AUSTRALIA’S NEXT GEN

The Florey looks to the future. Saving lives and preventing illness at a crucial time of life.
**Brain Matters Spring 2016**

**Director’s Report**

**Welcome to the latest edition of Brain Matters.**

While our researchers are seeking cures for many conditions related to older people, this edition is dedicated to our younger Australians – many of whom face huge challenges with great optimism and determination.

As a neurologist, I see patients who have suffered a stroke all too regularly. But as you will read in the story on this page, here at the Florey, we are developing a range of treatments that are transforming recovery – and for young patients like Lucas and Damian, the impact will be lifelong. They will be able to study, work and live healthy lives thanks to early intervention. The alternative could be terribly sad – perhaps a nursing home bed or a life dependent on welfare.

On a positive note, as the Director of the Florey, I am surrounded by brilliant young researchers who continually amaze me with their dedication and talent. We educate more than 150 neuroscience students each year. Many stay with us to climb the ranks so they can help cure the most serious of diseases of the brain and mind. They are mentored by those at the top of their game who are pushing at the boundaries of knowledge on the way the brain works. The Florey is a stimulating and rewarding place to be.

Young people reach a point – often in adolescence – when they are particularly susceptible to the onset of mental illness or addiction. Our researchers are embedded in the international quest to understand how sex differences, hormones and environments influence a young person’s journey into adulthood.

You will read how our scientists are studying the unique way youth respond to ice, cocaine and other drugs, and how drug use may lead to the development of mental illness.

Finally, congratulations to 11 year old Charlotte Di Toro who recently visited the Florey and was motivated to raise money for our research in the most surprising way. Yes, she held sausage sizzles and spoke to her school assembly about the Florey, but she also pledged to cut off her long hair in the name of research! To her amazement, she raised more than $3000. Thank you so much, Charlotte. You’re an inspiration to us all.

**Professor Geoffrey Donnan AO**

Director, the Florey Institute of Neuroscience & Mental Health

---

**Stroke: saving young lives**

**Doctors are changing the way they respond in the critical hours after a stroke thanks to stroke neurologist, Professor Geoffrey Donnan’s ground breaking research.**

Simone Street recognised the signs instantly.

Her son Lucas had lost all muscle tone. One side of the one-year-old’s face had dropped. He was heavy and hard to hold.

“I knew it was a stroke, but I didn’t say until I was in the ambulance. I didn’t want to scare everybody,” Ms Street said.

“I was lying on the stretcher and he was lying on top of me, and I could feel on one side that it wasn’t the same.”

With her suspicion revealed, paramedics alerted the Royal Children’s Hospital. Neurologists were waiting, and the CT scanner was cleared for the time-critical diagnosis to be made.

But such a quick response is rare.

Lucas is the only Victorian child to receive the clot-dissolving drug tissue plasminogen activator (tPA) after ischaemic stroke, despite it being used routinely in adults.
According to Florey Director and stroke neurologist, Professor Geoffrey Donnan, an international trial aiming to test the drug’s effectiveness in children recruited no-one in 18 months, for the simple reason that stroke is rarely suspected.

“Children typically aren’t diagnosed within the 4.5 hours thrombolytic drugs can be given, before the risks of brain bleeding outweigh the benefits for the most common type of stroke,” Prof Donnan said.

When reflecting on his career, Prof Donnan says Australians of all ages who suffer a stroke have gone from having no stroke treatments, to five proven therapies in the past 20 years. Yet, it remains a major cause of disability and death for 40,000 Australians each year.

A raft of national and international clinical trials, starting at the Florey, will treat more people, earlier. The $13.7 million National Health and Medical Research Council grant is lead by Professor Donnan and Royal Melbourne Hospital’s head of neurology, Professor Stephen Davis.

One multi-centre international trial is testing whether tPA can be given as late as nine hours after stroke, in patients whose brain scans show they still have sufficient viable brain tissue.

If successful, the big beneficiary of this trial, called EXTEND, will be the “wake up stroke” cohort; those who don’t know what time their stroke happened during the night and so don’t qualify for clot-dissolving treatments.

An alternative thrombolytic, one commonly used after heart attack, is being trialled as a more effective and safer first-line clot-buster.

“Our team is also testing whether tPA can be skipped altogether before invasive clot-retrieval surgery takes place – to reduce the risk of brain bleeding,”

A new mobile CT unit, the ‘stroke ambulance’, will arrive in Melbourne next year, another initiative of the dynamic Donnan-Davis partnership. It will be the first in the country.

“The first hour after stroke is the ‘golden hour’, “ Prof Donnan said. “You double the benefits by halving the time to treatment in most instances.”

Treating more of the 45 Victorian children and babies who have stroke each year during this “golden hour” is RCH neurologist Dr Mark Mackay’s aim. He is developing an app to help paramedics and emergency department staff better recognise symptoms.

While children usually arrive at hospital within an hour of stroke, his PhD research – completed under the supervision of Prof Donnan – found it can take 12 hours to confirm a diagnosis — too late for therapies to reduce brain damage.

“Children should be receiving the same treatment as adults, and the only way to improve access is to diagnose more rapidly,” Dr Mackay said.

“At least half of the children will have long-term disabilities after stroke.”

Now, 18 months on, Lucas’ speech is delayed and his right side is weaker. The three-year-old, whose treatment for a congenital heart defect had put him at higher risk of stroke, now talks to his right hand, urging it to work better. But he is back running around the playground.

“Without tPA it would have stayed like that,” Ms Street said.

So too, was the Stroke Chain of Recovery working the day Damian O’Brien collapsed at football training in May.

His teammates recognised the 22-year-old’s lopsided face, slurred speech and left-side weakness were stroke symptoms and called an ambulance.

Mr O’Brien’s local hospital in Traralgon had recently linked to the Victorian Stroke Telemedicine program, led by the Florey, being rolled-out across the state.

It allowed top neurologists to authorise time-critical treatment via a bedside video-link.

By the time he arrived by helicopter at the Royal Melbourne Hospital, the clot had dissolved. Surgery was avoided. Mr O’Brien walked out of hospital six days later. The diesel mechanic is back at work full-time and he returned to football last month.

The telemedicine program has treated almost 1000 Victorians since it launched two years ago.

“By the time I had woken up the next day I had pretty much regained most of my movement,” he said. “I’m 100% now, but it can happen to anyone.”

If you would like to help the Florey improve stroke recovery, please call 1800 063 693.

Cover photo credit: Eugene Hyland, News Corp.
Addiction

Jee’s research group, the Developmental Psychobiology laboratory, now has really good preclinical evidence showing this difficulty is related to a natural imbalance in dopamine signalling in teenage brains. Dopamine is the key signalling molecule involved in the brain’s reward-seeking pathway.

Sophia Luikinga is a PhD student with Dr Kim, who has recently completed some exciting experiments examining the hot-button issue of adolescent methamphetamine addiction (popularly known as “ice”).

Sophia gives adolescent and adult rats access to ice and waits for them to become addicted. Surprisingly, Sophia found that when given low doses of ice, both adults and adolescent animals consumed the same amounts. However, after becoming accustomed to that low dose, Sophia began to increase the amount of ice for each shot of the drug. At a certain level the adult rats stopped consuming ever-greater amounts, instead levelling off their consumption. In a fascinating finding, the adolescent animals kept taking greater and greater amounts of the drug, until the end of the experiment.

This habitual drug-taking behaviour implicated a particular part of the brain. Sophia used a cutting-edge technique to examine and characterise altered gene levels in the brains of those adult and adolescent animals, then compared them to each other and to similarly aged drug-free animals.

Jee says: “Ice use during adolescence causes dramatic negative changes in some gene levels compared to ice abuse in adulthood. This may lead to a lasting vulnerability to other psychiatric disorders”.

“These genes all help to transmit dopamine signals at the synapse – the junction between nerve cells. In humans, mutations in this pathway that decrease signalling levels are associated with bipolar disorder, depression and anxiety.”

Sophia’s experiments will now determine whether any existing pharmaceuticals can restore the signalling levels in the pathway. The aim? To reverse some of the changes in the drug addicted brain.

As well as their work on ice, a postdoctoral researcher in Jee’s lab, Dr Heather Madsen, looks at cocaine addiction. Most of us can relate to the cravings we feel when giving up things like alcohol or sweets. The longer we abstain, the more intense the cravings become. The same applies for cocaine consumption, where the cravings increase during a period of abstinence.

Dr Madsen has shown that both adolescent and adult rats that model heavy cocaine use display this craving increase. They respond to drug-associated cues much more strongly after a 30-day period of abstinence than a 1-day period. Importantly, these cravings can be reduced if the rats are shown cues associated with their drug use, but not actually given any cocaine, while abstaining.

“We believe this ‘cue extinction training’ can reduce smoking, drinking or drug cravings, and therefore the likelihood of relapse,” says Heather.
Schizophrenia

Schizophrenia is often considered the most notorious psychiatric disease to strike young people. The peak age of onset for schizophrenia in males is between 18 and 23 and in females, from 22 to 25 – with another group particularly vulnerable after menopause. Along with the well-known auditory and visual hallucinations commonly portrayed in film and TV, other symptoms include a flattening of people’s mood and emotional responsiveness. Most debilitating of all are deficits in their cognitive abilities, including short term memory and learning difficulties with literacy and numeracy – at a crucial period of their schooling and early careers.

Dr Andrea Gogos and Professor Brian Dean are looking for molecular pathways by investigating the role of genes involved in developing schizophrenia. Beginning with human samples from the Victorian Brain Bank at the Florey, Brian has examined gene changes in the brains of people who died with schizophrenia, and identified hundreds of genes that are increased or decreased compared to typical brains.

Female sex hormones, particularly oestrogen, are protective against schizophrenia. Fewer females suffer from schizophrenia, they get it later and they have less severe negative symptoms and cognitive deficits.

Current pharmacological treatments for illnesses like depression, bipolar disorder, anxiety, and eating disorders focus on altering levels of brain signalling molecules such as serotonin and dopamine, but often do little to improve the underlying causes. New treatment approaches – with fewer side effects – are required.

In this regard, The Florey has a long-standing interest in another brain signalling system – the relaxin-3 neuropeptide network. Relaxin-3 is a peptide (small protein) that is very similar to insulin. Relaxin-3 is produced in nerve cells in a small area at the base of the brain, but these neurons send projections to many forebrain areas, emphasising the broad role of relaxin-3 in brain function.

Cary Zhang, a PhD student from Professor Andrew Gundlach’s Peptide Neurobiology laboratory, is the latest emerging Florey scientist to explore the neural actions of relaxin-3. Cary says: “I showed that relaxin-3 signalling can regulate the ‘stress response’. By specifically activating the right pathway, I can enhance relaxin-3 signalling to reduce elevated anxiety in mice. Conversely, by blocking relaxin-3 activity I can increase anxiety-like behaviours”.

“Current treatments for eating disorders like anorexia and compulsive eating are not very effective. In addition to its effects on anxiety, I also showed that blocking relaxin activity reduced consumption of tasty food, high in fat and sugar, in mice.”

Professor Andrew Gundlach has praised Cary’s excellent work, saying: “The next step in developing relaxin-3-related therapies for mood and eating disorders is to develop new forms of the peptide that can be given easily and cross the protective blood-brain barrier”.

“We work closely with collaborators at The Florey, The University of Queensland and Monash University to describe these so-called ‘peripherally-active’ relaxin-3 analogues. Identifying new treatments for mental health disorders that so commonly afflict teenagers and young adults is a major research priority at The Florey.”

And the future of mental health therapies?

Current pharmacological treatments for illnesses like depression, bipolar disorder, anxiety, and eating disorders focus on altering levels of brain signalling molecules such as serotonin and dopamine, but often do little to improve the underlying causes. New treatment approaches – with fewer side effects – are required.

In this regard, The Florey has a long-standing interest in another brain signalling system – the relaxin-3 neuropeptide network. Relaxin-3 is a peptide (small protein) that is very similar to insulin. Relaxin-3 is produced in nerve cells in a small area at the base of the brain, but these neurons send projections to many forebrain areas, emphasising the broad role of relaxin-3 in brain function.

Cary Zhang, a PhD student from Professor Andrew Gundlach’s Peptide Neurobiology laboratory, is the latest emerging Florey scientist to explore the neural actions of relaxin-3. Cary says: “I showed that relaxin-3 signalling can regulate the ‘stress response’. By specifically activating the right pathway, I can enhance relaxin-3 signalling to reduce elevated anxiety in mice. Conversely, by blocking relaxin-3 activity I can increase anxiety-like behaviours”.

“Current treatments for eating disorders like anorexia and compulsive eating are not very effective. In addition to its effects on anxiety, I also showed that blocking relaxin activity reduced consumption of tasty food, high in fat and sugar, in mice.”

Professor Andrew Gundlach has praised Cary’s excellent work, saying: “The next step in developing relaxin-3-related therapies for mood and eating disorders is to develop new forms of the peptide that can be given easily and cross the protective blood-brain barrier”.

“We work closely with collaborators at The Florey, The University of Queensland and Monash University to describe these so-called ‘peripherally-active’ relaxin-3 analogues. Identifying new treatments for mental health disorders that so commonly afflict teenagers and young adults is a major research priority at The Florey.”

And the future of mental health therapies?

Current pharmacological treatments for illnesses like depression, bipolar disorder, anxiety, and eating disorders focus on altering levels of brain signalling molecules such as serotonin and dopamine, but often do little to improve the underlying causes. New treatment approaches – with fewer side effects – are required.

In this regard, The Florey has a long-standing interest in another brain signalling system – the relaxin-3 neuropeptide network. Relaxin-3 is a peptide (small protein) that is very similar to insulin. Relaxin-3 is produced in nerve cells in a small area at the base of the brain, but these neurons send projections to many forebrain areas, emphasising the broad role of relaxin-3 in brain function.

Cary Zhang, a PhD student from Professor Andrew Gundlach’s Peptide Neurobiology laboratory, is the latest emerging Florey scientist to explore the neural actions of relaxin-3. Cary says: “I showed that relaxin-3 signalling can regulate the ‘stress response’. By specifically activating the right pathway, I can enhance relaxin-3 signalling to reduce elevated anxiety in mice. Conversely, by blocking relaxin-3 activity I can increase anxiety-like behaviours”.

“Current treatments for eating disorders like anorexia and compulsive eating are not very effective. In addition to its effects on anxiety, I also showed that blocking relaxin activity reduced consumption of tasty food, high in fat and sugar, in mice.”

Professor Andrew Gundlach has praised Cary’s excellent work, saying: “The next step in developing relaxin-3-related therapies for mood and eating disorders is to develop new forms of the peptide that can be given easily and cross the protective blood-brain barrier”.

“We work closely with collaborators at The Florey, The University of Queensland and Monash University to describe these so-called ‘peripherally-active’ relaxin-3 analogues. Identifying new treatments for mental health disorders that so commonly afflict teenagers and young adults is a major research priority at The Florey.”

And the future of mental health therapies?

Current pharmacological treatments for illnesses like depression, bipolar disorder, anxiety, and eating disorders focus on altering levels of brain signalling molecules such as serotonin and dopamine, but often do little to improve the underlying causes. New treatment approaches – with fewer side effects – are required.

In this regard, The Florey has a long-standing interest in another brain signalling system – the relaxin-3 neuropeptide network. Relaxin-3 is a peptide (small protein) that is very similar to insulin. Relaxin-3 is produced in nerve cells in a small area at the base of the brain, but these neurons send projections to many forebrain areas, emphasising the broad role of relaxin-3 in brain function.

Cary Zhang, a PhD student from Professor Andrew Gundlach’s Peptide Neurobiology laboratory, is the latest emerging Florey scientist to explore the neural actions of relaxin-3. Cary says: “I showed that relaxin-3 signalling can regulate the ‘stress response’. By specifically activating the right pathway, I can enhance relaxin-3 signalling to reduce elevated anxiety in mice. Conversely, by blocking relaxin-3 activity I can increase anxiety-like behaviours”.

“Current treatments for eating disorders like anorexia and compulsive eating are not very effective. In addition to its effects on anxiety, I also showed that blocking relaxin activity reduced consumption of tasty food, high in fat and sugar, in mice.”

Professor Andrew Gundlach has praised Cary’s excellent work, saying: “The next step in developing relaxin-3-related therapies for mood and eating disorders is to develop new forms of the peptide that can be given easily and cross the protective blood-brain barrier”.

“We work closely with collaborators at The Florey, The University of Queensland and Monash University to describe these so-called ‘peripherally-active’ relaxin-3 analogues. Identifying new treatments for mental health disorders that so commonly afflict teenagers and young adults is a major research priority at The Florey.”
From little things...

Australians are renowned for being wonderfully generous, donating to appeals and good causes. So it comes as no surprise that the Florey is in contact with a growing number of families who recognise the need to support medical research, encouraging their children to give.

Drs Nicole Jenkins and Gawain McColl, who study ageing and brain degeneration at the Florey, have two young girls who are learning how to make a difference.

Aiden, 13, and Caely, 11, are already active in community fundraising efforts for Parkinson’s and other causes, particularly at Christmas time.

The girls also follow the ‘save-spend-donate’ model for their income. Any money they receive is divided into three ‘pots’. The first pot is their bank account, the second is for spending on hobbies or amusements, and the third is for donating to causes they are passionate about.

As mum Nicole says: “the girls are very aware that they are extremely privileged to grow up in a stable and prosperous country like Australia, and that not all kids are as fortunate. They recognise their ability to ‘pay it forward’, and we encourage them to use the money from their donation pot for any cause or charity they feel a particular affinity with”.

Charitable giving obviously runs in the family, with the girls’ grandmother, Dianne Jenkins, also giving regularly to the Florey.

...Big things grow

The Dowd family set up the Dowd Foundation 14 years ago with help and encouragement from Michael Andrew (KPMG) and under the Patronage of Professor Richard Smallwood AO.

In Carl Dowd’s own words:

“The board decided to direct our giving to three main areas – the arts, under the direction of our elder son Mitchell, education, to be handled by our daughter Lisa and medical research, which was and still is Wendy’s passion and responsibility. Investment decisions for the Foundation are handled by our younger son Jason together with me.”

“For many years prior to forming the Foundation, we have enjoyed a long term relationship with the Florey’s Director, Geoffrey Donnan, who over the years has helped open our eyes and minds to the fact that most families are impacted by some form of brain disease along their life’s journey.

“This led to our desire to support the Florey with yearly medical scholarships which in turn led to the creation of a Research Fellowship for Neuroscience three years ago. This three-year $360,000 Fellowship was to support an extremely talented researcher who was yet to receive a NHMRC senior research fellowship but who was slated to become a very successful career scientist. Associate Professor Chris Reid was unanimously chosen over 17 other candidates to become The Dowd Foundation Fellow at the Florey in 2014.

“Chris has taken every advantage of this opportunity and is now a member of the $16 million Genetic Epilepsy Program Grant with world leaders in the genetics of epilepsy.

“We feel proud and privileged to have Chris as our first recipient.”
An extreme result from an extreme challenge!

Community fundraisers, ONE IN FIVE, have done it for the Florey, once again. This dedicated bunch of athletes recently raised more than $17,000 to help us develop improved treatments for mental illness.

The Surf Coast Century for 2016 took place in Anglesea on the Great Ocean Road. Participants ran 100km, solo or as members of relay teams. As always, there was strong support from the crowd for the dedicated runners.

According to Gwen from ONE IN FIVE: “We had 24 runners this year. Many of them have competed before however we had a number of new participants. As a first time runner, I received great camaraderie and support; it was a terrific atmosphere. As well as a great day of fun and extreme exercise, we also raised important funds for mental health research.”

ONE IN FIVE chairperson Gabrielle Sheehan says: “We are passionate about raising money. Research into mental illnesses will lead to the development of targeted, and more effective drug treatments for depression, bipolar disorder and schizophrenia.”

On behalf of the Florey’s mental health researchers, thank you to all those who like to go extreme for the Florey!

Find out more at: www.oneinfive.com.au

Survey results are in

Thank you to all those who responded to our recent reader survey. We now have a much clearer picture on the way you like to donate, the sort of stories you like to read and how you like to be contacted.

We were heartened to receive so many positive and helpful comments. We’re looking forward to offering you interesting stories, public lectures and news on the website especially tailored to our valued donors and advocates.

We noted how many of you are driven to support our work as a result of personal experience with a disease or disorder of the brain and mind.

Your thoughts and comments drive our research and offer our team the motivation to persevere, despite the funding obstacles facing Australian scientists.

Thank you for contributing so we can fast forward our research – to find cures for brain diseases and disorders. With one in five Australians affected, we feel a deep obligation to use donated funds wisely, for the good of humanity.

Gifts in wills – thank you

Some of the most heartening comments from the recent survey came from the people who are thinking about the Florey’s long term future and are considering making a gift in their Will, or intend to do this the next time they revise their Will.

It is a common misunderstanding that only wealthy people can leave a gift in their Will. This is not true - anyone can do it. Just recently the Florey received a $100,000 gift from a supporter in country Victoria, a man whose largest previous gift had been $50. By gifting just a small percentage of his estate after he had taken care of his family, he was able to make a more significant gift than we ever anticipated.

If you are considering making a gift to the Florey in your Will, thank you. If you would like to talk about your intentions, need our help with the right wording, or would like to visit the Florey to see how we will invest your gift for the future, please call Irene Crebbin on 03 8344 1478.
I’D LIKE TO
IMPROVE LIVES
THROUGH
BRAIN RESEARCH

First name: 
Surname: 
Address: 
State: Postcode: 
Email: 

☐ I would like more information about making automatic regular donations.
☐ I would like more information about remembering the Florey Institute of Neuroscience & Mental Health in my will.
☐ I would like updates on brain research ☐ by mail ☐ by email

I would like to donate $ 
Enclosed is my ☐ cheque ☐ money order or debit my ☐ Mastercard ☐ Amex ☐ Visa

Card number: 
Expiry date: 
Signature: 

Other ways to donate:
• Call our free call credit card donation line on 1800 063 693
• Fax your donation to us on (03) 9035 3107
• Online at www.florey.edu.au
• 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.

Please let us know if you wish to change any of your personal details, contact preferences, or opt out, using any of the above contact methods. The Florey Institute of Neuroscience & Mental Health records information about its supporters that includes address and donation details, and is used solely by the institute but is not sold, traded or passed on to any third parties.
Dr Scott Ayton has been named the 2016 Young Researcher of the Year by the Bethlehem Griffiths Research Foundation.

Scott was recognised by the foundation’s Chairman, William Clancy AM, for his impressive work on dementia and the great potential he has as a future medical research educator and leader. During his stellar career at the Florey, Scott has attracted an impressive $3 million in grants and fellowships and has supervised numerous PhD and honours students.

The Bethlehem Griffiths Research Foundation was established in 1994 through a bequest from the estate of the late Mr Glen W A Griffiths, in appreciation for the care he received at Calvary Health Care Bethlehem for motor neurone disease. His will provided for the establishment of a foundation to fund Victorians researching life-threatening neurological illnesses such as multiple sclerosis and MND as well as palliative care and stroke.

We would like to welcome a new member to the Florey fraternity.

Psychiatrist Richard Kanaan is the co-head of our Biological Psychiatry and Mental Health division. Richard has special interests in unexplained syndromes and in schizophrenia. He is Chair of Psychiatry at the Austin Hospital and has worked across a number of disciplines, including neuroimaging, neuropsychology, philosophy, and social psychiatry. Richard’s current work focuses on building explanations for rare syndromes such as conversion disorder using functional neuroimaging. Welcome to the team, Richard.

Thank You

The Florey thanks our recent donors who kindly donated $500 or more between June and September 2016.*

Donations in memory of

Patricia Bertram
Peter Marsh
Betty Pritchard
*Correct at time of publication.