BRAIN MATTERS

THE FUTURE OF HEALTH: THE RESEARCHERS ADVANCING PRECISION MEDICINE
In the previous edition of Brain Matters, Professor Stephen Petrou said there was a lot to be excited about in 2022. Reflecting on that sentiment months into my Directorship at The Florey, I can confirm he was absolutely right.

With the return of some normality, The Florey is buzzing with ideas and innovations. It is great to witness, in-person, our researchers stepping up to solve the greatest brain and mind questions of our era.

Some of the biggest questions lie in mental health. The national, and even international, conversation on mental health has certainly shone a new light on our research in this area. It has highlighted a greater need for improved knowledge and new treatment options.

Our cover story, featuring my colleague Associate Professor Jess Nithianantharajah, presents the work we are undertaking to understand what happens in the brain when a person experiences a mental health condition. Knowing precisely what is happening on a biological level will help us find those much-needed new treatments.

Supporters who have followed us for a while will know that our work in dementia research is a jewel in The Florey’s crown. With an estimated 500,000 Australians living with this disease, our researchers remain committed to finding solutions that prevent and slow dementia progression, and even put an end to dementia altogether. We know science is the key to this mission, which is why we’re tackling it from multiple angles, something you can read more about on page 5.

And like all great research, we’re getting it out there. In fact, The Florey prides itself in taking its efforts from the lab bench right through to the bedside. We share three fantastic examples of this on page 7.

I’d like to thank you for your unwavering support of our work at The Florey, it is because of you that The Florey is able to transform lives. I hope you enjoy this edition of Brain Matters.

Professor Trevor Kilpatrick MBBS PhD FRACP FAHMS
Director, The Florey Institute of Neuroscience and Mental Health

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News from The Florey

Our teams have been working hard on research breakthroughs, connecting with our community, and advancing humanity through brain and mind science. Read on to learn about what’s been keeping us busy.

1. New research has provided a better understanding of how mutations in genes, important for controlling DNA expression, can result in epilepsy.

Professor Chris Reid and an international team of researchers explored this emerging field of interest—known as epigenetics—the study of how external factors such as experiences during development can change the way our genes are expressed. It is hoped that further research into epigenetic causes of epilepsy could lead to new pathways to prevent, treat and diagnose the condition.

2. The Australian Stroke Clinical Registry achieved a major milestone, recording 150,000 cases of stroke care.

Thanks to the 70 hospitals who provide their data, the registry can monitor the acute care given to patients during and after their stroke. Every case entered into the registry helps to inform improvement initiatives which aim to decrease disability, reduce the risk of recurrent stroke, and even prevent death. The registry, based at The Florey, is also used in research as a nationally representative data set of stroke information.

3. Multiple Sclerosis (MS) researcher Michele Binder and her team published new research which advances a path to restore brain function in people living with MS.

Investigating myelin, the protective covering on some nerves in the brain and spinal cord, Michele’s team demonstrated that the brain can withstand some myelin damage and maintain normal function. Their research indicates that repairing this protective sheath could have therapeutic potential in a range of demyelinating diseases including MS and even motor neurone disease.

4. The Florey hosted an in-person philanthropy function for the first time in two years.

A panel featuring Professor Anne-Louise Ponsonby, Professor Graeme Jackson and Associate Professor Scott Ayton discussed the effects of plastics on the developing brain, new technology changing brain imaging and recent advances in dementia research. Executive Manager of Philanthropy Eric Cheng said the event was a great opportunity for significant supporters of the Institute to connect with researchers and learn first-hand how they are making a difference.

5. A proof-of-principle study from Professor Lachlan Thompson and Dr Niamh Moriarty represents a new chapter in pioneering stem cell research.

Aiming to advance treatments in Parkinson’s disease, the team successfully reconstructed long-distance brain connections. Previously damaged in the Parkinson’s disease brain, these connections restored lost movement. At the heart of the research is the combination of two novel techniques the team have been developing over several years. Their findings set a new benchmark for the potential of stem-cell therapies to treat a range of neurological conditions.
Antidepressant medications remain one of the primary treatments for anxiety disorders, even for individuals who are not experiencing depression. Concerningly, these treatments only work for a small proportion of people prescribed them.

“We have not seen sufficient strides in developing new, improved and targeted treatments that specifically address anxiety symptoms with less side-effects,” said Associate Professor Jess Nithianantharajah, a leading mental health researcher at The Florey.

Associate Professor Nithianantharajah is on a mission to rectify this, identifying new treatment options for anxiety through precision medicine - moving away from a historical one-size-fits-all approach.

To do so, her team are using refined animal behavioural models combined with new brain imaging tools to investigate the underlying neurobiological processes that occur in the brain in a range of mental health conditions.

She says these behavioural models are essential for being able to investigate complex behaviours like decision-making and explore changes in neural connections that occur during anxiety.

“In anxiety disorders the brain’s ‘watchman’, the amygdala, becomes over-activated. It can send out false alarms for non-threatening situations that are mistakenly interpreted as threats. At the same time, connectivity with the prefrontal cortex becomes under-activated,” said Associate Professor Nithianantharajah.

Considered a master controller for the rest of the brain and key centre for decision-making, the prefrontal cortex is critical for regulating emotions and weighing up consequences.

“Anxiety can strongly impact our mental and cognitive processing. When prefrontal connectivity is compromised, it inhibits the prefrontal cortex from being able to ‘apply the brakes’ and dampen down the unnecessary overactivity of brain circuits,” she explained.

Fortunately, the brain has an incredible ability to re-wire and grow new connections, known as brain plasticity, meaning the right treatment options can help reshape these brain changes.

“Anxiety, like all health conditions, is the result of biological changes to the body - in this case the brain. By using our advanced behavioural and imaging tools to measure how and where these changes are occurring, we hope to develop better treatments that directly target and reverse these changes,” said Associate Professor Nithianantharajah.

“Unlocking the biology of what changes in our brains in anxiety and other mental health conditions is key for how we refine diagnosis and generate new treatments. It will be the start of a new era in mental health care, one where we can provide better support for the individual using more tailored medicine.”
An estimated 400,000 Australians currently live with Alzheimer’s disease – the nation’s second leading cause of death. With this figure expected to double in the next 30 years, researchers like those at The Florey are broadening this field of research to include new theories, cutting-edge technology and different treatment pathways.

“While we have become better at diagnosing Alzheimer’s, it is still one of the most difficult diseases to treat. The challenge we face is to find treatments that are effective and well tolerated. This is what The Florey is working towards. By adopting these new approaches, we hope to finally begin reducing the impact this disease has on the millions of people affected by it,” said Professor Ashley Bush, Head of The Florey’s Aging Brain Division.

**Targeting genetic mutations**

Associate Professor Scott Ayton and his team are exploring the underlying causes of neurodegenerative diseases. They are investigating a new theory which looks at the impact Alzheimer’s disease genes have on a process known as ferroptosis. This natural function occurs when iron is activated within a cell, resulting in its ‘self-destruction’. Associate Professor Ayton’s team believe certain gene mutations may activate ferroptosis prematurely, accelerating neurodegeneration and Alzheimer’s disease. Their theory could lead to new treatments which target these genetic mutations slowing Alzheimer’s disease-related neurodegeneration.

**Traversing the blood-brain barrier**

New research by Dr Rebecca Nisbet and her team focuses on developing next-generation treatments for Alzheimer’s disease. Currently any treatments for the disease are limited in their effectiveness as they struggle to pass the blood-brain barrier - designed to protect the brain from any infections or germs in the blood. To overcome this challenge her team is investigating new drug delivery strategies to improve the ability of drugs to enter the brain. This includes packaging up the genetic information of the drug into drug delivery vehicles. Once delivered, brain cells can read this information and produce the drug themselves. Her team is also testing methods such as focused ultrasound which briefly opens the blood-brain barrier, allowing treatments to enter the brain.

**Slowing disease progression**

Dr Abdel Ali Belaidi and his team of researchers are examining excess iron in the brain as a contributor to neurodegenerative diseases like Alzheimer’s disease. His team are investigating the link between a protein known as Apolipoprotein E (APOE) and iron in the brain. While some types of APOE act as an indicator of a higher risk of developing Alzheimer’s disease, other types were found to be effective at regulating ferroptosis. Dr Belaidi and his team are exploring if the latter could provide an alternative treatment approach to Alzheimer’s disease. Their hope is that regulating and preventing premature ferroptosis, and the resulting iron build up, could slow neurodegeneration and Alzheimer’s disease progression.
Around 250,000 Australians live with epilepsy, and it is one of the most common neurological conditions in the world.

A lack of access to the right healthcare and a disjointed approach to testing can result in years of delay until the right intervention is found; years when a patient’s quality of life can be impacted.

Started at The Florey, the Australian Epilepsy Project (AEP) aims to change this - cutting time to diagnosis and delivering precision reporting to clinicians, to improve patient outcomes.

Amanda started having seizures at the age of 23. Her seizures got worse, occurring daily. She received third-degree burns from a seizure while cooking, suffered infected cheeks and tongue due to seizure-related biting and by the age of 30 felt completely isolated.

Her diagnosis journey included three hospitals, three neurologists, a neuropsychologist, GP visits, more tests than she can remember, four different anti-seizure medications, a visit to the Emergency Department, a naturopath, doctor of Chinese medicine and various diets.

“I spent seven years on medication that didn't work. I'll never get that time back,” said Amanda.

Amanda eventually found her way to advanced MRI testing, similar to that offered as part of the AEP. It was discovered she had scar tissue on her right temporal lobe caused by encephalitis as a nine-month-old.

Ten years after surgery Amanda has regained her quality of life and is now a Lived Experience Ambassador at the AEP.

Amanda’s story is all too common; years plagued with uncertainty and long delays in diagnosis and in receiving effective treatment.

The AEP strives to change this and transform the lives of people living with epilepsy by shortening their diagnosis journey, resulting in improved outcomes and quality of life.

“Everyone living with epilepsy should have access to the best possible care.” - Amanda Anderson

The AEP is currently recruiting participants as part of a large-scale study that seeks to better understand epilepsy and seizures. Through advanced testing and Artificial Intelligence (AI) technology they will establish a new model of care for people living with epilepsy.

Giving access, changing lives
Finding the pathway to impact

With 5 million Australians affected by neurological conditions each year, the need for personalised treatments and better care is critically important.

Our researchers are proactively working to achieve these ambitious goals, collaborating with like-minded individuals, research institutions and community groups. Through their efforts they hope to expedite discoveries from bench to bedside – making an impact for all Australians.

Better Stroke Care

Leading Florey stroke researchers Professor Vincent Thijs, Professor Julie Bernhardt, Professor Dominique Cadilhac and Dr Kate Hayward are part of a nationwide collaboration to deliver better healthcare for stroke patients.

Working as a Centre of Research Excellence (CRE) to accelerate stroke trial innovation and translation, the collaboration brings together partners from 12 Universities and Research Institutes, as well as lived experience advocates and the Stroke Foundation.

The CRE, led by Professor Richard Lindley at University of Sydney, will transform stroke research in Australia by translating research faster and more efficiently into better clinical care and support nationally for all those who experience a stroke.

LASEREDD Therapeutics

A biotech spin-out led by scientists at The Florey hopes to address the needs of people living with schizophrenia from a completely new angle.

LASEREDD Therapeutics, launched by Associate Professor Daniel Scott, Dr Christopher Draper-Joyce and Professor Ross Bathgate, will utilise internally developed technology as part of a new platform to undertake next-generation drug discovery.

Funded by CUREator, a biotech incubator arm of the Australian Government’s Medical Research Future Fund, LASEREDD will enable the identification and development of medicines with improved effectiveness and reduced side-effects.

The team hope their platform approach will open new drug discovery avenues, overcoming significant barriers that have hindered previous efforts.

Measuring Ataxia

Ataxias are a group of neurological conditions which cause significant imbalance and impaired coordination.

Treatments for these conditions have been hampered by the inability to accurately measure progression or improvement of these disorders.

Thanks to a partnership between scientists, clinicians and engineers from The Florey, Deakin University and Murdoch Children’s Research Institute, this is about to change.

Associate Professor David Szmulewicz and Professor Malcolm Horne have led a team which includes Professor Pubudu Pathirana and Associate Professor Louise Corben to develop a system of devices to accurately measure ataxia.

Funded by MTPConnect, Friedreich Ataxia Research Alliance USA, Association Française de l’Ataxie de Friedreich and the NHMRC, the team have spent five years developing the devices that use sensors and machine learning to assess ataxia progression and improvement.

They hope the device will be used in routine care and help fast-track new treatments.
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Your gift provides a lasting contribution to help advance our knowledge beyond the 21st century in stroke, dementia, Parkinson’s disease, addiction, schizophrenia, and other conditions of the brain and mind experienced all over the world.

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About The Florey

The Florey Institute of Neuroscience and Mental Health is the largest brain research centre in the Southern hemisphere specialising in diseases of the brain and mind. Over 4.7 million Australians each year are directly affected by the illnesses we study. We are a world leader in discovery science, imaging technologies, clinical trials, population studies, data analytics and more. Our scientists share a common goal - to improve the lives of people through our brain and mind research.

Conditions we study include:
- Addiction
- Alzheimer’s disease and other dementias
- Anxiety
- Autism
- Bipolar disorder
- Cardiovascular disease
- Concussion
- COVID-19
- Depression
- Digestive diseases
- Epilepsy
- Huntington’s disease
- Motor neurone disease
- Multiple sclerosis
- Parkinson’s disease
- Schizophrenia
- Stroke
- Traumatic brain & spinal cord injury

Some of the ways you can help fund our research:
- Future-proof research through The Florey Future Fund
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