

# Brain Matters

News from the Florey Institute of Neuroscience & Mental Health



## IMAGING A WORLD WITHOUT ALZHEIMER'S

THE FLOREY LOOKS INSIDE THE BRAIN FOR ANSWERS

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## Director's Report



**R**esearch into the workings of the brain is a slow and methodical process but, as Director of the Florey, exhilarating on a daily basis. As neuroscientists, we know we must take incremental steps towards an understanding of the brain's machinations. But with 650 people based at the Florey, we have exciting news coming through regularly.

By example, perhaps you saw the recent media coverage of the development of a blood test to identify those with the beginnings of Alzheimer's disease? You can read about this fascinating science on page 3.

Last week, Melburnians filled our auditorium to hear Florey Honorary, Professor Tomás Ryan from Trinity College, Dublin. His lecture about memory was one to remember as he explained in riveting detail how memories are formed and lost...and whether it is possible to retrieve a memory stored deeply in our brains. Another extraordinary moment in the life of the Florey. Prof Ryan is working closely with our own Professor Anthony Hannan and Dr Lucy Palmer to accelerate our research in this area.

Another area attracting attention is concussion and acquired brain damage. One of our neurologists, Associate Professor Paul McCrory, recently received a \$577,000 Clinical Practitioner Fellowship through the Medical Research Future Fund. This funding will help Prof McCrory and colleagues push ahead with our world-first study to recognise the risk of long-term damage and degeneration of the brain after a mild traumatic brain injury. We are making great strides in the way we can pick-up the initial signs of brain trauma and the extent of recovery, knowing every person responds differently.

Melbourne's first stroke ambulance is in full operation, undertaking approximately 40 trips per week. Personally, I am very proud to be involved in this initiative, assessing the value of the ambulance which has a CT scanner on-board, allowing us to treat a suspected stroke patient faster.

There are so many important and varied projects underway and I can only mention a few here. I do hope you enjoy reading Brain Matters as, together, we embark on another year of discovery.

If you are thinking about supporting the Florey, our new Major Gifts and Philanthropy Manager, Elouise Homes, would be very happy to discuss your interests. Please feel free to call Elouise on 03 8344 0678.

Warm regards,

**Professor Geoffrey Donnan AO**

Director, The Florey Institute of Neuroscience & Mental Health

## Imaging shows Alzheimer's decline



PhD student Remika Mito with Professor Alan Connelly, co-head, Florey Imaging team.

**R**esearchers at the Florey have invented a breakthrough imaging technique to describe in micro-detail the brain degeneration occurring in people with early Alzheimer's and the full-blown disease.

By using our powerful MRI machines, researchers have identified the precise locations of brain degeneration in a cohort of living Alzheimer's patients. The work is important as it sheds new light on the underlying cognitive degeneration in Alzheimer's, helping us focus our efforts to slow the decline.

To develop the technique, the team analysed brain scans from 177 Australians as part of the Australian Imaging, Biomarkers and Lifestyle study, who were either healthy, had an early form of Alzheimer's or had the full-blown disease.

The brain pathways identified by the team have all been implicated in Alzheimer's disease previously; those known to be crucial for memory formation, emotion and reasoning.

Alzheimer's disease is usually thought to be caused by abnormal production and buildup of a peptide called amyloid beta.

Professor Alan Connelly, who led the study, said, "Interestingly, the mildly affected patients with low amyloid had more fibre degeneration in particular brain regions than

those with high amyloid levels. This suggests that firstly, specific degeneration of certain brain areas will not necessarily be useful in predicting which mildly impaired individuals will progress to Alzheimer's disease, and secondly that degeneration of this pathway is related to cognitive impairment, regardless of the buildup of the amyloid peptide.

"This is an important advance for a field still struggling to come to grips with what exactly causes Alzheimer's. Our study shows we still have a way to go in interrogating the natural history of this insidious disease," Alan says.

Lead author Remika Mito says, "This study was conducted by comparing the averages of each group of patients against each other, in order to give us the most statistically, and biologically, relevant results. In the future, we want to be able to compare an individual patient against a normal, healthy standard, to see how far along the disease trajectory they are. Or we could compare back to their previous scans to determine what effect a new medication is having as part of a clinical trial for example."

Remika recently explained her results in an online abstract for *Brain*. If you would like to hear more about the details of the study, head over to Youtube (<https://youtu.be/15X6zbDUQrg>) to view Remika explain her work. [📺](#)

# A blood test to detect Alzheimer's: a world first

**A** new blood test could detect Alzheimer's many years before the disease symptoms appear – with more than 90 per cent accuracy – thanks to a Florey and Japanese collaboration.

The test will not be available for use in general medical practice for at least five years but may be used in medical research within a year.

Alzheimer's is set to affect more than one million Australians by 2056.

Currently, dementia costs Australia more than \$15 billion and by 2056, it is predicted to skyrocket to \$36.8 billion if a treatment or cure is not found.

With these terrible human and financial costs in mind, the need to track and monitor the disease has created a huge demand from researchers and the pharmaceutical industry as they seek treatments. The problem with current tests, like PET scans (positron emission topography) and lumbar puncture samples, is that they are expensive and invasive.

The new blood test measures a specific peptide in the blood, beta amyloid, to inform scientists if a patient has the very earliest stages of Alzheimer's disease.

The latest research compared blood samples from patients in Japan to those of Australians who are part of the Florey-based Australian Imaging, Biomarker and Lifestyle Study of Ageing.

**Currently, dementia costs Australia more than \$15 billion and by 2056, it is predicted to skyrocket to \$36.8 billion if a treatment or cure is not found.**



Professor Colin Masters AO.

One of the essential hallmarks of Alzheimer's disease is the build-up of beta-amyloid in the brain. The process starts about 30 years before outward signs of dementia, like memory loss or cognitive decline, have begun.

The Florey's Professor Colin Masters AO has been at the forefront of Alzheimer's research since the 1980s. Colin, who co-led the research published in the latest issue of *Nature*, says: "This new test will be an invaluable tool in increasing the speed of screening potential patients for new drug trials."

"Beta-amyloid takes many years to build up in the brain. As you age, the clearance mechanisms in the brain fail by 10 or 15 per cent. And slowly but surely over a 30-year period this protein builds up in the brain and causes extensive degeneration in the synapses. And that's the whole basis of Alzheimer's disease," he says.

"Progress in developing new therapeutic strategies for Alzheimer's disease has been disappointingly slow. None of the three drugs currently on the market treat the underlying disease. New drugs are urgently required, and the only way to do that is to speed up the whole process. That requires trials with rigorous and economical patient selection. Due to the long timespans involved, pharmaceutical companies require accurate predictions of who is most at risk," Colin says.

**“ This new test will be an invaluable tool in increasing the speed of screening potential patients for new drug trials. ”**

The power of being able to detect this biomarker early could revolutionise how clinical trials are done and how the disease is monitored in patients. It will provide scientists with a way to determine if experimental early intervention techniques are working. If the amyloid ratio goes up, researchers will know the treatment is working even before a person starts to show cognitive decline. It will also allow someone to determine how fast the disease is progressing after symptoms start to show. This may allow those suffering from the disease to plan for a future.

For a disease that has no known treatment or cure, a lot of people may simply not want to know. Even Colin has no desire to take the test. "Personally, I wouldn't have the test right now because even though I am in my early seventies, I would wait until there's clear evidence of a therapeutic intervention."

He is hopeful that researchers will soon prove that lifestyle changes to diet, sleep and exercise can slow the process of the disease. "If the data can be confirmed then I would do the blood test and make appropriate environmental modifications of my lifestyle."

The research is available to view on the Nature website: <http://dx.doi.org/10.1038/nature25456>



# A sleeping pill to slow Alzheimer's and addiction?



Professor Andrew Lawrence and Dr Laura Jacobson.

**W**hat does sleep have to do with Alzheimer's disease, and addiction? We all know how important a good night's sleep is for us to feel rested and energetic for the day ahead, but evidence is building that sleep is integral to many other brain functions.

While we might feel we've had a great night's sleep, our brain has been beavering away, clearing out the cellular rubbish accumulated during the day's hard work and pruning back the unneeded synaptic branches created during each and every interaction.

Dr Laura Jacobson heads the Florey's sleep and cognition laboratory, and is fascinated by the extensive role sleep plays in keeping us healthy, and how disordered sleep may in fact be a contributor, not just a symptom, of many brain diseases, including dementia and post-traumatic stress disorder.

Alzheimer's and fronto-temporal dementia are characterised by abnormal build-ups of two proteins, amyloid and tau. These clumps of protein then cause brain cells to die.

Laura is particularly interested in two forms of dementia, Alzheimer's disease and fronto-temporal dementia. Sleep disturbances are one of the earliest symptoms of Alzheimer's, even before memory problems

begin, although the underlying reasons for this are still unknown.

Therefore, reasons Laura, improving sleep in people with Alzheimer's or fronto-temporal dementia may also improve their memory, mood and cognitive ability. Traditional sleeping pills are unsuitable though, because they can leave you feeling groggy the next day, increase the risk of a nasty fall, as well as actually disrupting memory formation.

Instead, Laura has become interested in the orexin system, which not only controls our sleep-wake cycles, but also plays a major role in our appetite and eating behaviours – which are also commonly affected in patients with dementia.

The orexins are molecules produced in a very specific region of the brain, which then signal to other brain cells and networks in all parts of the brain. Increasing activity in the orexin system reduces sleep, pushing us towards a waking state.

Laura says: "Higher levels of orexin in the fluid surrounding the brain match up with higher levels of clumping tau in the brain. I suspect that these pathological forms of tau, brought on by Alzheimer's or fronto-temporal dementia, may be causing orexin levels to similarly rise, thereby disrupting patients' sleep."

## A new drug for insomnia, suvorexant, blocks the orexin system from telling our bodies to wake up.

A new drug for insomnia, suvorexant, blocks the orexin system from telling our bodies to wake up. Laura is evaluating whether suvorexant may be useful for people suffering from dementias caused by a build-up of tau, not only to improve their sleep without increasing risk of physical injury, but perhaps by slowing the disease process directly.

Professor Andrew Lawrence, head of the Florey's addiction biology laboratory is also interested in suvorexant, for a completely different reason. He has evidence that blocking the orexin system prevents alcoholic rats from relapsing in response to either alcohol-related cues or stressful stimuli after a prolonged period of abstinence. Andrew now has plans to begin an in-patient clinical trial in 2018 with the department of addiction medicine at St Vincents Hospital, in collaboration with Dr Yvonne Bonomo.

"There are only three pharmaceuticals on the market at the moment for alcohol addiction, and none of them work well at a population level," says Andrew. "When you consider that alcohol hospitalises 430 Australians every day and kills 15 of them, and alcohol use disorder affects 76 million people around the world, we really need a new way of tackling this devastating medical condition."

Laura Jacobson recently spoke to Lindy Burns on ABC Radio's Evening program about sleep and memory. You can listen back here: [www.abc.net.au/radio/melbourne/programs/evenings/andrea-currie/8661534](http://www.abc.net.au/radio/melbourne/programs/evenings/andrea-currie/8661534). Andrew Lawrence spoke to Robbie Buck on ABC radio Sydney about alcohol addiction and his new trial. Listen back here: [www.facebook.com/TheFlorey/posts/1551818441602816](http://www.facebook.com/TheFlorey/posts/1551818441602816).



## Mobile stroke unit: a FAST solution

**V**ictorian stroke patients are being offered the very best chance of survival as Australia's first dedicated stroke ambulance hits the road. Four months into its five-year trial, it is attending an average of 40 suspected strokes each week.

The Florey is proud to be a member of a consortium delivering the on-the-road trial designed to fast-track treatment to people suffering a suspected stroke. It's a rapid response medical service and while

it looks like an ambulance, it's more like an emergency department on wheels.

As many of us know, expert stroke care needs to be delivered as soon as possible if life-saving clot-busting drugs are to be given to a patient within a golden window of opportunity.

The mobile stroke unit takes the technology to the patient. It's loaded with a CT scanner, telemedicine equipment and a mobile laboratory.

The staff on-board are primed and ready to go. A neurologist, stroke nurse, radiographer and a paramedic travel to the patient and start treatment after an on-the-spot evaluation. Until now, this sort of assessment couldn't have

happened until an ambulance delivered the patient to a hospital.

The \$8 million, five-year trial is the result of a close research collaboration between Florey Director Professor Geoffrey Donnan and Professor of Translational Neuroscience, Stephen Davis at the University of Melbourne and Melbourne Health. Funding came from the National Health and Medical Research Council, private philanthropy, the Stroke Foundation, the Royal Melbourne Hospital and Ambulance Victoria.

Studies overseas have delivered stunning results with 70 per cent of patients in Houston USA treated within 90 minutes of symptoms, including 40 per cent in the first hour. In the hospital setting, only one per cent of patients are treated in the first hour. In Houston, economists are predicting a \$2-\$4 million saving in post-acute stroke therapy thanks to faster recovery and more lives saved each year.

The trial will run for several years, assessing the impact of the service in Melbourne before a more extensive roll-out is considered by the Victorian Government.

Although early days, we are seeing earlier treatment using clot-dissolving drugs and more efficient transport of patients to an appropriate hospital. 📱

## Digital health: on the road and in the clinic

**W**e're often told that we spend way too much time with our heads buried in our devices – smartphones, tablets and computers.

But one Florey researcher, neurologist Professor Chris Bladin, believes our tech can be a force for good.

Chris co-leads the Victorian Stroke Telemedicine program, a ground-breaking technology that has enabled over 90 per cent of Victorians to receive treatment within one hour of a suspected stroke. The program has been so successful, it has the potential to be rolled out nationwide.

Chris is also working with Ambulance Victoria and regional hospitals to trial a new phone-based tool called Pulsara. Pulsara seamlessly connects paramedics attending a stroke call-out with the hospital's emergency department and associated radiological, neurological or cardiac experts.

By the time the patient arrives at emergency, everyone has seen the patient's vital stats in advance so the emergency

staff are ready to start treatment, shaving over 30 minutes off the time it takes for a patient to receive life-saving treatment. Preliminary results also show that the ambulance crew is back out on the road, on average, 10 minutes earlier.

The importance of this work can't be underestimated as this sort of technological leap has the potential to improve health care around the world, saving countless lives.

Chris says it's all about diagnosis, development and distribution. "With the Florey's clinical expertise and extensive partnerships with tertiary hospitals in Melbourne and around Australia, we aim to develop technologies that will improve the speed and accuracy of diagnoses for all the major brain and mind diseases.

"To do this we will partner with organisations that are experts in developing tools, applications and devices, and ultimately build our in-house capacity.

"Finally, we aim to become a distribution hub for healthcare technologies, becoming



Neurologist, Professor Chris Bladin.

the commercial partner that disseminates new technologies, and their applications, through the clinical environment as well as into the community, as we have done with Pulsara."

Although in its infancy, the team is in discussions with some of the major names in healthcare tech, government and other medical research institutes to develop partnering opportunities.

By the glow of a smartphone's screen, the future does, in fact, look healthier. 📱



## MND Research Institute of Australia grants



The Florey enjoyed another summer of tennis, donning visors from Fight MND. Our own motor neurone disease researchers are relentless in their quest to "smash MND".

**T**he Motor Neurone Disease Research Institute of Australia recently announced its grants and fellowships for 2018, with several Florey researchers fortunate enough to be recognised.

Leading the group was Dr Nirma Perera who received the Bill Gole MND Fellowship – the first Victorian to receive this fellowship in its almost 20-year history. Nirma works in the MND laboratory, headed

by Associate Professor Brad Turner, who received a grant-in-aid in the same funding round.

Other Florey recipients included: Dr Dominic Hare, Dr Lachlan Thompson, Dr Tom Oxley, and Associate Professor Justin Rubio.

Congratulations all, and thank you to the Motor Neurone Disease Research Institute of Australia. 🇺🇸

## Stopping MS degeneration

**P**rofessor Trevor Kilpatrick has been awarded a project grant of \$225,000 for three years by MS Research Australia.

The funding will allow Trevor and his team to investigate a protein called Tyro3 which, in the laboratory, has been shown to improve the natural repair process in the brain by causing the production of myelin, the protective coating around nerve cells. They hope to reverse the damage associated with MS.

Thanks to MS Research Australia for helping the Florey fast track this important work. 🇺🇸



Professor Trevor Kilpatrick.

## Clinical trial for adolescents

Researchers from the Developmental Psychobiology laboratory are looking for healthy people between the ages of 18 – 45 to participate in a trial looking at the effects of methamphetamine (ice) use on the brain.

Importantly, participants need to have had no lifetime history of drug use disorder or dependence.

Participants would need to come to the Florey for approximately three hours. They would undertake an interview, cognitive tasks and a blood sample, for which they will receive reimbursement. No drug use would be involved.

To register your interest email [jee.kim@florey.edu.au](mailto:jee.kim@florey.edu.au)



Professor Dominique Cadilhac.

“It’s estimated there will be more than 56,000 strokes across the country in 2018 – that is one every nine minutes.”

## Stroke care funding

**C**ongratulations to Professor Dominique Cadilhac and Dr Kathryn Hayward who have each received \$50,000 grants from the Stroke Foundation.

Dominique will study the factors that influence pre-hospital and hospital patient care to improve access to high quality stroke care.

Kate will run a phase II trial to assess the impact of very early rehabilitation for upper limbs after stroke.

According to Stroke Foundation Chief Executive Officer, Sharon McGowan:

“Stroke is largely preventable and treatable. High quality evidence-based research will help us stop this terrible disease and reduce the spiralling costs to the community and health system.”

- Sharon McGowan

“Tragically, it’s estimated there will be more than 56,000 strokes across the country in 2018 – that is one every nine minutes. Too many Australians are dying or being left with an ongoing disability as a result of stroke.

“Stroke is largely preventable and treatable. High quality evidence-based research will help us stop this terrible disease and reduce the spiralling costs to the community and health system.”

Kate has also received a Heart Foundation Vanguard grant of \$75,000 to continue her investigation of early rehabilitation after stroke. The one-year funding is designed to support those with innovative concepts that aim to improve public health.

The Florey thanks the Stroke Foundation and the Heart Foundation for this brilliant support. 🙌



Dr Kathryn Hayward.

## Welcome to Elouise Homes



Elouise Holmes, our new Major Gifts and Philanthropy manager.

**I** have recently joined the Florey as Major Gifts and Philanthropy Manager, after a stint as Head of Private Giving and Memberships at Arts Centre Melbourne.

I look forward to developing relationships with current and prospective major gift donors and philanthropists. I plan to help them discover the intersection between their philanthropic passions and the Florey’s critical work, which they may wish to support.

It is my responsibility to ensure that engagement with current and potential donors increases their awareness and understanding of the impact and value of our research, as well as the importance of their strong and continued support.

It is a great privilege to witness the significant difference philanthropists can make in their support of worthwhile causes. It is even more fulfilling when I see philanthropists find great satisfaction and meaning through their involvement. I am looking forward to sharing the transformative power of philanthropy at the Florey. 🙌

“It is a great privilege to witness the significant difference philanthropists can make in their support of worthwhile causes. It is even more fulfilling when I see philanthropists find great satisfaction and meaning through their involvement.”



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- Send your donation to The Florey Institute of Neuroscience & Mental Health, Reply Paid 83037, 30 Royal Parade, Parkville, VIC 3052

Thank you for your valuable support. All donations are tax deductible.

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## Come along to a free public lecture

### The latest in stroke research

Come and hear two legends of stroke research, Florey Director Prof Geoffrey Donnan AO and Prof Stephen Davis AO from the University of Melbourne, when they discuss the latest in global stroke research. How does Australian research stack up?

**Date:** Wednesday, April 18

**Time:** 6pm

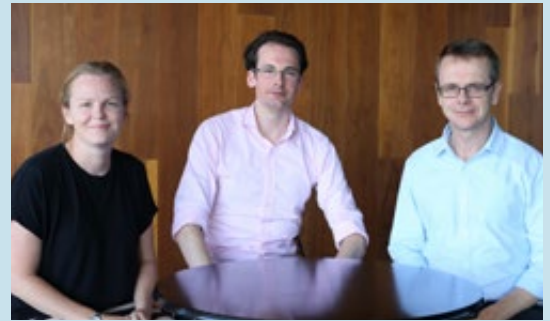
### The future of motor neurone disease research is here

Hear the latest from Associate Professor Brad Turner on our fight to beat MND. From patient stem cells to clever robots, the Florey is at the cutting edge of the world's search for a cure.

**Date:** Tuesday, June 5

**Time:** 11am

All lectures take place in the Florey's auditorium on the ground floor of 30 Royal Parade, Parkville. The full lecture program, booking details and travel information can be found on the Florey website.



### Did you forget to come?

If you missed the first public lecture of the year, you might like to visit the Florey website where you will find a YouTube link to Professor Tomás Ryan's fascinating discussion of memory.

Tomás explained his discovery that memories, thought to disappear in mouse models of amnesia, might actually remain intact and are potentially retrievable.

Challenging conventional notions of memory storage, retrieval, and brain damage, he set the stage for potential memory recall in patients with amnesia due to trauma, stress, alcohol and drug abuse, dementia, and ageing.

Pictured: The Florey's Dr Lucy Palmer and Professor Anthony Hannan hosted Florey honorary and Professor at Trinity College in Dublin, Tomás Ryan (centre).

## Thank You

The Florey thanks our recent donors who kindly donated \$250 or more between 6 Sept 2017 and 12 Feb 2018

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Birthdays of Simon Gomalinski and George Braitberg	70th Birthday of Wendy Taggart
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For more information contact the editor,  
Amanda Place: amanda.place@florey.edu.au or +61 411 204 526

Find us on Facebook and Twitter at our website: florey.edu.au

The Florey Institute of Neuroscience and Mental Health conducts its research on the lands of the Wurundjeri people of the Kulin Nation. We pay our respects to the traditional owners of this country, their ancestors, their children and the lore of the creator spirit Bunjil.

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