2019 DEMENTIA GRANTS PROGRAM

Project Grants (for funding commencing in 2020)*

LEAD INVESTIGATOR	PROJECT TITLE	INSTITUTION
AAG Research Trust – Dementia Australia Research Foundation Strategic Research Grant		
Dr Emily Reeve^	Consumer and clinician led priority setting for the NNIDR MEDicines and DEMentia (MEDDEM) National Research Action Plan	University of South Australia
Back Block Bards Project Grant		
Dr Patricio Opazo	In-vivo synaptic correlates of cognitive reserve	The University of Queensland
Bondi2Berry and Bondi2Brighton Project Grant		
Dr Andrew Care	"Cage vs Age": Development of an innovative nanotechnology to halt the spread of hyperphosphorylated Tau protein in Alzheimer's disease	Macquarie University
Dementia Australia Research Foundation Project Grant		
Dr Angel Lee	Is there a role for gait aids to improve stability and reduce falls risk for older people with dementia?	Monash University
Dr Yijun Pan	Personalising dosage regimens of medicines in Alzheimer's disease	Monash University
Dr Sarah Rea	Enhancing the TBK1-p62 axis as a therapeutic strategy for frontotemporal lobar degeneration	Murdoch University
Dr Duncan Sinclair	Investigating stress-related therapeutic targets for Alzheimer's disease in human neuronal cells	University of Tasmania
Dementia Australia Research Foundation – Norma Beaconsfield Project Grant		
Dr Pat Metharom	Investigating the effect of Factor Xa anticoagulant on dementia risk	Perth Blood Institute
Dementia Australia Research Foundation – Victoria Project Grant		
Dr Jenni Ilomaki	Preventing recurrent hip fractures: are people with dementia prescribed evidence-based treatments?	Monash University
Dementia Centre for Research Collaboration – Dementia Australia Research Foundation Pilot Grant		
Dr Sophie Andrews	Harnessing habits to increase physical activity in people with Mild Cognitive Impairment and Subjective Cognitive Decline	UNSW Sydney
Dr Belinda Brown	Sustaining exercise to enhance cognition: A feasibility study	Murdoch University
Dr Louise Mewton	Clarifying the relationship between alcohol use and dementia	UNSW Sydney
Dr Claudia Meyer	Respite care and transition to permanent residential care for people living with dementia and informal carers: Mind the Gap!	Bolton Clarke Research Institute
Dementia Centre for Research Collaboration – Dementia Australia Research Foundation Pilot Grant & Dementia Advocates' Award		
Dr Jade Cartwright	Evaluating the feasibility and effectiveness of a novel discourse intervention to improve everyday communication in people with dementia	Curtin University
Hazel Hawke Research Grant in Dementia Care		
Dr Sandra Garrido	Personalising care of people with dementia through music: Development and testing of a training program for aged care workers	Western Sydney University

* Valued at $75,000 over 1-2 years; ^ Valued up to $30,000 over 1.5 years

2019 DEMENTIA GRANTS PROGRAM

PhD Scholarships (for funding commencing in 2020)*

LEAD INVESTIGATOR	PROJECT TITLE	INSTITUTION
Bondi2Berry and Bondi2Brighton PhD Scholarship		
Ms India Boyton^	"Cage vs Age": Development of an innovative nanotechnology to halt the spread of hyperphosphorylated Tau protein in Alzheimer's disease	Macquarie University
Dementia Australia Research Foundation PhD Scholarship		
Ms Maddison Mellow	Optimising daily activity patterns for brain health in older adults	University of South Australia
Ms Claire Spargo	Driving in people with mild cognitive impairment (MCI): current practice and perspectives amongst people with MCI, occupational therapists and medical practitioners	Flinders University
Henry Brodaty PhD Scholarship		
Ms Lisa Bransby	The impact of modifiable risk factors on cognitive decline and Alzheimer's disease dementia	The Florey Institute of Neuroscience & Mental Health

* Award funding is $30,000 per year up to 3.5 years; ^ This PhD project will extend the work to be undertaken by Project Grant recipient Dr Andrew Care.

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PROJECT GRANT SUMMARIES

AAG Research Trust – Dementia Australia Research Foundation Strategic Research Grant

Dr Emily Reeve, University of South Australia

Consumer and clinician led priority setting for the NNIDR MEDicines and DEMentia (MEDDEM) National Research Action Plan

This project aims to identify the top 10 unanswered quality use of medicines (QUM) questions for people living with dementia. These questions will be generated and prioritised by Australians living with dementia, carers, and health care providers (clinicians). QUM means using medicines safely, effectively and when they are needed to get the best possible health outcomes. We will determine priorities using a multi-step research process. A national survey conducted with stakeholders and championed by a stakeholder Steering Group will determine what questions participants have had about medicines and dementia. These questions will be assessed to determine if there is already an 'answer' – has high quality research already been done? A second questionnaire followed by a workshop will prioritise the unanswered questions, resulting in a top 10 list. In the past, health research questions have been led by drug companies or researchers, with little involvement of clinicians and consumers. We aim to determine which questions are important to people living with dementia and their care team, to prioritise research in these areas and ensure that outcomes of research are directly relevant to the care of people living with dementia. This will lead to improving how medicines are used which in turn will improve health outcomes in people living with dementia.

Back Block Bards Project Grant

Dr Patricio Opazo, The University of Queensland

In-vivo synaptic correlates of cognitive reserve

Given that the incidence of Alzheimer's disease increases with age, it has been estimated that delaying dementia onset by 5 years would decrease the prevalence of late-onset dementia by 50%. In this project we will investigate the biological basis of Cognitive Reserve, a protective property of the brain known to delay dementia onset, but whose underlying mechanisms remain a mystery. Because the cognitive deficits in Alzheimer's disease are strongly associated with a loss of synapses – the point of communications between neurons – we believe that Cognitive Reserve is first implemented at the synaptic level as a way to preserve neuronal communication. In this project we will take a state-of-the-art microscopy approach to directly visualise the loss of synapses inside the brain of a living Alzheimer's disease animal model and the compensatory and regenerative events that follows that might serve as the basis of Cognitive Reserve. Given that therapeutics targeting the formation of amyloid pathology have failed in numerous clinical trials, we will focus on the protective mechanisms of the brain to cope with pathology rather than on those leading to pathology in the first place. The outcomes of this project may be instrumental in developing effective therapeutics harnessing these protective mechanisms as a way to delay the onset of dementia.

Bondi2Berry and Bondi2Brighton Project Grant

Dr Andrew Care, Macquarie University

"Cage vs Age": Development of an innovative nanotechnology to halt the spread of hyperphosphorylated Tau protein in Alzheimer's disease

Alzheimer's disease is the most common cause of dementia, accounting for 60-70% of all cases. Current medications prescribed for Alzheimer's disease alleviate the symptoms of the disease but do not alter the brain mechanisms underpinning it. Hence, a disease modifying treatment for Alzheimer's disease remains a major unmet clinical need. A major contributor to the spread of Alzheimer's disease inside the brain is the transmission of abnormal forms of a protein called tau. In this process, abnormal tau is released from diseased brain cells and taken up by neighbouring healthy brain cells, triggering the misfolding of the normal tau inside those cells. Nanoparticles are extremely small spheres that can be modified to encapsulate and deliver drugs to a specific target within the body, which therefore enhances the efficacy of a treatment and the outcomes for patients. This project aims to harness the properties of unique nanoparticles found inside bacteria by re-engineering them into a novel nanotechnology to treat Alzheimer's. These naturally-occurring nanoparticles will be designed to become drug carriers that target and disrupt tau pathology, halting the progression Alzheimer's disease inside the brain. We will take a multidisciplinary approach to achieve this goal, combining modern tools and techniques from protein engineering, materials science, pharmacology and neurobiology. This research has the potential to provide a disease-modifying treatment that would be of significant benefit to the millions of individuals living with Alzheimer's disease.

Dementia Australia Research Foundation Project Grant

Dr Den-Ching Angel Lee, Monash University

Is there a role for gait aids to improve stability and reduce falls risk for older people with dementia?

Balance impairment and falls are common among people living with dementia. Walking aids are frequently used to improve stability and reduce risk of falls for older people. However, there is often confusion about walking aid use by older people living with dementia, due to concerns about safety and their ability to learn this new skill. This research aims to fill the evidence gap to improve practice and guide decision-making by hospital and community care staff, and informal caregivers regarding walking aid use for people living with dementia who have balance impairments. A sequential investigation will be undertaken: 1) a survey to identify practice and rationales of hospital and community care staff and informal caregivers about walking aid use for older people living with dementia; 2) developing an algorithm to facilitate decision-making in hospitals and community; and 3) piloting a walking aid training program for people living with dementia to validate the algorithm. It is expected that the algorithm can guide practice and decision-making and identify people living with dementia who can achieve safe and effective walking aid use, which in turn may improve stability and reduce fall risks in older people living with dementia.

Dr Yijun Pan, Monash University

Personalising dosage regimens of medicines in Alzheimer's disease

Alzheimer's disease is a medical condition affecting the brain. However, recent evidence suggests that our body is also affected by Alzheimer's disease and as such, may absorb or metabolise medicines differently.

Compared to those who do not have the disease, people living with Alzheimer's disease tend to have more medical conditions and consume more medicines. Therefore, they are more likely to experience undesirable effects from medicine(s) or, as the body does not handle medicines in the same way as someone without

Alzheimer's disease, suffer the effects of under or overdosing. Prescribing practices can be improved if we understand what changes actually happen in our body when we have Alzheimer's disease. Our project uses cutting-edge technology to thoroughly screen for the changes in a mouse model of Alzheimer's disease as well as in human tissues. This information will be used to generate pharmacokinetic profiles of medications of interest. The profiles will promote medication safety and effectiveness in people with Alzheimer's disease by helping doctors to decide the best treatment, with the least number of medicines, at the right dose.

Dr Sarah Rea, Murdoch University

Enhancing the TBK1-p62 axis as a therapeutic strategy for frontotemporal lobar degeneration

Frontotemporal lobar degeneration (FTLD) is the most common cause of dementia in younger people. Autophagy is a natural process where damaged proteins and mitochondria (tiny specialised structures responsible for energy production) are removed from the cell. In FTLD, autophagy is reduced, which leads to a build-up of damaged proteins (TDP-43) and damaged mitochondria in brain cells, causing them to die. Autophagy requires a protein called p62, which is activated by another protein,TBK1. In 3-4% of FTLD cases a change in the TBK1 gene leads to a mutated TBK1 protein being produced. Researchers don't yet know how mutant TBK1 proteins cause FTLD. However, we found that two mutant TBK1 proteins did not activate p62, which reduced autophagy and caused TDP-43 to build-up in the brain. We will now test whether other mutant TBK1 proteins fail to activate p62 and cause TDP-43 and mitochondria to build-up. Our study will help researchers to understand exactly how TBK1 gene mutations cause FTLD. Increasing TBK1 levels may reduce the build-up of TDP-43 and damaged mitochondria in the brain and this could be beneficial in FTLD. Therefore, we will also test potential therapeutic compounds to find those that enhance TBK1 levels.

Dr Duncan Sinclair, University of Tasmania

Investigating stress-related therapeutic targets for Alzheimer's disease in human neuronal cells

Stressful experiences are all around us. These experiences can make us more likely to develop Alzheimer's disease and, if we have Alzheimer's disease, can speed up its progression. So it's vital to understand how stress impacts the brain in Alzheimer's disease. To do this in the laboratory, we are using brain-like human cells from adult donors to model Alzheimer's disease. We are investigating how these cells respond to stress hormones called glucocorticoids, which are released when we're stressed. So far our work has suggested that cells in the brain may respond differently to stress hormones in people living with Alzheimer's disease. It has also revealed that some aspects of these stress hormone responses may be helpful, and others harmful. This new study will dig deeper into stress, the brain and Alzheimer's disease. What happens inside the brain-like cells which model Alzheimer's disease when they are exposed to stress hormones? When, how and why can stress hormones can be beneficial or damaging? By answering these questions we hope to enable development of drugs and environmental interventions which target stress hormones to decrease risk for Alzheimer's disease and improve the lives of all of us as we age.

Dementia Australia Research Foundation – Norma Beaconsfield Project Grant

Dr Pat Metharom, Perth Blood Institute

Investigating the effect of Factor Xa anticoagulant on dementia risk

Individuals with an irregular heartbeat or recurrent blood clots are often prescribed drugs that thin the blood long-term. Some of these treatments include drugs inhibiting FXa, an important protein of the blood clotting process. However, FXa is known to be capable of performing multiple tasks besides regulating clots. In platelets, a type of blood cells that are important in wound healing and clot formation, FXa is capable of controlling ADAM10, a protein responsible for managing the breakdown of Amyloid Precursor Protein (APP) into harmless fragments. Reduced function of FXa may potentially cause incorrect processing of APP into Amyloid Beta (Aβ) peptides, a sticky toxic substance that drives the development of Alzheimer's disease. As platelets are the main producer of APP in the blood, we first aim to investigate, in test-tube settings, the processing of APP in healthy platelets after exposure to FXa inhibitors. Next, we will give anti-FXa drugs to mice, and then analyse their blood for signs associated with Aβ production. Finally, we will compare the blood of patients on long-term FXa inhibitor and other anticoagulants for levels of Aβ peptides. As direct FXa inhibitors are now widely used, we must understand how these drugs may increase the risk of dementia.

Dementia Australia Research Foundation – Victoria Project Grant

Dr Jenni Ilomaki, Monash University

Preventing recurrent hip fractures: are people with dementia prescribed evidence-based treatments?

People living with dementia are at an increased risk osteoporosis and hip fracture compared to people without dementia. However, recent reports suggest people with dementia are less likely to be prescribed evidence-based treatments for osteoporosis to prevent recurrent fractures. Our aim is to determine patterns and predictors of receiving guideline-recommended medications for osteoporosis after hip fracture in people with and without dementia, and to determine whether use of guideline recommended medications prevents subsequent hip fracture. We will conduct a large multinational cohort study across Australia, UK, US and Hong Kong. This will be achieved by building a common data model based on a previously funded project via the Dementia Australia Research Foundation. We will include people discharged from a hospital for hip fracture between 2012 and 2018. Dementia will be identified through ICD-10 codes from hospitals and medication dispensing data. Osteoporosis medications after hospital discharge will be captured from pharmacy dispensing data. Rehospitalisation for hip fracture will be captured from ICD-10 codes. By utilising large population-based databases in four countries we will produce generalisable results with a high likelihood of impacting policy and practice. Advocates will be engaged throughout the project to maximise the benefits of this research directly to people living with dementia.

Dementia Centre for Research Collaboration – Dementia Australia Research Foundation Pilot Grant

Dr Sophie Andrews, UNSW Sydney

Harnessing habits to increase physical activity in people with Mild Cognitive Impairment and Subjective Cognitive Decline

For older people experiencing decline to their memory and thinking skills, keeping physically active is important to maintain brain health and reduce risk of dementia. Despite this, over 80% of older Australians do not do enough physical activity in their daily lives. To date, interventions to help people increase their physical activity levels have involved setting goals, planning and self-monitoring, which are challenging for people with thinking and memory difficulties. Recent research suggests that automatic, every-day habits play an important

role in maintaining physical activity levels over the long-term. The current project aims to target these habits to help people with mild cognitive impairments create healthy, automatic habits of regular physical activity, that are easy to maintain over the long-term. To achieve this, we will develop and pilot the Harnessing Automatic Behaviours Intervention Trial (HABIT), a personalised physical activity behaviour change intervention for people with mild cognitive impairment. The results of the HABIT pilot will be used to guide a larger community trial of the intervention, and produce practical advice for people experiencing thinking and memory declines about how to use habit to increase their everyday physical activity to levels that are beneficial for brain and cognitive health.

Dr Belinda Brown, Murdoch University

Sustaining exercise to enhance cognition: A feasibility study

Over the past two decades, research has consistently shown that older adults undertaking regular physical activity have better memory and thinking skills and a lower risk of dementia. However, in studies where people are allocated to exercise interventions, there are not always observed effects on memory and thinking. One contributing factor to the varied results across previous studies may be the lack of high-intensity exercise delivered within interventions, which has been shown to provide significant benefits to the brain. In addition, although supervised exercise studies in older adults usually report good attendance, they often don't contribute to long-term changes in exercise habits. Prior to undertaking a large-scale study that would address the above, it is necessary to conduct a smaller, 'pilot' study. We will determine the feasibility of delivering high-intensity exercise coupled with behavioural change techniques and education to older adults, with the ultimate aim of enhancing brain health. The programme will include behavioural change techniques and education, with the objective of giving individuals the tools required to change their long-term exercise habits.

Dr Jade Cartwright, Curtin University

Evaluating the feasibility and effectiveness of a novel discourse intervention to improve everyday communication in people with dementia

Communicating and staying socially connected with others is important to people with dementia, yet there are very few evidence-based interventions to help people living with dementia to retain skills needed for everyday conversations and to engage socially. This study will adapt a highly novel intervention approach that has been trialled with other neurological conditions, such as after stroke, in hope of improving the everyday communication and quality of life of people with dementia. This structured, yet interactive, approach aims to improve how people organise and structure their everyday talking, for example, when giving opinions, sharing personal stories, recounting events, and explaining procedures, all of which occur in daily conversations. If found to be effective, the treatment protocol refined through this study will have significant implications and be widely disseminated to speech pathologists. This study hopes to enable better access to evidence-based communication interventions that have potential to make a meaningful difference to the social connectedness and wellbeing of people living with dementia.

Dr Louise Mewton, UNSW Sydney

Clarifying the relationship between alcohol use and dementia

Whilst heavy alcohol use has been identified as a key modifiable risk factor for dementia, previous studies have shown that low to moderate alcohol use is beneficial when compared with both abstaining and heavy alcohol use. However, previous research has limitations. With alcohol use increasing among older adults, further research is needed to clarify the relationship between low to moderate alcohol use and the risk of dementia. Using large-scale data combined across 15 international studies (48,965 people), the current project aims to investigate the relationship between different patterns of alcohol use and dementia in adults aged over 65 years. The use of large-scale data will allow an unprecedented examination of the relationship between patterns of alcohol use and dementia, and how these may differ according to key clinical and demographic characteristics. This project will contribute to evidence-based recommendations on the number of standard drinks associated with minimal dementia risk. These practical recommendations will have a clear benefit in terms of dementia risk reduction in the wider community.

Dr Claudia Meyer, Bolton Clarke Research Institute

Respite care and transition to permanent residential care for people living with dementia and informal carers: Mind the Gap!

People living with dementia often have specific care needs that are provided (mostly) by informal carers (that is, family and/or friends). There may come a time, however, when the physical and/or emotional demands of caregiving are no longer manageable, hence the importance of supportive residential respite care without transition to permanent care. Respite can be defined as a pause, or an interval of rest, from the duties of caring, but doesn't necessarily require a physical distancing from the person living with dementia. For the carer, transition of a person living with dependency to permanent care, can be laden with a combination of guilt, confusion and relief, but this will vary from person to person. This project aims to co-design a new and novel approach to short-term residential respite care and transition into permanent care in conjunction with people living with dementia and their carers, residential care staff and management. This project is exploratory and, as such, it is unclear what the exact program will look like. The project is designed to generate ideas on what might work, rather than testing a known intervention. A prototype program will be generated from the co-design sessions, followed by the testing of assumptions related to the program, to identify how to make the program better.

Hazel Hawke Research Grant in Dementia Care

Dr Sandra Garrido, Western Sydney University

Personalising care of people with dementia through music: Development and testing of a training program for aged care workers

People living with dementia often experience mood disturbances such as depression or agitation, which can have a big impact on quality of life and carer stress levels. The use of drug-based treatments for these mood disturbances are often undesirable because of side-effects, so the development of cost-effective non-pharmaceutical treatments is highly important. There is considerable evidence that music can have a positive influence on the mood of people living with dementia. However staff buy-in and knowledge are significant barriers to the effective use of music programs in aged care facilities in Australia. This project will merge the experience of Western Sydney University and HammondCare to develop an online training program for aged care staff and home-based carers of people living with dementia. The course, to be developed in close partnership with end users and people with lived experience of dementia, will help caregivers to understand

the potential for music to be used as part of individual care plans to manage mood-related symptoms in dementia.

PHD SCHOLARSHIP SUMMARIES

Bondi2Berry and Bondi2Brighton PhD Scholarship

Ms India Boyton, Macquarie University

"Cage vs Age": Development of an innovative nanotechnology to halt the spread of hyperphosphorylated Tau protein in Alzheimer's disease

Alzheimer's disease is the most common cause of dementia, accounting for 60-70% of all cases. Current Alzheimer's disease medications only alleviate symptoms and do not modify the underlying mechanisms that cause the disease. Consequently, finding an effective therapeutic for Alzheimer's disease is of critical importance. One major contributor to the spread of Alzheimer's disease within the brain is the transmission of abnormal forms of a protein called tau. In this process, abnormal tau is released from diseased brain cells and taken up by neighbouring healthy brain cells, triggering the misfolding of the normal tau inside those cells. Thus, Alzheimer's disease progressively spreads throughout the brain. Nanoparticles are tiny balls that can be engineered to package drugs and deliver them precisely to diseased tissue inside a patient, thus enhancing a drug treatment's efficacy and improving the outcomes of patients. This project aims to harness the properties of unique nanoparticles found inside bacteria by re-engineering them into a novel nanotechnology that can be utilised to treat dementia. These naturally-occurring nanoparticles will be altered into tiny drug carriers that selectively target and disrupt tau pathology, halting the progression Alzheimer's disease inside the brain. To reach this goal, I will combine a set of novel tools and techniques found in protein engineering, drug delivery, pharmacology and neurobiology. This research has the potential to provide a disease-modifying treatment that would be of significant benefit to the millions of individuals living with Alzheimer's disease.

Dementia Australia Research Foundation PhD Scholarship

Ms Maddison Mellow, University of South Australia

Optimising daily activity patterns for brain health in older adults

Achieving enough physical activity and sleep, and limiting sedentary behaviour (e.g. prolonged sitting), improves brain function and reduces dementia risk in older adults. These three behaviours coexist to make up the 24-hour day, and to increase time spent in one of these, time must be taken away from another. We still do not know the best combination of these behaviours within a 24-hour time period for cognition or dementia risk in older adults. This project will investigate how brain health and function in older adults is affected by how much time is spent sleeping, engaging in physical activity or being sedentary across the 24-hour day. This information will be collated to understand "best day" patterns for optimal brain health and function in healthy older adults. The findings will contribute to the development of an interactive app which will predict how changing time use (e.g. reducing sitting time and increasing sleep) affects an individual's brain health and function.

Ms Claire Spargo, Flinders University

Driving in people with mild cognitive impairment (MCI): current practice and perspectives amongst people with MCI, occupational therapists and medical practitioners

Research has shown that many people living with mild cognitive impairment have only minor driving problems, whereas other people demonstrate unsafe driving behaviours such as difficulty positioning the vehicle within the correct lane. However, it is not known what driving recommendations are made by the health professionals who see these people when they attend memory and driving clinics. It is unclear what proportion of these people are suspended from driving, recommended to continue driving or referred for on-road driving assessments. This project will involve an audit of medical records that are written by doctors working in these clinics to find out what driving recommendations they make. People living with mild cognitive impairment, doctors and occupational therapists will also be interviewed to obtain different perspectives about current practice and gaps. We will address the gaps identified by developing a tool to assist with decision making about fitness to drive. It is anticipated that this will lead to improved safety for all road users and reduce negative outcomes for people living with mild cognitive impairment who demonstrate the ability to continue driving safely.

Henry Brodaty PhD Scholarship

Ms Lisa Bransby, The Florey Institute of Neuroscience and Mental Health

The impact of modifiable risk factors on cognitive decline and Alzheimer's disease dementia

As the search for a cure for Alzheimer's disease dementia remains unsuccessful, it is important to consider other ways to delay or prevent it. A range of modifiable risk factors, such as obesity, physical inactivity, low mood, disrupted sleep, social isolation and low cognitive engagement have been found to be related to cognitive impairment and dementia risk. However, most studies have only examined the contribution of these risk factors to cognitive dysfunction and dementia risk individually. As these risk factors are highly related to each other, a more comprehensive understanding of the contribution of modifiable risk factors to cognitive dysfunction and dementia risk would be achieved by examining the combined effects of these risk factors. The aim of the proposed project is to examine the additive or interactive contributions of each modifiable risk factor to determine their effect on cognitive dysfunction and dementia risk. The contribution of key genetic risk factors, such as the apolipoprotein E (APOE) E4 allele, to this relationship will also be explored. The results of this project will have the potential to inform the design of future multi-modal lifestyle intervention trials that aim to prevent or delay dementia.