, Australia [Oral Presentation].

APPENDIX J: WORKSHOPS & INVITED SPEAKING ENGAGEMENTS

Affleck AJ. Anti-hypertensive medication usage and effects on Alzheimer's disease pathology. *St George and Sutherland Clinical School*, Research in Progress Meeting. 4 Sep 2019; St George and Sutherland Clinical School, Sydney.

Affleck AJ. Antihypertensive medications usage associates with spread of Alzheimer's disease pathology. *Brain and Mind Centre, Genetic Clinical Work and Research Meeting*. 11 Oct 2019; Sydney.

Brodaty H. Maintain Your Brain: The Secret to Healthy Brain Ageing. *Learn@Lunch*. 8 May 2019; UNSW Sydney.

Brodaty H. Strategies for Maintaining Memory and Brain Health. *Strategies for Healthy Ageing Forum*, hosted by Older Persons' Mental Health Service, Eastern Suburbs Mental Health Services, South Eastern Sydney Local Health District in collaboration with CHeBA. 30 Oct 2019; The Juniors, Kingsford.

Brodaty H. Maintain Your Brain. *Inaugural UNSW Ageing Futures Institute Symposium*. 11 Dec 2019; UNSW Sydney.

Browning C. Remembering to Remember – Prospective Memory in our Daily Life. *University of the Third Age (U3A) Public Talk*. Oct 2019; Waverly Library, Waverly, Sydney.

Browning C. The Sydney Centenarian Study – Progress to Date. *Montefiore Home Forum*. Nov 2019; Montefiore Home, Randwick.

Casey A-N. Perceptions of social relationships and BPSD. *Dementia Centre for Research Collaboration (DCRC) Behaviours and Psychological Symptoms associated with Dementia (BPSD) Workshop*. 26 Nov 2019; Randwick, Sydney.

Chenoweth L. *Applying person-centred principles in care of the person with dementia in the hospital setting*. 3-day workshops for PiP Study Champions (nurses and allied health staff) at St Vincent's Public Hospital, Sydney; 4, 11, 18 Oct 2019.

Chenoweth L, Endean E. Preventing and responding to delirium in the person with dementia in the hospital setting. 15 x 1.5-hour sessions for Nurses and allied health staff (5-8/session) at St Vincent's Public Hospital, Sydney; Aug–Oct 2019.

Chenoweth L. *Preventing and responding to agitation in the person with dementia in the hospital setting*. 15 x 1.5-hour sessions for Nurses and allied health staff (5-8/session) at St Vincent's Public Hospital, Sydney; Oct–Nov 2019.

Chenoweth L. *Practicing person-centred care of the person with dementia in the hospital setting*. 30 x 1.5-hour sessions for Nurses and allied health staff (5-8/session) at St Vincent's Public Hospital, Sydney; Nov– Dec 2019.

Cleary R. The Social Cognition Study. *Montefiore Forum*. 28 Nov 2019; Sydney, Australia.

Connors MH, Teixeira-Pinto A, Loy C. Psychosis in Huntington disease: A longitudinal study. Paper presented at the *Neuropsychiatric Syndromes Symposium of the International Society to Advance Alzheimer's Research and Treatment (ISTAART) Professional Interest Area day at the Alzheimer's Association International Conference (AAIC)*. July 2019; Los Angeles, CA, USA.

Kochan NA. Neuropsychological data harmonization and formation of cognitive domain scores. *Joint Symposium of the Epidemiology Research Council of the Korean Stroke Society and the Korean Vascular Cognitive Impairment Research Group*. 12 Jan, 2019; Seoul, Korea.

Kochan NA. Approaches to the problem of missing data, drop-outs and attrition bias in longitudinal cognitive studies. *Joint Symposium of the Epidemiology Research Council of the Korean Stroke Society and the Korean Vascular Cognitive Impairment Research Group*. 12 Jan, 2019; Seoul, Korea.

Kochan NA. Healthy brain ageing and brain fitness. *University of the Third Age (U3A)*. 18 Oct 2019; Waverley, Sydney.

Koncz R. Neuroimaging for psychiatrists. Invited lecture for registrars completing a Masters in Psychiatry. *Brain and Mind Centre Symposium*, University of Sydney.

Koncz R. Seminar in Intellectual Disability Mental Health. Invited lecture for registrars completing a Masters in Psychiatry. *Health Education & Training Institute (HETI)*

Koncz R. Obstructive sleep apnoea in severe mental illness. *Collaborative Centre for Cardiometabolic Health in Psychosis 2019 Symposium*. 11 Oct 2019;

Kondo M. Decoding the Information from Our Senses. Workshop at Garran Primary School. 23 Sep 2019; Canberra, ACT.

Kondo M. Cultural Heritage and Identity Development in Children. Canberra Japan Club Community Language School. 14 Sep 2019; Canberra ACT.

Kondo M. The Role of Physical Activity in Healthy Ageing. University House ANU. 31 Jul 2019; Canberra, ACT.

Kondo M. Achieving Healthy Ageing. *Australian National University Visiting Fellows Dinner*. 11 Jun 2019; Australian Studies Institute, Canberra, ACT.

Kondo M. Working Like a Scientist. Workshop series at Garran Primary School. 11 Jun - 2 Jul 2019; Canberra, ACT.

Lo J. Profile and Risk Factors of Post-Stroke Cognitive Impairment in Diverse Ethno-Regional Groups: the STROKOG consortium. *Vascular Neurodegeneration Symposium*. 22 Feb 2019; Florey Institute of Neuroscience and Mental Health, University of Melbourne.

Lo J. Profile of and risk factors for post-stroke cognitive impairment in diverse ethno-regional groups: findings from the international Stroke and Cognition (STROKOG) consortium. *UNSW Medicine Research in Progress Meeting*. 23 Oct 2019; St George and Sutherland Clinical School, Sydney.

Mewton L. Substance use and mental illness in young people. *Rotary District Conference*. 16 March 2019; Bankstown Sports Club, Sydney.

Paradise MB. Vascular cognitive disorders. *UNSW Medicine Research in Progress Meeting*. 23 Oct 2019; St George and Sutherland Clinical School, Sydney.

Sachdev P. Tourette's syndrome and tic disorders: Insights into phenomenology, pathophysiology and treatment. *Movement Disorder Society of Australia & New Zealand*. 13 Mar 2019; Sydney.

Sachdev P. Talk title TBC. *Hunters' Hill Ladies Probus*. 26 Aug 2019; Sydney.

Trollor J. Responding to the health needs of people with intellectual disability- from research to action in PHNs. *Roundtable on the Health of People with Intellectual Disability*. 2 Aug 2019; Rydges Hotel Sydney Airport.

Trollor J. Out of sight, out of mind… The health and wellbeing of people on the autism spectrum. *School of Psychiatry, Academic Forum*. 26 June 2019; UNSW Sydney.

Arnold, Stevens, Trollor J. Health and wellbeing in autistic adults and their carers. *Sutherland Hospital Mental Health Grand Rounds*. 10 April 2019; Sutherland Hospital.

Trollor J. Mental health and wellbeing in people with intellectual disability. *Central Coast Intellectual Disability, Mental Health- creating pathways*. 28 Oct 2019; Crowne Plaza Terrigal, NSW.

Trollor J. Emerging findings in autism in adulthood. *AADDM Conference*. 4 Oct 2019; Telethon Kids Institute, Perth.

Trollor J, Evans L. Dementia in Down syndrome. *Down Syndrome Conference*. 27 Sept 2019; Novotel Central Hotel, Sydney.

Trollor J, Arnold S, Stevens A. Autism in adulthood: what future psychiatrists should know about assessment and management. 13 Sept 2019; St George Mental Health Unit.

Trollor J. Mental health and wellbeing of people with intellectual or developmental disability: challenges in the provision of integrated supports. *ACT Government Senior Practitioner Forum*. 31 May 2019; Canberra, ACT.

Trollor J. Re-building capacity in the psychiatry of intellectual and developmental disability: NSW and National Developments. *RANZCP Congress 2019*. 14 May 2019; Cairns Convention Centre.

Trollor J. Old Dog, New Tricks. An adult psychiatrist's view on using the new National Guideline for the Assessment and Diagnosis of Autism Spectrum Disorders in Australia in clinical practice. *RANZCP Congress 2019*; 13 May 2019; Cairns Convention Centre.

Trollor J. Intellectual Disability Mental Health; Understanding Intellectual Disability and Mental Health. *HETI Health Education Training Institute*. 9 May 2019; Online.

Trollor J. Intellectual Disability Mental Health, Assessment & Management of Mental Ill Health in People with ID. *HETI Health Education Training Institute*. 9 May 2019; Online.

Trollor J. Intellectual Disability Mental Health, Assessing and Managing Challenging Behaviour. *HETI Health Education Training Institute*. 9 May 2019; Online.

Trollor J. Responding to the Health Needs of People with Intellectual Disability: Role and Responsibility of PHNs. *Australian Government Primary Health Network Mental Health Stepped Care Workshop*. 7 March 2019; AAMI Park Olympic Boulevard, Melbourne.