

Neuroscience Research Australia

Profile 2019

### Discovery brings hope, changes lives

We have discovered a new way to prevent freezing of gait and falls, and maximise mobility, independence and quality of life for people with Parkinson's disease using Smart Garment technology.

- Dr Matt Brodie

We have discovered the first direct evidence that a key chemical messenger interferes with neuronal function in people with schizophrenia.

- Professor Cyndi Shannon Weickert

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Cur research is the first to discover a potential treatment for chemobrain by disrupting the tumour-to-brain communication using anti-inflammatories such as aspirin.

- Dr Adam Walker

We have discovered the first evidence that shows a link between chronic pain, glutamate levels and mental health disorders in humans.

- Associate Professor Sylvia Gustin



Discovery brings hope, changes lives

#### 2019 marks a year of great optimism and outstanding achievements at NeuRA.

#### New MRI scanner

A new state-of-the-art *Philips Ingenia CX 3T* MRI scanner has arrived at NeuRA, enabling researchers to see the brain in exquisite detail. Located in a new facility in the Margarete Ainsworth Building, the scanner will support an active community of local, national and international researchers. Imaging has been at the forefront of NeuRA's research since 2003 with our MRI facilities supporting over 100 research projects, which have produced more than 300 research publications.

#### Schizophrenia breakthrough

Associate Professor Tom Weickert and Professor Cyndi Shannon Weickert and their team have recently identified changes in the inflammationrelated biochemical pathways in schizophrenia. These changes interfere with proper nerve-cell communication. The discovery underpins new approaches for the development of medications to treat schizophrenia and its symptoms.

#### Parkinson's disease – Smart Garment technology

NeuRA researchers are testing innovative new Smart Socks for people with Parkinson's to help prevent falls and improve quality of life. Dr Matthew Brodie and Associate Professor Kim Delbaere are developing the technology, which uses visual, audio and sensory cues to engage the feet when an altered pattern of walking is detected that may lead to a fall. The program works by building new connections in regions of the brain less affected by Parkinson's.

#### New partnerships for healthcare innovation

We were recently joined by the NSW Minister for Health and Medical Research, the Hon Brad Hazzard MP, to announce the latest results from the Transurban Road Safety Centre based at NeuRA. The research, led by Professor Lynne Bilston, has shown a potential safety benefit in using plastic chest clips on child restraints, as they keep shoulder straps together. We are also excited to announce an Australian-first partnership between NeuRA and the Mark Moran Group. The partnership aims to improve the health and wellbeing outcomes of older Australians and facilitate the translation of NeuRA's age-related research into real-world outcomes. Through colocation and collaboration, we are demonstrating how research can deliver tangible and practical improvements in caring for people in retirement and aged-care living.

#### Mindgardens Neuroscience Network

The partnership between South Eastern Sydney Local Health District, UNSW Sydney, Black Dog Institute and NeuRA to establish the Mindgardens Neuroscience Network has developed substantially over the past year under the Chairmanship of Mr John Grill AO. Scientia Professor Helen Christensen AO of the Black Dog Institute and I have been serving as the Joint Interim CEOs of Mindgardens, progressing our aim to establish a world-first Comprehensive Brain Disorders Centre. We were delighted that the Federal Health Minister, the Hon Greg Hunt, supported our vision by providing \$7M in the 2019 Federal Budget to Mindgardens to implement its vision.

#### NeuRA Governing Council and Foundation

With the company board focusing its efforts on bringing the Mindgardens project to fruition, it has established the NeuRA Governing Council to provide leadership of the NeuRA enterprise. I want to thank the Hon Justice Anna Katzman as Chair and Ms Alice Kase as Deputy Chair, and all Councillors for their diligent governance of the institute. I also want to thank Mr Norbert Schweizer OAM, Chairman of the NeuRA Foundation and his fellow Foundation Directors for their outstanding efforts in fundraising to support NeuRA.



#### Neuroscience recognised in Australia Day Honours

I was truly humbled and deeply honoured to be appointed an Officer of the Order of Australia in the Australia Day 2019 Honours List for my service to medical and scientific research in the field of neuroscience. I want to thank and acknowledge my colleagues at NeuRA and at many other wonderful organisations that I have had the privilege to serve, recognising that the award reflects the combined efforts of all of these people. I hope this award helps to shine a light on the urgent need for a strong, collective and integrated response to tackle brain disorders in Australia. Did you know the cost of all brain disorders in Australia was \$74 billion in 2017? Now is the time for critical investment in neuroscience research, given the current impact of mental illness, and especially as the number of people with dementia is expected to triple by 2050. I hope you will join me in the effort for more funding to support research into brain disorders in Australia.

Thefield

Professor Peter R Schofield AO FAHMS PhD DSc CEO

Scientific discovery is the process or product of successful scientific inquiry. Objects of discovery can be things, events, processes, causes and properties, as well as theories and hypotheses.

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### MIND OVER MEDITERRANEAN: A DIET THAT REDUCES THE RISK OF DEMENTIA

A diet designed to increase brain health has been shown to reduce the odds of cognitive impairment and disorders including Alzheimer's and dementia.

In a study led by NeuRA's Professor Kaarin Anstey, researchers reviewed the potential protective effects of the Mediterranean-DASH Intervention for Neurodegenerative Delay diet, also known as the MIND diet.

The composition of the MIND diet is based partially on the Mediterranean diet but incorporates foods specifically relevant to brain health.

The MIND diet is characterised by 15 dietary components with a focus on green leafy vegetables, whole grains, olive oil and small amounts of red meat.

The investigation followed 1,220 adults aged 60 and older, for a period of 12 years. It linked the MIND diet to a 19 per cent reduction of developing clinically diagnosed mild cognitive impairment or dementia. In contrast, no benefit was found for adhering to the Mediterranean dietary pattern.

"This study has shown for the first time, outside of the United States, that the MIND diet reduces the risk of dementia," says Professor Kaarin Anstey.



Professor Anstey hopes the study will help researchers develop concrete recommendations for reducing the risk of dementia in Australia and around the world.

The findings come from a 12-year longitudinal cohort study, the PATH Through Life project, which is based in Canberra and Queanbeyan, NSW. Participants were interviewed about their dietary intake using the CSIRO food frequency questionnaire at the commencement of the study. Their cognitive abilities were monitored over time and they were also assessed for cognitive impairment. Their diets were scored to see whether the participant's dietary patterns followed the MIND or Mediterranean pattern.

Professor Martha Morris developed the MIND diet in the US. What sets it apart from other diets is the detailed specification of foods thought to be neuroprotective, such as green leafy vegetables and berries. The scoring also has a category for cakes and pastries, which were hallmarks of a westernised diet. This allowed researchers to better capture the dietary pattern and behaviour of participants.

Professor Anstey says the next steps are to evaluate the diet in randomised controlled trials and to conduct studies that reveal the protective mechanisms and pathways associated with the MIND diet.

Professor Anstey's research group has a strong interest in identifying ways to reduce the risk of dementia and improve healthy ageing.



### NEURA RESEARCHER RECEIVES WESTPAC FUTURE LEADERS SCHOLARSHIP

Westpac Scholars Trust announced its 2019 Westpac Future Leaders Scholars, awarding over \$2 million to 17 outstanding postgraduate students investigating solutions to some of Australia's most complex issues. Amongst this year's recipients is NeuRA researcher, Nicole Ee. Nicole is a member of Professor Kaarin Anstey's multi-disciplinary ageing research team and plans to use her scholarship to explore the relationship between social engagement and dementia risk. Nicole's research is focused on whether early intervention and increased social engagement may mitigate the onset or progression of dementia.



"The scholarship will provide me with exciting collaborative networks, global opportunities for learning, mentorship and a platform to advocate for and disseminate my research," says Nicole Ee.

### AGE-RELATED HEARING LOSS AND DEMENTIA RISK

Age-related hearing loss happens to most of us as we grow older. Over half of Australians aged 60 years and older experience some kind of hearing difficulty. Hearing loss can occur gradually as we age and despite affecting many aspects of daily life, is often unnoticed and undertreated.

Research has shown that hearing loss with age is associated with faster rates of cognitive decline and increased risk of future dementia incidence. Older adults with mild symptoms of hearing loss may be twice as likely to develop dementia as those with hearing in a normal range. However, we do not currently know the reason for this.

"Hearing difficulties may reduce quality of life through communication difficulties, social withdrawal, feelings of loneliness and depression, as well as a loss of independence," says NeuRA Research Fellow Dr Kim Kiely. "These factors may increase the risk of developing dementia."

Dr Kiely's research aims to better understand the link between hearing loss and dementia to inform interventions to prevent cognitive decline.



"Our best bet at this stage is prevention and that will help reduce the rates of dementia over time," says Dr Kiely.



DIAN Study team Jacob Bechara, Dr Bill Brooks, Professor Peter Schofield AO and Mirelle D'Mello

### GLOBAL COLLABORATION DRIVES NEW BLOOD TEST TO PREDICT GENETIC ALZHEIMER'S DISEASE

A recent study from the Dominantly Inherited Alzheimer Network (DIAN) details evidence for a blood test that can predict familial Alzheimer's disease 16 years before clinical symptoms appear.

The collaborative research study, led by Professor Mathias Jucker from the German Centre for Neurodegenerative Diseases (DZNE) and the University of Tubingen Germany, has provided encouraging results that will drive the development of an early detection program for Alzheimer's disease.

The DIAN study involves a global network of researchers, led by Professors John Morris and Randall Bateman at Washington University, St Louis, Missouri, with study sites in the US, England, Germany and three research teams in Australia – NeuRA, The Florey Institute and Edith Cowen University. Professor Peter Schofield AO leads the Sydney study site at NeuRA.

"The DIAN study has allowed us to track families with the rare inherited Alzheimer's gene," says Professor Schofield.

This research has provided critical insight into the biomarkers for Alzheimer's.

"Identifying a particular signature in the blood is the first step in the early detection and treatment of this devastating disorder of the brain," says Professor Schofield. Next steps for the test include replicating the results in sporadic Alzheimer's disease patients, who are older and often have other health issues.

"We hope that a test could become part of a routine medical checkup in the future, providing a cost-effective and efficient early warning system for the disease," says Professor Schofield.



# CAN HUMANS LIVE TO 150?

As our population ages, the number of centenarians will increase exponentially. Estimates suggest that there will be approximately 12,000 centenarians in Australia by 2020 and 50,000 by 2050. Worldwide, the number of centenarians is projected to increase 15-fold to 2.2 million by 2050.



Living to 100 guest centenarians Michael Harvey, Eileen Kramer, Tom Sample and Helena Goldstein

The second international *Living* to 100 Conference, hosted by the Centre for Healthy Brain Ageing (CHeBA), brought together internationally recognised experts in ageing to deliberate on the latest research on exceptionally long-lived individuals, in particular centenarians and supercentenarians.

The internationally acclaimed lineup of 32 speakers included NeuRA's CEO Professor Peter Schofield AO, NeuRA Senior Research Scientist and CHeBA Senior Research Fellow, Dr Karen Mather, and the Director of NeuRA's Brain Bank, Dr Claire Shepherd.

Dr Mather's presentation focused on the complex roles that epigenetic factors may play in longevity. Epigenetics refers to mechanisms that influence gene expression that are not due to changes in the DNA coding sequence and include DNA methylation and non-coding RNAs.

"The field of epigenetics shows much promise for intervention and preventive strategies to improve human health, since it may be influenced by environmental changes. However, much more research is required to move this field forward," says Dr Mather. One of the conference highlights involved the discussion of whether humans can live to the age of 150. While some experts were pessimistic, Professor Schofield, who has been studying the brain for decades, is optimistic.

"The things that may make it possible to conceive that humans will live to 150 are probably going to have to be quite innovative – they are probably going to need things like potential genetic therapies and drug therapies," Professor Schofield told SBS News.

# What is the benefit of studying exceptionally long-lived individuals?

Exceptionally long-lived individuals are the ultimate examples of successful ageing, as many of these people have survived or even escaped agerelated decline and disease until very late in their lives. "Unlocking the secrets of successful ageing in centenarians will suggest pathways to promote health in our ageing population," says Dr Mather.

"Revealing genetic variants associated with exceptional longevity will give us a better understanding of the biological mechanisms leading to successful ageing. In future we may be able to target individuals for interventions to promote healthy ageing."



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### NEURA LEADS WORLD FIRST AGED-DRIVER STUDY

NeuRA researchers have conducted a large study at the Transurban Road Safety Centre to test the effect of comfort and orthopaedic accessories used by older drivers, for the first time.

Real-world research shows almost a third of older drivers use a variety of accessories including cushions, comforters on the seatbelt and an array of back and lumbar supports.

"We've tested over 40 different accessories to clearly identify those that are safe and those that should never be used in the car," says Associate Professor Julie Brown.

"This type of testing has never been done before and is only possible with the state-of-the-art equipment at the Transurban Road Safety Centre," says Crash Test Engineer Nicholas Kent. "We're interested in the protection of older people in cars because they are overrepresented in injury statistics, and are much more likely to be seriously injured than younger drivers," says Associate Professor Brown. "We want to keep older drivers as safe as possible on the road, for longer."

In this study, crash test dummies travelling at speeds of up to 49 kilometres per hour demonstrated the potential injury risk of each accessory in a simulated crash. "The cameras at the Transurban Road Safety Centre at NeuRA record up to 1,200 frames per second, which allows us to see what is really going on in a highspeed collision," says Mr Kent.

A panel of industry experts are analysing the data from the study to provide clear recommendations about when comfort and orthopaedic accessories should be used by older drivers in the car, and which ones are safe to use.

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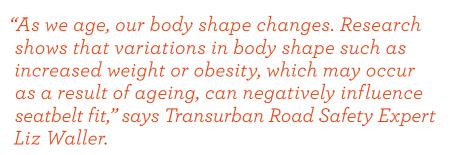
### NEURA UNVEILS NEW GUIDELINES FOR SENIORS AND SEATBELTS

NeuRA has developed an information brochure on the correct use of seatbelts for seniors, in partnership with the Transurban Road Safety Centre. This follows research that shows, on average, 250 Australians aged over 65 die every year in car crashes, and more than 4,000 are hospitalised.

Injuries sustained by older drivers are more severe than those in younger age groups. It is estimated the injury risk is nine times higher per kilometre travelled in drivers 85 years and over, compared to drivers aged between 25 and 69.

"Cars are a primary means of transport for senior Australians enabling independent living and social engagement. Car safety is therefore a critical component of healthy ageing," says Associate Professor Julie Brown.

The Transurban Road Safety Centre is a state-of-the-art crash lab based at NeuRA that allows researchers to understand how vehicles and crash protection devices, like seatbelts, can best protect drivers in a collision.



"Mobility is so important for healthy ageing, so one of our key focus areas is understanding how we can keep seniors as safe as possible on the roads as they age," says Ms Waller.

The goal of the brochure is to bring greater awareness to the importance of good seatbelt fit and deliver tips on senior driver safety.

To request a FREE digital copy of the Seniors and Seatbelts Brochure, visit foundation.neura.edu.au/ seatbelt





Elizabeth Waller, Transurban Road Safety Specialist

### WHAT ARE WE DOING ABOUT THE HIGH RATE OF DEMENTIA IN ABORIGINAL AND TORRES STRAIT ISLANDER AUSTRALIANS?

Rates of dementia in Aboriginal and Torres Strait Islander Australians are three to five times higher than in the general Australian population and the onset of dementia starts earlier. However, the major causes and risk factors for dementia in Indigenous communities are not well understood. Identifying causes and risk factors of dementia in these populations is essential for developing targeted, effective dementia prevention strategies. NeuRA's Aboriginal Health and Ageing team has initiated a number of projects to translate research findings to Aboriginal healthcare workers, community partners and community Elders. The team recently hosted the Growing Old Well Gathering to share best-practice advice for dementia assessment, highlight healthy ageing, and discuss strategies for preventing the early onset of dementia. "Close community engagement is the cornerstone of our research. This event is an important opportunity for researchers, health professionals, service providers, and community members to come together to exchange ideas on how to support the increasing numbers of older people in these communities to age well," says Dr Kylie Radford, Aboriginal Health and Ageing Program Leader.



Smoking Ceremony opens Gathering

### SHARING THE WISDOM OF OUR ELDERS



Core Dreaming (Strong Women, Strong Future) by Glenny Naden

Sharing the Wisdom of Our Elders is a project emerging from NeuRA's epidemiological Koori Growing Old Well Study (KGOWS), supported by The Lowitja Institute. The project documents health, resilience and social connectedness with Aboriginal and Torres Strait Islander people who are growing old well. The project shares Elders' insights into the meaning of healthy ageing, and is identifying current services and programs that align with the needs and expectations of the ageing Aboriginal and Torres Strait Islander population.

The project has worked closely with Elders, local artists, Aboriginal Community Controlled Health Services, and other organisations to produce an Aboriginal-specific ageing well education resource.

"The resources aim to preserve and share Aboriginal Elders' knowledge and stories about ageing well for both present and future generations," says Dr Radford. The project is also identifying ways in which current services and decision makers can better meet the needs of an ageing Aboriginal population. Importantly, the project foregrounds and honours the stories of older Aboriginal and Torres Strait Islander people, in their own words, alongside extensive research data.

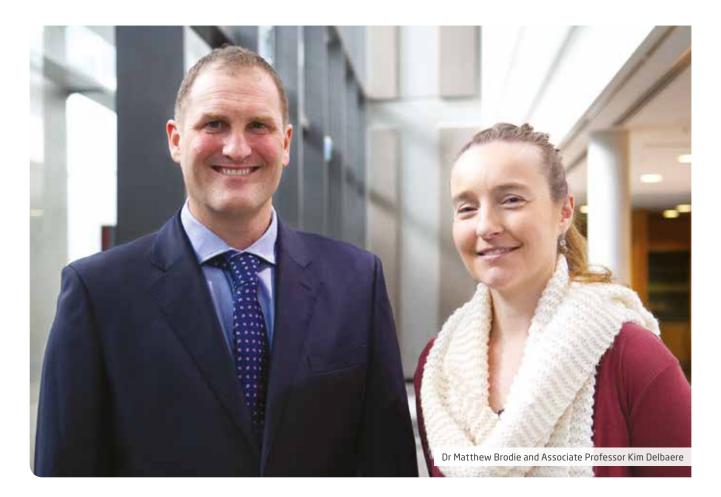


Waadjaa-da (We Are The Land) by Alison Williams

### CARING FOR SPIRIT

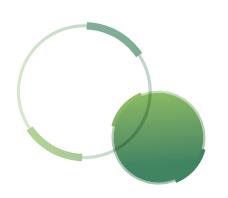


Caring for Spirit is a project supported by the Australian Government's Department of Health Dementia and Aged Care Services Fund. The project has developed a website **(www.CaringForSpirit.org.au)** and online training resources for Aboriginal and Torres Strait Islander health workers, caregivers and communities to improve dementia awareness and access to high quality evidence-based and culturally appropriate information about dementia. This project is being coordinated by Lauren Poulos, a Biripi woman, in conjunction with the Aboriginal Health and Ageing team at NeuRA. The team has worked closely with Aboriginal designers and content consultants to develop the Caring for Spirit website. The site features novel information and audio-visual content that has been developed with the support of our national network of collaborators.



### DEVELOPING SMART GARMENT TECHNOLOGIES TO PREVENT FALLS IN PEOPLE WITH PARKINSON'S DISEASE

Researchers at NeuRA have partnered with The Michael J. Fox Foundation to test eHealth and smart garment technologies to prevent falls in people with Parkinson's disease.



NeuRA's Dr Matthew Brodie and Associate Professor Kim Delbaere, who lead the study, are partnering with Sensoria Health and aim to make their neuro-rehabilitation program *WalkingTall with PD* the leading eHealth solution for maximising mobility and preventing falls in people with Parkinson's disease.

Falls are a common and often devastating event in the lives of people with Parkinson's disease. They are frequently caused by gait impairments, postural instability and freezing of gait, a brief absence of forward momentum of the feet despite the intention to walk. WalkingTall with PD uses visual, audio and haptic sensory cues to help rewire the parts of the brain that control walking in people with Parkinson's. The program aims to prevent freezing-ofgait and falls, and enhance participants' independence.



#### How does the program work?

Participants are given a NeuRA training mat with colour-coded stepping targets, a pair of Sensoria Smart Socks, an iPad and phone. The program, practised daily, encourages participants to step on coloured stepping targets that match a series of colours displayed on their iPad. At the same time, they listen to rhythmic auditory cues such as music and a metronome beat that are synchronised with the vibrating Smart Socks.

The combination of visual, audio and sensory elements helps to form new connections in the parts of the brain less affected by Parkinson's disease, leading to improved walking ability.

The program enables participants to manage and monitor their own progress via an app on their phone. The app can also trigger stimuli during everyday activities, such as vibration in their Smart Socks if they are in danger of experiencing freezing of gait, falls or if they show signs of shuffling feet.

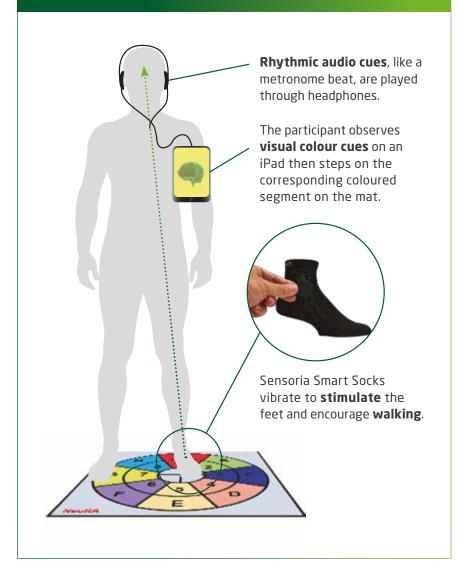
Clinicians can also monitor participants' progress remotely and adjust the program to provide ongoing and personalised continuity of care.

#### Improving quality of life for people with Parkinson's

"People with Parkinson's disease have substantial barriers to maintaining their independence. Our program has individuallytailored tools to empower all people with Parkinson's to manage their symptoms, increase capacity to remain independent and enjoy the highest possible quality of life," says Dr Brodie.

Associate Professor Delbaere says the grant gives hope to people with Parkinson's.

#### INNOVATIVE TECHNOLOGY PROGRAM SUPPORTS PARKINSON'S DISEASE



"WalkingTall with PD could transform the management of gait impairments for those with the disease," says Associate Professor Delbaere.

"The global uptake of mobile technology makes our user-friendly product suitable for widespread community application."



Dr Matt Brodie soldering the Smart Socks

### NEW RESEARCH PROGRAM REDUCING FALLS-RISK IN PEOPLE WITH PARKINSON'S

Researchers at NeuRA have published encouraging results of their reactive balance-training program that shows a 60 per cent risk reduction in falls due to trips and slips in older adults. This program is now being adapted to help those with Parkinson's disease and people with multiple sclerosis, and early indicators show promising results.

The reactive balance training program works on a retrainingthe-brain protocol developed from learning on a purposebuilt slip-and-trip walkway, the only one of its kind in the world. Participants, supported by a safety harness, walk along a pathway that has a series of unexpected booby traps in the form of boards that spring up and sliding tiles. These cause trips and slips, to which the brain and the body need to respond quickly. The learned response mechanism helps to retrain the brain to stay agile, respond faster to potential hazards, and correct balance to prevent a fall.

Following a series of devastating falls, Peter Marshall (*pictured with NeuRA's Dr Yoshiro Okubo*) was diagnosed with Parkinson's disease. Peter found out about NeuRA's research from a story in the media and decided to participate in the program to see if he could improve his balance.

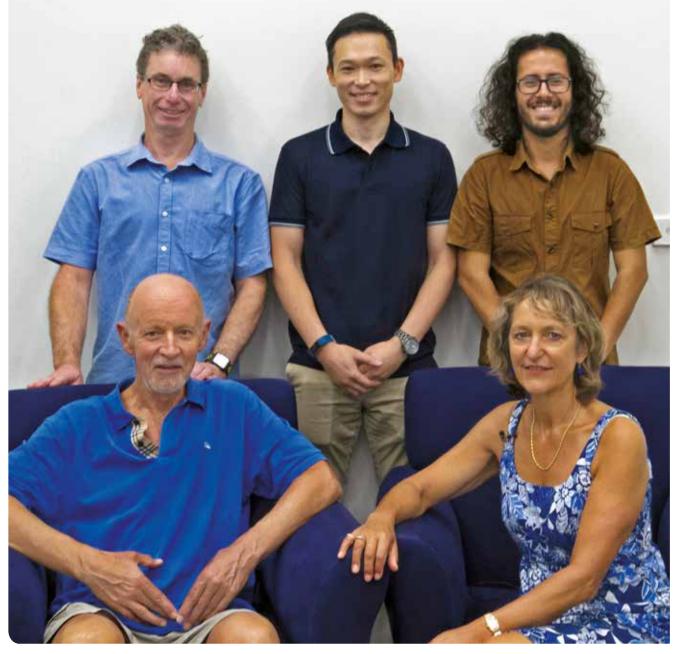
At his first visit to NeuRA, Peter was fitted with a comfortable safety harness. He then completed 20 walks on the walkway and attempted to keep his balance as he negotiated unpredictable slips and trip hazards – the harness safely catching him when these slips and trips triggered a fall.



Dr Yoshiro Okubo fitting Peter Marshall into the harness

As part of the study, Peter also practiced complementary step training exergames at home. These required him to perform quick and accurate steps on a step mat to play fun virtual games such as shooting aliens, squashing cockroaches and performing dance steps to music.

When Peter returned to NeuRA several weeks later and walked on the trip and slip walkway again, he recovered his balance without relying on the harness. The researchers noted Peter's gait had improved and he had become quicker at responding to hazards. "There are some positive signs to indicate that our new stepping program using exergames and the trip and slip obstacle courses may be effective in preventing falls in people with Parkinson's disease," says Professor Stephen Lord, Director of NeuRA's Falls, Balance and Injury Research Centre.



Back row (L-R): Professor Stephen Lord, Dr Yoshiro Okubo, Paulo Pelicioni; Front row (L-R): Peter and Janice Marshall

Janice Marshall, Peter's wife, has also seen the improvements in Peter's walking as a result of the study and the positive effect it has had on his mood.

"I feel like he is getting back to the old Peter who used to enjoy many things," says Janice. More than 80,000 people are living with Parkinson's disease in Australia, and of these, approximately two thirds will fall each year, resulting in injuries, hospitalisations and even death. NeuRA's goal is to continue to develop innovative therapies to improve balance and prevent falls to improve the quality of life for older Australians and those living with Parkinson's and multiple sclerosis.

More than 80,000 people are living with Parkinson's disease in Australia, and of these, approximately two thirds will fall each year, resulting in injuries, hospitalisations and even death.



### DR YOSHIRO OKUBO YOUNG RESEARCHER PROFILE

Dr Yoshiro Okubo obtained his PhD at the University of Tsukuba, Japan, where he investigated the influence walking had on falls in seniors. He was presented the Graduate School of Comprehensive Human Sciences Chair Award from the University of Tsukuba as well as a Postdoctoral Fellowship for Research Abroad by the Japan Society for the Promotion of Science. At NeuRA, Dr Okubo's research focuses on helping older people and those with Parkinson's and multiple sclerosis learn to better respond to and prevent trips, slips and falls. He is hopeful that this work will ensure people in these groups can maintain their independence as they age.

"There are many exercises for falls prevention, but it is important to train in a context similar to real life," says Dr Okubo. "Repeated exposure to trips and slips can help people better respond to fall hazards in daily life."

The advances in fall prevention made by Dr Okubo and NeuRA's Falls and Balance team has the potential to reduce personal and financial costs to individuals, their families and healthcare providers. Advances may also improve the quality of life for older people and people with neurological diseases who are at risk of falling.

Repeated exposure to trips and slips can help people better respond to fall hazards in daily life.

### NEW PARTNERSHIP FOR HEALTH INNOVATION IN AGED-CARE



The Mark Moran Group (MMG) and NeuRA have entered an Australian-first partnership to improve the health and wellbeing outcomes of older Australians. The partnership will be the first to facilitate the translation of NeuRA's age-related research into real-world outcomes for MMG residents. Through co-location and collaboration, we are demonstrating how research can deliver tangible and practical improvements in caring for people in retirement and aged-care living. The partnership will customise age-related health services of the future and show how these could be widely delivered.

"A huge challenge in taking research from the lab to the community is finding the right people and organisations with a shared vision and capacity to innovate. That's why we have partnered with Mark Moran Group," says NeuRA CEO Professor Peter Schofield AO.

The first project of the new partnership will be a customised app-based aged-care wellbeing assessment tool, the first of its kind in Australia. The assessment tool will equip care staff to evaluate the falls risk and psychological wellbeing of residents and will help identify specific clinical and allied health treatments required by the individual.

NeuRA is also working with MMG to develop an innovative new health and wellness centre at its new Caringbah location, which is planned to open in 2022. This will be the first time a 'living lab' has been created in an aged-care facility – an innovative concept designed to improve the health and wellness of MMG's residents, the surrounding community and to advance NeuRA's research discoveries.



"Mark Moran's state of the art facilities are the perfect setting for us to apply our Falls and Balance research in a real-world setting to prevent falls," says the Director of NeuRA's Falls, Balance and Injury Centre, Professor Stephen Lord.



### CLOSING THE OSTEOPOROSIS CARE GAP

The Australian and New Zealand Hip Fracture Registry (ANZHFR), based at NeuRA, is calling for hospitals to make osteoporosis plans a priority for patients leaving hospital after a hip fracture.



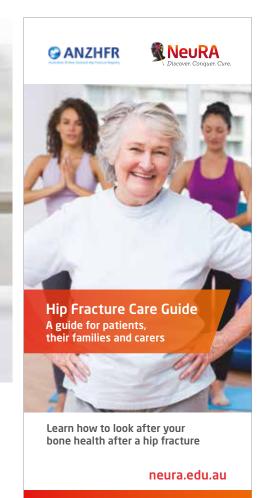
Data from ANZHFR's 2018 annual report shows only 25 per cent of hip fracture patients leave hospital on active treatment for osteoporosis and only 24 per cent of hospitals provide individualised written information on how to prevent future falls and fractures.

Professor Jacqueline Close, Geriatrician and ANZHFR Co-Chair, says while the data showed an improvement of 9 per cent compared to the 2017 report, Australia is still significantly behind other countries in closing the osteoporosis care gap.

"There are huge opportunities to further improve hip fracture care, including the prevention of future falls and fractures. Strong evidence exists to support treatment of osteoporosis in this population, but all too frequently we fail to offer treatments that can positively impact on people's lives," says Professor Close.

"Hospitals need to work toward closing the care gap to ensure hip fracture patients go home with an individualised care plan designed to prevent future fractures," says Professor Close.

"General Practitioners and other medical specialists also play a critical role in ensuring that bone health is addressed and that treatments are offered on an ongoing basis for older Australians unfortunate enough to break a bone from a fall," she says.



The number of hip fractures continues to increase due to the rising number of older adults. Current projections suggest that by 2022 there will be more than 30,000 hip fractures each year with a projected cost of \$1.12 billion.

These findings prompted NeuRA to publish a Hip Fracture Care Guide for patients, their families and carers. This guide addresses frequently asked questions about hip fractures. It also highlights the importance of preventing secondary fractures by treating osteoporosis and preventing falls.

ANZHFR is working collaboratively with other national organisations to ensure osteoporosis is recognised as a treatable chronic disease.



Hip Festival attendees and organisers

### HIP FESTIVAL GOES ON THE ROAD

The increasing global burden of hip fractures is significant. The Asia-Pacific region alone is predicted to account for half of the world's hip fractures by 2050.

The Australian and New Zealand Hip Fracture Registry (ANZHFR) has initiated a series of Hip Festivals to harness the collective knowledge of key stakeholders and to inspire and enable those involved in the provision of care.

Attendees have the opportunity to share experiences and innovative solutions to improve care in their local context. Presentations from clinicians from both regional and city-based services highlight the challenges and the many possible solutions to improve hip fracture care.

"I enjoyed getting together with colleagues who share a like-minded goal to achieve improved care for hip fracture patients and sharing stories," – Orthopaedic Clinical Nurse Consultant, NSW.

"All the presentations were relevant and informative. It was really useful to hear how other sites manage care. Great to have the opportunity to workshop in the afternoon," – Sub Acute Care Coordinator, WA.

"Very well organised event and an insight into the bigger state-wide picture for hip fracture management. Looking forward to next year," – Consultant Orthopaedic Surgeon, WA.

### AUSTRALIA NEEDS TO PRIORITISE SLEEP TO IMPROVE NATIONAL HEALTH AND PRODUCTIVITY

Four out of 10 Australians do not get enough sleep, and without adequate, restorative sleep the human body cannot function optimally.

Professor Danny Eckert, Director of the Sleep Program at NeuRA, is calling for a \$200 million strategic investment into sleep health over the next 5-10 years to be funded by the Australian Government's Medical Research Futures Fund.

The health, safety and economic consequences of inadequate sleep in Australia were estimated to be in excess of \$66 billion last year alone, according to a Deloitte Economics report commissioned by the Sleep Health Foundation.

Inadequate sleep can be caused by sleep disorders including sleep apnoea and insomnia, medical conditions that disrupt sleep like back pain or routinely not getting enough sleep because of lifestyle or life challenges. This leads to sleep deprivation and can result in daytime sleepiness and impaired alertness.

Inadequate sleep is associated with obesity, cardiovascular disease, cancer, impaired brain function, neurodegenerative disease including dementia and Alzheimer's disease, mental illness, diabetes, impaired immune function and more.

"We know that optimal sleep health requires the skills of a range of disciplines including sleep physicians, nurses, dentists, surgeons, psychologists, neurologists and pharmacists," says Professor Eckert.

"However, due to the high burden of disease, limited treatment options and lack of sleep health services available in the current health care system, wait times to see a sleep health professional can be more than a year, which limits Australians' access to high quality sleep services."

Professor Eckert's submission to the Federal Government's Inquiry into Sleep Health Awareness in Australia recommends that the Government should focus on innovative strategies and comprehensive services to improve sleep through a multidisciplinary systems approach.



"Improving sleep health will both improve the health and wellbeing of the nation and be economically advantageous," says Professor Eckert.





#### Recommendations

- Identify novel therapeutic targets and develop muchneeded targeted therapies for sleep disorders.
- 2. Targeted sleep research in understudied and underrepresented populations including sleep health in Aboriginal and Torres Strait Islander Australians, women, children and the elderly.
- **3.** Translational research studies that involve combination therapies to provide treatment options for the thousands of Australians who do not respond to first line therapies.
- 4. Development and implementation of novel sleep awareness programs for school children and training and education programs for health care professionals.
- Sleep-specific research fellowships for early and midcareer scientists and clinicians to create career pathways to expand the sleep research workforce in Australia.

6. Development of new approaches to clinical care and health care delivery models for sleep problems including the integration of research scientists into major public hospitals.

#### Better sleep for better health

Drinking, smoking and the light from your phone are just some of the reasons you can't get to sleep at night.

"Disrupted or inadequate sleep can negatively impact every organ in your body and is associated with anxiety, depression and other mental health disorders," says NeuRA sleep scientist Dr Hanna Hensen.

A lack of sleep will also influence our ability to work, making us less creative and efficient, and impacting on our motivation, judgment and decision-making.

#### Tips for a better sleep

Here are the top tips for improving sleep quality from NeuRA's Sleep Lab:

- Go to bed and wake up at the same time each day
- Avoid naps longer than 20-30 minutes
- **3.** Dim bright lights in your room
- **4.** Switch off your mobile phone and monitors before bed
- 5. Avoid caffeine, sugar treats, or cigarettes at least four hours before bed
- 6. Avoid eating heavy or rich foods including fried meals, spicy dishes, citrus fruits, and carbonated drinks, which can all trigger indigestion.



# **PREVENTING INFANT FALLS**

Among all children in Australia, infants under 12 months have the highest rates of death because of injury. Falls are the leading cause of injury hospitalisations, accounting for almost 50 per cent of hospitalised injuries for this age group.

Most falls among infants are from short heights less than one metre, and occur in the child's home. Around 80 per cent of infants under 12 months admitted to hospital after a fall have sustained a head injury, with approximately one third sustaining traumatic brain injury.

Despite the widespread nature of this problem and the potential for lifelong impact, recent research and previous systematic reviews have shown there is no evidence, worldwide, for any effective countermeasures.

There are currently no formal, targeted measures in place to prevent falls in infants in Australia. There is an urgent global need to identify effective ways to reduce the burden associated with falls among infants.

Infants at this age are under parental supervision most of the time. Therefore, interventions to prevent injury need to be targeted at parents and parental behaviours that can minimise the risk of falls. NeuRA researchers are developing a digital behaviour change intervention to help encourage those behaviours that will minimise falls risk to ultimately prevent infant fall incidents.

Associate Professor Julie Brown and Dr Susan Adams are leading research that explores the problem and identifies target behaviours that will provide a foundation for the digital intervention components. With PhD student Nipuna Cooray, they will then use best-practice methods for ensuring user understanding and acceptability. This will involve repetitively testing the content with new parents.

During 2019 and 2020, NeuRA will mainly focus on intervention material development and iteratively testing them with new parents recruited from the Royal Hospital for Women in Sydney. NeuRA's goal is to develop a set of materials that is easily understood by parents, with the long-term aim of creating a smartphone app to help reduce falls among young children.

Around 80 per cent of infants under 12 months admitted to hospital after a fall have sustained a head injury, with approximately one third sustaining traumatic brain injury.





### RESEARCHERS REVIEW CHEST CLIPS ON CHILD CAR RESTRAINTS IN AUSTRALIA



Research using child-sized crash test dummies has shown, for the first time, a potential safety benefit in using plastic chest clips on child car restraints, as they keep shoulder straps together, reducing the risk of serious injury in a crash.

Despite chest clips being widely used in the US, they do not meet Australian safety standards due to concerns they may cause neck injuries in a crash. However, researchers at the Transurban Road Safety Centre at NeuRA have found no sign of serious injury related to the chest clips when tested on Australian child restraints.

Researchers reviewed real-world data from an American crash database to see if there were any signs of injury in children up to the age of four. "We found that there was actually a reduction in the risk of moderate to serious injury of all types in children under one when chest clips were used properly," says Professor Lynne Bilston, Senior Principal Research Scientist at NeuRA.

This review of American data prompted Professor Bilston to study the performance of Australian car seats in crash tests using the same type of chest clips used in the US. Professor Bilston and her team conducted crash tests using small childsized crash test dummies at the Transurban Road Safety Centre based at NeuRA.

"We tested chest clips in frontal crashes, using a crash test dummy that represents the smallest child who would normally be forward facing," says Professor Bilston.



The crash tests were done at 49 kilometres per hour in a frontal direction, both with a tight harness and with a looser harness. Analysis of high-speed crash test footage showed the plastic clips tended to slide down the straps during the crash, meaning they are unlikely to be forcefully touching a child's neck. There was no difference in the neck forces with the clips in place.

The results of this research will be submitted for consideration by the Australian Standards Committee to determine whether plastic chest clips might have a net benefit, allowing them to be supplied with Australian child car restraints.





### BETTER LABELLING ON CHILD CAR RESTRAINTS COULD INCREASE CORRECT USAGE

A study led by NeuRA's Associate Professor Julie Brown has shown improved design of child restraint instructional materials could increase the correct use of these restraints by up to 27 per cent, saving lives and preventing injuries.

Associate Professor Brown's study revealed that nearly half of Australian parents using restraints are using them incorrectly, increasing the risk of serious injury to children by up to three times.

In a survey of 400 Australian parents, 90 per cent reported that they had read the instructions supplied with the restraints. Despite this, there were high rates of incorrect use.

"Research outcomes suggest instructional materials in their current form may not be effective in communicating how to use restraints correctly," says Associate Professor Brown.

"Our findings tell us that increasing comprehension of child restraint instructions is an effective measure to counter misuse, and that users should be involved in every step of the design and testing."

As part of the study, researchers at NeuRA looked at the range of instructional materials provided by manufacturers of restraints, citing these as a leading cause of errors in use. Following their review, Associate Professor Brown and her team developed a new set of prototype instructional materials for correctly using child restraints.

The instructions differ from other instructions because they were designed with a user-driven approach and were tested and refined until at least 80 per cent of study participants achieved correct comprehension and proper use. "Instead of a group of experts sitting around a table developing user guidelines, we asked parents to work with us to develop new instructions, and to then road test them as part of our ongoing research to review and deliver correct comprehension and proper use of installation guidelines," says Associate Professor Brown.



Professor Lynne Bilston and Associate Professor Julie Brown at the Transurban Road Safety Centre

### INFLAMMATION LINKED TO NEUROTRANSMITTER BLOCKADE IN SCHIZOPHRENIA



Clinicians have long recognised that street drugs such as ketamine and phencyclidine (also known as PCP) block a key neurotransmitter receptor, which can cause schizophrenialike hallucinations and delusions.

Understanding how this is mimicked in the brains of people with schizophrenia who are not on drugs has been a mystery. But now, NeuRA's Professor Cyndi Shannon Weickert and Associate Professor Tom Weickert, along with their research partners, have discovered the first direct evidence that finally solves this decade-long puzzle.

Their research has shown that elevated levels of kynurenic acid in the brains of people with schizophrenia block the excitatory neurotransmitter receptor, known as the N-methyl-D-aspartate receptor (NMDAR), which can lead to psychosis. "This is exciting for the field of schizophrenia research because we have now identified a key chemical messenger used by immune cells to interfere directly with neuronal function in the brain," says Professor Cyndi Shannon Weickert.

This study provides a better understanding of the molecular and cellular mechanisms underlying the harmful effects of neuroinflammation, and paves the way for better-targeted therapies with fewer side effects for people with schizophrenia.

It has long-been suspected that metabolism of the amino acid tryptophan, commonly known to produce the "feel-good" neurotransmitter serotonin, is involved in schizophrenia. During inflammation, tryptophan is broken down into kynurenine, which can form one of two chemical compounds: quinolinic acid or kynurenic acid. There is debate about which chemical compound is involved in the brain pathology of schizophrenia.

But the research team, led by Professor Shannon Weickert, has found the first evidence that the culprit is elevated levels of kynurenic acid. This acid plays an important role in protecting brain cells from overstimulation by blocking NMDAR, but in some instances, this can also lead to psychosis.

This study also demonstrated that biochemical markers in blood could reflect brain abnormalities related to schizophrenia, such as volume loss of the prefrontal cortex and attention impairment.



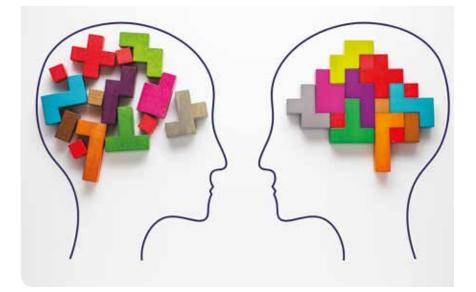
Helen Cai and Professor Cyndi Shannon Weickert

This suggests that the kynurenine pathway may be a viable target for the development of a clinical blood biomarker to help predict brain and cognitive changes in schizophrenia.

Researchers have been seeking a biomarker of schizophrenia for a long time, says Associate Professor Weickert.

"Our work suggests blood kynurenine and tryptophan levels may be able to quickly and simply inform clinicians of the presence of schizophrenia. This opens the possibility of developing new drug therapies that can block the entry of kynurenine into the brain," he says.

"This could stop the overproduction of the deleterious NMDAR blocker in the brain and would be a totally new approach to try to stop hallucinations and delusions," he says.



Gour work suggests blood kynurenine and tryptophan levels may be able to quickly and simply inform clinicians of the presence of schizophrenia. This opens the possibility of developing new drug therapies that can block the entry of kynurenine into the brain.



L-R: Javad Jamshidi, Dr Haeme Park, Dr Justine Gatt, Arthur Montalto and Miranda Chilver

## IDENTIFYING FACTORS THAT MAXIMISE MENTAL RESILIENCE

The neurobiology of resilience is complex. But neuroscience research is revealing an understanding of its biological mechanisms to help guide healthy emotional and cognitive functioning.

Resilience is defined as the process of positive adaptation in the face of adversity or stressful life events, and is crucial in the recovery from traumatic events.

NeuRA researchers led by Dr Justine Gatt, are embarking on a new project known as TWIN-10, which involves a 10-year follow-up of a cohort of twins. Researchers will evaluate changes in wellbeing and mental health outcomes to develop predictive trajectories of risk versus resilience. They aim to map the corresponding patterns in brain structure and function that predict resilience onto these trajectories.

Dr Gatt's previous research of the twin cohort showed genetic and environmental factors contribute almost equally to our level of wellbeing. Research also showed associations between wellbeing and other measures, including brain structure and cognitive function. "We observed a negative relationship between a part of the brainstem called the pons and levels of wellbeing, as well as a positive association between wellbeing and specific cognitive factors like working memory," says Dr Gatt.

By using the same twin sample as the original cohort, the team will be able to observe the longitudinal changes in neurocognitive mechanisms.

"We will be looking at the corresponding changes in brain plasticity over time that may predict risk versus resilience by using functional and structural imaging data," says Dr Gatt.

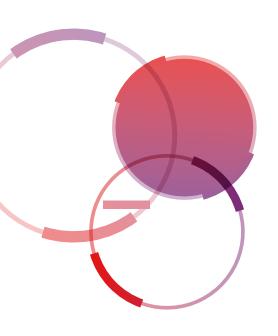
The research will also explore the relative contribution of genetics and environmental factors in modulating these shared neurocognitive and brain networks in both identical and non-identical twins. The research aims to identify individuals who may be at risk of developing a mental disorder. This will allow researchers to develop tailored interventions that target significant adverse environmental biomarkers.

"By identifying factors that maximise mental resilience from adversity, we hope to transform current clinical practice and move away from treatments that serve to only reduce clinical symptoms. We hope to move towards treatment plans that also incorporate a flourishing state of mind and promote overall mental wellbeing," says Dr Gatt.



### UNDERSTANDING THE BIOLOGY OF CHILDHOOD TRAUMA IN PSYCHOTIC DISORDERS

Research from the Stress-related Psychopathology research group led by NeuRA's Professor Melissa Green and Dr Yann Quidé, aims to determine the neurobiological consequences of childhood maltreatment.



Most mental disorders have strong genetic foundations, but exposure to adverse environmental factors are also strong contributors to their development.

Childhood trauma is a form of chronic stress often characterised by repeated forms of emotional, physical and/or sexual abuse. It is now a well-established risk factor for the development of schizophrenia and bipolar disorder, and is prevalent in over 50 per cent of these populations.

Research in this area led by Dr Quidé has recently shown differences in brain structure and function, social cognitive skills, and schizophrenia-proneness among people exposed to childhood trauma. In addition, increased levels of inflammation in patients with schizophrenia were associated with childhood experiences of sexual abuse. However, the mechanisms by which childhood trauma exposure impacts brain development or other neurobiological markers – and their potential interaction with genetic risk for psychotic disorders – remain unclear.

In line with NeuRA's vision, the team is actively working on the discovery of these mechanisms to contribute to the detection of new targets for the development of personalised pharmacological and psychological treatments for psychotic disorders.

### EXPLORING THE IMMUNE-BRAIN CONVERSATION



Until a few decades ago, it was thought that the brain and the immune system existed as separate entities. But we now know this could not be further from the truth.

Immune-signaling molecules are involved in regulating many aspects of brain function. Importantly, when you have an infection like the flu, the brain needs to know you are sick so that it can induce a fever to help fight off the infection. The brain also tells the body to rest and recover, which we experience as fatigue, sleepiness or other changes in our behaviour.

However, there are times when the immune system can hijack the brain and cause long-term mental health issues such as depression, anxiety and a reduction in cognitive abilities. For some people this happens when inflammation is high or becomes chronic. Dr Adam Walker, head of NeuRA's Laboratory of Immunopsychiatry, is working to identify ways to prevent and treat inflammationinduced psychiatric illness.

Immune-brain communication is bidirectional, meaning the brain can talk to the immune system and vice versa. Humans have two major stress systems; the sympathetic nervous system commonly known as our fight or flight response, and the hypothalamic pituitary adrenal axis, which is our energy mobilisation response.

Research shows that these stress response pathways modulate immune function and can suppress immunity. This makes people more vulnerable to diseases and can even increase inflammation.

There is growing evidence that nerves talk to immune cells that have been laid down for adaptive reasons. But with chronic psychological stress and continued activation of neural pathways, the brain can subvert the immune system and impair its function. This communication plays a pivotal role in daily life.

Dr Walker is working to identify how to target immune-to-brain signaling to improve health and wellbeing. He is currently researching drugs that may be repurposed or designed to help treat inflammationinduced depression.

Research shows that these stress response pathways modulate immune function and can suppress immunity. This makes people more vulnerable to diseases and can even increase inflammation.

### NEUROSCIENTIST DISCOVERS POTENTIAL TREATMENT FOR 'CHEMOBRAIN'



Breast cancer advocate Karen Foster and Dr Adam Walker

In a discovery that could one day help breast cancer patients, NeuRA's Dr Adam Walker has found a potential treatment for 'chemobrain', a condition that affects up to 60 per cent of women after they receive chemotherapy for breast cancer.

The study has the potential to transform cancer treatment research and eradicate some of the most common negative side-effects of cancer and chemotherapy.

Dr Walker says that until now, scientists believed that chemotherapy was the only cause of cancer-associated cognitive impairment such as memory, learning and concentration difficulties, commonly dubbed as 'chemobrain'. "However, studies have observed cognitive impairment in cancer patients prior to treatment," says Dr Walker.

"This suggests the cancer alone may be sufficient to induce cognitive impairment, but the mechanisms through which this occurs were unknown." In his study using animal models, Dr Walker found that a low dose of anti-inflammatories completely blocked breast cancer cells from causing memory loss without affecting other aspects of the disease.

"This suggests that the tumour itself can actually hijack the brain via inflammation to cause cognitive impairment. But we may be able to use anti-inflammatories to block this process," he says.

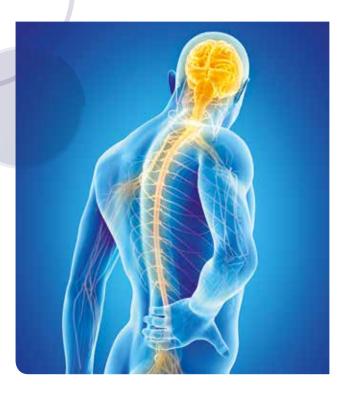
"This is the first study to show that we can disrupt tumourto-brain communication using anti-inflammatory agents such as aspirin to reduce the inflammation that causes cognitive impairment."

The next phase of Dr Walker's work is to look at how antiinflammatories might block other aspects of 'chemobrain,' such as learning and concentration difficulties.

"We think anti-inflammatory drugs could be a potentially cheap and safe intervention to prevent and treat chemobrain, but we need to learn more about when during the cancer journey patients should take them," says Dr Walker.



### RESEARCHERS CHALLENGE GUIDELINES FOR TREATING ACUTE LOW BACK PAIN



NeuRA's pain researchers are calling for a review of clinical guidelines for treating acute low back pain following their study that showed the early, specialised care that is recommended in global guidelines does nothing to help a patient's recovery.

This is the first randomised, placebo-controlled trial for testing the effectiveness of early, specialised patient education for acute low back pain. NeuRA's Associate Professor James McAuley says recommendations to include intensive early management in treatment for acute low back pain may be premature.

"Most people recover from acute low back pain without medical intervention. In our study, we were interested in treating those who were at risk of not recovering," he says.

"Globally, major clinical guidelines recommend that health practitioners provide patient education to manage acute low back pain. This is the treatment for back pain that is currently the most accepted and recommended." The study followed 202 participants in Sydney who had experienced low back pain for less than six weeks and showed a high risk of developing chronic low back pain. Participants also saw their regular health practitioner during the study.

Participants in the intervention group received early, specialised care involving patient education over two one-hour sessions. The education focused on pain and contributing factors, and self-management techniques.

Participants in the control group received placebo patient education – active listening, but without information or advice.

The trial showed that adding two one-hour sessions of specialised patient education to usual care of patients did not reduce pain intensity or lead to a meaningful reduction in the development of disability. "These results challenge a widespread belief that patient education is an effective strategy for treatment of acute low back pain," says Associate Professor McAuley.

"Adding specialised, time-consuming treatment to primary-care is unnecessary for most patients with acute low back pain," he says.

"This has the potential to fundamentally change the way acute low back pain is managed in primary care."

Key outcomes of this research suggest a basic approach to acute low back pain treatment should include simple advice on how to remain calm and be reassured that your pain will get better, keep active and remain at work, avoid strong medications, and avoid imaging tests.



Associate Professor James McAuley and Associate Professor Sylvia Gustin

#### NEURA PAIN RESEARCH RECEIVES A \$2.3 MILLION FUNDING BOOST

Pain research at NeuRA is set to benefit from a \$2.3 million-dollar funding boost with Associate Professors James McAuley and Sylvia Gustin leading a global research collaboration to test interventions for complex regional pain syndrome (CRPS). "Of all the chronic pain conditions, CRPS is the most devastating," says Associate Professor McAuley.

"It's characterised by unbearable and terrifying burning or stinging pain, and there is currently no available treatment," he says.

Approximately 75 per cent of patients report suicidal thoughts, plans or actions. There are no high-quality trials to guide management. "Our aim is to develop low-cost, evidence-based interventions that can be easily translated into clinical practice," says Associate Professor McAuley.

The project is part of NeuRA's MEMOIR research program that involves multi-national randomised controlled trials to test the most promising interventions for chronic pain.



••• Our aim is to develop low-cost, evidence-based interventions that can be easily translated into clinical practice.



# **RESOLVE CHRONIC LOW BACK PAIN**

Research shows that there are changes in the brain when someone has pain for a long time. NeuRA's pain researchers believe it is these changes that could make recovery from pain slower and more difficult.

Using this knowledge of the brain and how it changes with pain, Associate Professor James McAuley developed two treatment programs for chronic low back pain. These treatment programs target how the brain and central nervous system process information to produce low back pain. In the RESOLVE trial, an NHMRC-funded randomised controlled trial, Associate Professor McAuley and his team are comparing these treatment programs to determine if back pain can be reduced through retraining the brain and central nervous system.

Back pain is the leading cause of disability worldwide, and second only to the common cold as a reason for visiting a general practitioner. "The interventions used in the RESOLVE study could have a significant and lifechanging impact on the quality of life for people living with low back pain," says Associate Professor McAuley.

Back pain is the leading cause of disability worldwide, and second only to the common cold as a reason for visiting a general practitioner.

PAIN

#### RESEARCH SUGGESTS CHRONIC PAIN CAN NEGATIVELY CHANGE YOUR PERSONALITY



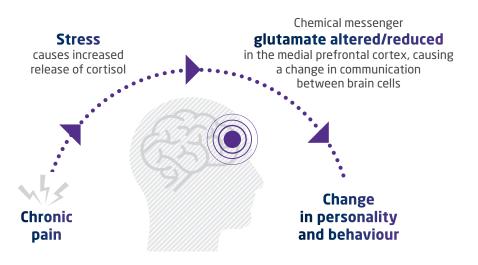
New research has shown for the first time that communication between brain cells is disrupted in people with chronic pain, which can lead to a change in their personality.

The study, led by Associate Professor Sylvia Gustin from NeuRA and UNSW, found that people with chronic pain have a reduction of the brain's key chemical messenger, glutamate, in the brain region responsible for regulating thoughts, beliefs and emotions. Using cutting edge brain imaging, Associate Professor Gustin identified a reduction in glutamate in participants' medial prefrontal cortex. This is the first study to identify a communication error in the brain cells of humans with chronic pain, and shows associated personality and behaviour changes, including constant worry, pessimism, fear and a lack of motivation.

"The study shows people with chronic pain see everything through a filter of fear, worry and pessimism, which affects all aspects of their lives," says Associate Professor Gustin. Associate Professor Gustin says her study is a step towards reducing the stigma around chronic pain.

"People with chronic pain are often labelled as having certain personality traits that make them more likely to experience pain, but we now know that's not true," says Associate Professor Gustin.

Associate Professor Gustin hopes to build on her ground-breaking research to develop clinically accessible brain-computer interface systems to help regulate thoughts, beliefs and emotions in people with chronic pain. Better functioning of the brain's key chemical messenger, glutamate, could reduce people's pain, and improve associated mental health disorders.



#### PERCEIVED HAND SIZE HOLDS KEY TO UNDERSTANDING BRAIN-HAND COMMUNICATION

Research shows that healthy individuals, when asked to locate the position of the tips and knuckles of each finger on their hand while not looking at it, consistently misjudge the shape of their hand.

Specifically, they overestimate the width of their hand and underestimate the length of their fingers. This would also imply that the same individuals misjudge the actual location of at least some parts of their hand during the task.

A new study, led by NeuRA researchers Professor Simon Gandevia and Dr Annie Butler, aimed to determine whether healthy individuals could accurately locate the actual position of their hand when hidden from view. They wanted to find out whether accuracy depended on the type of task used, the orientation of the hidden hand, and which hand was tested.

The study revealed that healthy participants consistently misjudged the location of their hidden hand as closer towards their wrist (proximal bias) and, to a lesser extent, away from the thumb (ulnar bias). Results also showed that participants' perceived location of their hand drifted closer towards the wrist (proximal proprioceptive drift) over time, while remaining stable along the long axis of the hand.

#### Significance and implications

Position sense is a crucial component of proprioception, which is the innate ability to be aware of where our body parts are located, allowing us to interact with our environment. Proprioception is negatively affected in a wide range of neurological conditions, such as stroke and Parkinson's disease as well as many orthopaedic conditions, such as chronic low back pain. At present, there exists a gap between research and clinical settings regarding the assessment of proprioception.

One limitation to widespread detailed testing of proprioception is the complexity, cost and time-consuming nature of proprioceptive measures used in the laboratory. A refined version of the hand localisation task used in this study offers potential as a simple, quick measurement of one aspect of proprioception. By establishing data from healthy populations, future studies could investigate specific disorders in which proprioception is negatively affected to help determine the validity of the landmark localisation task as a means of differentiating between normal and impaired proprioceptive acuity.

### WORLD'S FIRST INTERNATIONAL MOTOR IMPAIRMENT CONFERENCE

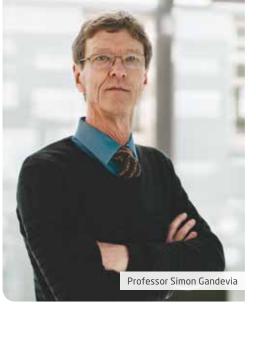
#### NeuRA hosted the first international conference on motor impairment in late 2018.

The three-day conference brought together leaders in motor impairment from around the globe, with world-renowned researchers from the UK, Canada, the US, the Netherlands and Australia.

The conference focused on all aspects of motor impairment, from ground-breaking research to translational medicine and clinical trials.

Deputy Director of NeuRA and Foundation Scientist Professor Simon Gandevia says motor impairment is a major cause of physical disability. "Motor impairment impacts a range of conditions from stroke and multiple sclerosis to cerebral palsy and spinal injury, and it can also be part of normal ageing," says Professor Gandevia.

"This conference was the first time we have established an international focus on motor impairment. It was a significant step towards filling the gaps in our knowledge by bringing together global experts for conversation and collaboration," he says.



"Our vision is to advance the transfer of new understanding of physiology and pathophysiology in motor impairment toward the clinical outcome of improved motor function."

Motor impairment research at NeuRA focuses on three key themes that relate to leading causes of disability including weakness and fatigue, impaired sensation and balance, and muscle contracture.



Conference attendees

#### UNDERSTANDING MUSCLE GROWTH AND CONTRACTURE IN CEREBRAL PALSY

People with cerebral palsy often develop muscle contractures, which is the tightening and shortening of muscles. Muscle contractures reduce joint mobility, impair performance of motor tasks such as walking and grasping, and cause deformity and pain. Muscle contractures are not present at birth. Instead, children with cerebral palsy develop muscle contractures during childhood. Little is known about how human muscles grow, or about how muscle growth is disordered in children with cerebral palsy. But NeuRA researchers, led by Professor Rob Herbert, are embarking on research that is the first of its kind to describe growth-related changes of leg muscles in children with and without cerebral palsy. The MUGgLE (Muscle Growth in the Lower Extremity) Study is the first large-scale longitudinal study of growth in human muscles, the first longitudinal study of muscle growth in children with cerebral palsy, and the first study of muscle growth to use magnetic resonance imaging (MRI).







The insights gained from this project are fundamental to our understanding of human biology and for developmental medicine. Ultimately, the findings of the study may help in the development of new interventions to prevent and treat muscle contractures.

In the study, the lower legs of more than 300 children will be scanned using cuttingedge imaging protocols, which have recently been developed at NeuRA. These techniques are based on diffusion tensor imaging - an MRI technique - to obtain high-resolution, large-field, three-dimensional measurements of the structure of whole human muscles. Measurements will be obtained both from children with and without cerebral palsy so that differences in muscle growth between these groups can be compared.

NeuRA's Professor Rob Herbert is leading the study and says the findings could assist health professionals in the prevention and treatment of muscle contractures in children with cerebral palsy.

"While it is clear muscle contractures in children with cerebral palsy represent a failure of muscle growth, it is not known if contractures are due to failure of longitudinal growth of muscle fibres or tendons, or other mechanisms," says Professor Herbert.

L-R: Brian Chow, Professor Rob Herbert, Bart Bolsterlee

The study will also expand knowledge of human development, biomechanics and muscle physiology.

"This data is important to biologists seeking to understand regulation of muscle growth, computational biomechanists simulating motor tasks in children, and researchers seeking to understand factors that influence motor development, motor control and motor performance," says Professor Herbert.



Endorestiform nucleus discovered

#### RENOWNED NEUROSCIENTIST DISCOVERS HIDDEN REGION OF THE HUMAN BRAIN

World-renowned cartographer of the brain, Scientia Professor George Paxinos AO, has discovered a hidden region of the human brain. This region is found near the brain-spinal cord junction and Professor Paxinos has named it the *endorestiform nucleus*.

Professor Paxinos suspected the existence of the *endorestiform nucleus* 30 years ago, but has only now been able to see it with better staining and imaging techniques.

"There is nothing more pleasant for a neuroscientist than identifying a hitherto unknown area of the human brain. In this case, there is also the intrigue that this area is absent in monkeys and other animals," says Professor Paxinos, adding, "there have to be some things that are unique about the human brain besides its larger size, and this may be one of them."

The discovery of new brain regions helps researchers to explore cures for diseases including Alzheimer's, Parkinson's and motor neuron diseases.

The *endorestiform nucleus* was noticed when Professor Paxinos

introduced the use of chemical stains, combined with imaging techniques, in the production of his latest atlas mapping the human brainstem.

The endorestiform nucleus is located within the inferior cerebellar peduncle, an area that integrates sensory and motor information to refine our posture, balance and fine movements.



Scientia Professor George Paxinos AO

"I can only guess as to its function, but given the part of the brain where it has been found, it might be involved in fine motor control," says Professor Paxinos.

Most neuroscientists researching neurological or psychiatric diseases in humans or animal models use Professor Paxinos' brain atlases as guides for their work. His human brain atlases are heralded as the most accurate for the identification of brain structures and are routinely used by brain surgeons.

An increasingly detailed understanding of the architecture and connectivity of the nervous system has been central to most major discoveries in neuroscience in the past 100 years. "Professor Paxinos' atlases, showing detailed morphology and connections of the human brain and spinal cord, provide a critical framework for researchers to test hypotheses from synaptic function to treatments for diseases of the brain," says NeuRA's CEO Professor Peter Schofield AO.

Professor Paxinos is the author of the most-cited publication in neuroscience and 52 other books of highly detailed maps of the brain. The maps chart the course for neurosurgery and neuroscience research, enabling exploration, discovery and the development of treatments for diseases and disorders of the brain. The endorestiform nucleus is located within the inferior cerebellar peduncle, an area that integrates sensory and motor information to refine our posture, balance and fine movements.



Dr Lucette Cysique and Professor Sean Rourke

# THE NEUROLOGICAL COMPLICATIONS OF HIV

Professor Sean Rourke from the University of Toronto, Canada, and Dr Lucette Cysique from NeuRA are leading an international taskforce to update the classification of the neurocognitive complications from HIV. In this Q&A, Dr Rourke and Dr Cysique talk about their latest collaboration.

#### What are you working on?

We are revising a document that was developed 10 years ago that details the way neurocognitive complications that occur in HIV are characterised.

We are also coediting a book that brings together all the leading clinicians and researchers of HIV around the world to talk about where we are with understanding how the brain is affected by HIV and identify gaps in knowledge.

#### Why is this work important?

It is an excellent opportunity to work together and to also work with people from around the world to restructure the diagnostic criteria for the neurocognitive complications of HIV and bring to bear what we have learned in 10 years.

#### What are you hoping to achieve with this work?

One of the major things we are trying to do is bring the international HIV research community together and work with other research disciplines around the world to understand how HIV impacts the brain, especially as people with the condition age. We want to see how we can bring that expertise and knowledge into the context of HIV because we think that is going to be really important as people with HIV live longer.

It would be great to be able to prevent many of the neurocognitive complications of HIV including difficulty in making decisions and learning, attention, concentration, and memory difficulties. It is good to be proactive in educating health care providers and patients with HIV about what they can do to keep the brain healthy.

#### BREAKTHROUGH IN CLEFT LIP AND PALATE RESEARCH

New genes have been identified that play a role in the development of cleft lip and palate, in an international research collaboration led by NeuRA.

The study provides the first evidence that a significant number of non-syndromic clefts have a single gene basis.

Representing about 70 per cent of cleft lip and palate cases worldwide, non-syndromic cleft lip and palate typically occur in isolation without other physical abnormalities. This craniofacial malformation has long been thought to be caused by a combination of many common genetic variants and environmental factors, each contributing a small amount to the risk of a child being born with a cleft.

Using next-generation sequencing, the research team, led by NeuRA's Associate Professor Tony Roscioli, identified variants in four new genes, each representing a primary cause of non-syndromic cleft lip and palate. These genes are known to encode proteins that work together in a network. Cleft lip and palate is one of the most common human malformations, occurring in one in 800 children.

"That equates to about 250 Australian children each year and one affected child born every three minutes worldwide," says Associate Professor Roscioli.

The genetic pathway that emerged from the data gathered through collaboration with clinical teams from around the world is arguably one of the most significant advances in cleft lip and palate genetics in the past 15 years.

"Knowing the genes and the way these impact lip and palate formation opens the door for further research to understand how these genes work, and to develop treatments," says Associate Professor Roscioli.



Cleft lip and cleft palates are repaired with corrective surgery. Future research will further investigate the biology and link the findings to future potential therapies. These discoveries will allow geneticists to provide more accurate information to families.

The National Health and Medical Research Council-funded project was led by Associate Professor Tony Roscioli from NeuRA, Sydney Children's Hospital and UNSW Sydney; and Professor Timothy Cox, from Seattle Children's Research Institute and the University of Washington School of Medicine in the US.

Cleft lip and palate is one of the most common human malformations, occurring in one in 800 children.



# THE 1,000 BRAINS PROJECT

The 1,000 Brains Study is a research project seeking to identify the genetic factors in the brain that cause life-changing neurodegenerative diseases like Alzheimer's disease and Parkinson's disease, and other types of movement disorders and dementias. This study will focus on the key unresolved question: why do some of us develop devastating neurodegenerative diseases, while others retain good brain health?

The study will compare the genomes of people who successfully reached healthy old age with those who have died from neurodegenerative disease. It will also compare the brain tissue in these groups through microscopic examination. The collection, examination and research of brain tissue will take place at NeuRA's Sydney Brain Bank. Director of the Sydney Brain Bank, Dr Claire Shepherd, says brain banks are essential to underpin research into neurodegenerative disorders.

"We collect the tissue to enable national and international world-class research, and to conduct our own research here at NeuRA in the hope that we can find a cure or a treatment for these diseases and disorders," says Dr Shepherd.

"Human brain tissue is the gold standard for ageing and neurodegeneration research as it gives a true indication of the human condition. We plan to sequence the genome of the brain and understand what genetic risk factors and what genes contribute to the disease process," she says.

Holding the genetic information associated with the brain tissue greatly enriches the research outcomes that can be achieved by investigators using tissue from the Sydney Brain Bank.

"Research organisations like NeuRA are at the forefront of neuroscience research. That's why I support them because dementia is going to affect so many people and it's not just the person who gets it, it affects the whole family and the community," says Mrs Janet Cameron OAM of Grant Broadcasters and a key NeuRA supporter.

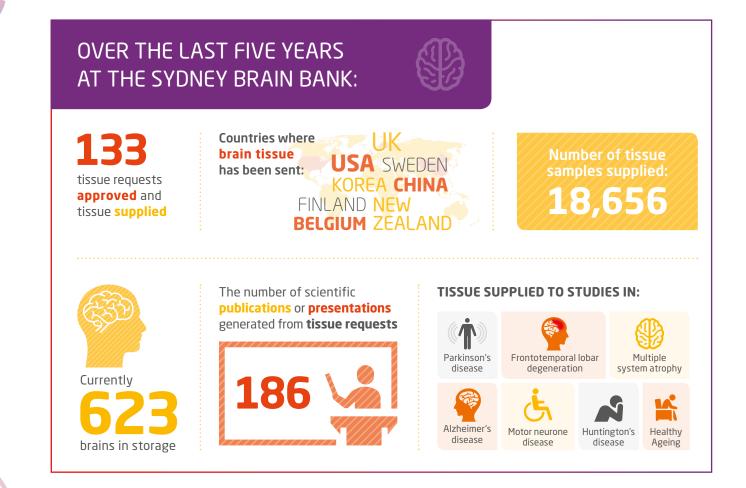




Sydney Brain Bank team: (L-R) Heather McCann, Carla Scicluna, Andrew Affleck, Dr Claire Shepherd, Francine Carew-Jones and Adèle Lusson

#### WHY DO WE NEED BRAIN BANKS IN AUSTRALIA?

- The human brain tissue collected by brain banks is essential to **provide insight into the unique cellular biology of human brain disease,** which can't be done as accurately using other models.
- Brain banking assists clinical practice by providing neuropathological assessment of brain tissue, which is then used to inform clinicians on the accuracy of patient diagnoses.
- Researchers rely on brain banks to access well-characterised brain tissue to drive neurodegeneration research efforts towards the development of clinical interventions and cures.
- Advances in dementia research will **reduce the cost** of dementia in Australia, which is estimated to reach \$36.8 billion by 2056.
- Some types of dementia research that require access
  to brain tissue are only possible through brain banks.



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The Neuroscience Research Australia Board exercises overall governance of the entire company's range of activities, NeuRA, NeuRA Foundation and the Mindgardens Neuroscience Network. The Board's current focus is the development of the Mindgardens Neuroscience Network, therefore the Board established the NeuRA Governing Council in 2018 to oversee all NeuRA and NeuRA Foundation activities.



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The Hon John Watkins AM LLB, MA, DipEd, HonDLitt Macq The NeuRA Governing Council has delegated powers to oversee the operations and functions of NeuRA, including setting and monitoring the strategic direction, use of resources, budget and performance.



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Mr Lee Valentine



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The NeuRA Foundation Board is the corporate trustee of the NeuRA Foundation trust fund. The Foundation's sole objective is to raise donations to enhance the development of NeuRA through financial support of its research programs, infrastructure and facilities.

# MESSAGE FROM THE FOUNDATION DIRECTOR

**Grant Simpson** 

Working together to make a difference in life and achieve something meaningful inspires us all.

Many of us aspire to do our part, in whatever small way, to make the world a healthier and safer place for those we love, for the vulnerable, and for the generations who will follow us.

The NeuRA Foundation exists as a channel for our partners to work with NeuRA in tangible and meaningful ways to support our mission to discover, conquer and cure.

I am particularly delighted to see the ways in which our donors, supporters and partners are working alongside NeuRA to build hope through our research. The 1,000 Brains Project is one such example. This project seeks to accurately identify the causes of neurodegenerative diseases like dementia earlier in order to halt or delay their progression. The 1,000 Brains Project is a collaborative initiative that combines the neuropathological work of The Sydney Brain Bank, together with genome analysis. This is possible thanks to funding from generous donors including Jackie Waterhouse and her family who have made this important project possible.

NeuRA is also looking at technology to provide solutions to treat the symptoms of Parkinson's



disease. Our work on 'Smart Garments' uses app-based technology to control electrical stimulation to sensors built into socks. This sensation stimulates movement and is designed to prevent freezing of gait and falls in people with Parkinson's disease. This ground-breaking research is enabled through a partnership with US manufacturer Sensoria, funding from The Michael J. Fox Foundation and the Shake It Up Foundation, and the generosity of other major benefactors.

We are extremely proud of our partnerships with leading businesses such as Transurban, who partner with us in facilitating research at The Transurban Road Safety Centre, which is located at NeuRA. The goal of the Centre is to make our roads safer for all. We are also delighted to be forming a new partnership in the aged-care sector with the Mark Moran Group, who are working with us to enhance the wellbeing of older Australians.

Finally, I would like to acknowledge that this work could not be achieved without the ongoing partnership and generosity of our donors, particularly our major donors, regular givers and bequest partners. It is the passion and selflessness of our supporters that inspires us to strive towards achieving our mission. It is through your support and partnership that NeuRA is able to provide hope to the millions who are living with a devastating disease or disorder of the brain. We are extremely thankful to you all.

FOOD FOR THOUGHT DINNER 2019

On 16 May, NeuRA held its annual Food for Thought dinner in the Margarete Ainsworth Building. The night was dedicated to raising funds for dementia research, and included the launch of the 1,000 Brains Project. The NeuRA Foundation was thrilled to host 145 guests and to begin fundraising efforts for the \$5 million needed for the project.



Katie Little speaking

The highlight of the evening was guest speaker Katie Little who shared her story of growing up with her mother and Australian television icon, Jeanne Little. In 2009, Jeanne was diagnosed with Alzheimer's disease and since then life has changed significantly for the star and her family. Katie spoke about Jeanne's journey and the hardship of watching her

mother's decline. Katie closed the night with a message of hope about the collective research effort to "discover, conquer and cure" this devastating disease, and by highlighting the importance of funding research and "getting behind all the smart people at NeuRA".

### A GIFT FOR DISCOVERY

Joan Hume passed away at 69 after having lived as a quadriplegic for 46 years. All her life she was active in advocacy for people with disabilities. Joan believed in innovative research and the impact it could have in providing benefits for people living with spinal cord injuries. She even volunteered for a number of NeuRA's spinal injury research projects.



L-R: Prof John Niland AC, Dr Carmel Niland and Prof Schofield AO

Joan's belief in the power of research will live on through a legacy gift left in her will. The gift will support researchers at NeuRA working on spinal injury research.

"Joan would like her gift to support out-of-the-box research," says Joan's sister, Carmel. By leaving a gift in your will, you too can influence the future development of significant and life-changing medical research.

To discuss leaving a gift in your will, please contact NeuRA's Gifts in Wills Manager, Stephanie Grove, on +61 2 9399 1270 or by email s.grove@neura.edu.au

#### A MESSAGE FROM KATIE LITTLE

My mum, Jeanne Little, has Alzheimer's disease. She has had it for thirteen long years, with eleven of those in full-time care.

What strikes me the most is the difference between mum in life, and mum today. When we visit it is like I'm visiting a different person – a shell of the person she was who looks at me through a blank and distant stare. Alzheimer's stole my mum.

Even Tom, my young son – mature beyond his years – says she wouldn't want this, and he's right. Who would?

One million Australians will have dementia by 2050 - that's one in three of us! I feel it is our responsibility to rid our community of this beast. No one deserves their final years - any years for that matter - 'living' like this. That's why I'm supporting NeuRA and their 1,000 Brains Study.



Katie is the daughter of Australian television icon and Gold Logie Winner Jeanne Little (pictured with her mother and two children). Katie has written a book about her mum called Catch a Falling Star

NeuRA's research in preventive lifestyle measures, together with the 1,000 Brains Study, makes me feel hopeful that they can break the back of this insidious disease.

NeuRA is where all the smart people are, so we all need to get behind them and help them as much as possible. With your help, they can find out how to prevent and cure this illness, so no one in future generations has to lose someone they love, like my mother Jeanne Little.

Alzheimer's is awful. It has robbed me and my family of so many things. But the one thing it will not take is my sense of humour – the tougher life is the darker it gets.

Mum wasn't just the life of the party, she was the party.

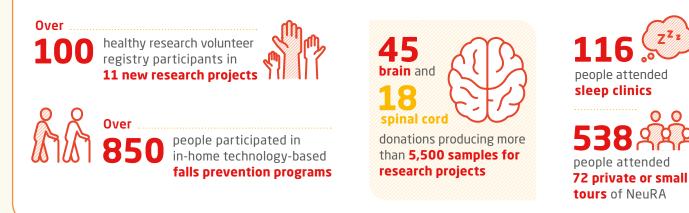
> Katie Little, Jeanne's daughter



Jeanne was born in Sydney, Australia and made her television debut on Network Ten's *The Mike Walsh Show* in September 1974. She was diagnosed with Alzheimer's disease in 2009, and is now being cared for in a Sydney nursing home.

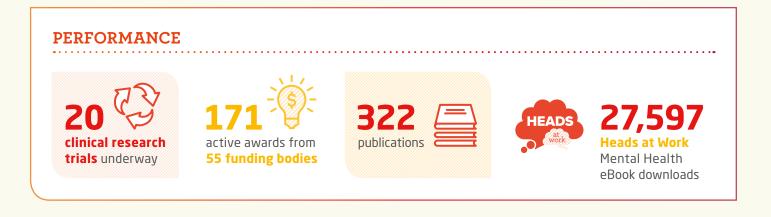
### PUBLIC ENGAGEMENT: A LOOK AT THE PAST 12 MONTHS

#### PUBLIC AND COMMUNITY INVOLVEMENT



#### SOCIAL MEDIA ENGAGEMENT





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NeuRA is a leader in brain and nervous system research, harnessing the excellence and passion of a worldclass team.

*Cour team continues to discover new ways to prevent, treat and cure disease and disorders of the brain and nervous system.*