OUR MISSION
To improve lives through brain research

OUR VISION
To create significant knowledge about the brain

OUR VALUES
Generate scientific knowledge to improve global health
Innovate and problem-solve
Work together with integrity
Share our discoveries with our supporters and partners

Cover Image: Professor Ingrid Scheffer AO has had a long-standing interest in childhood epilepsy, identifying the first “epilepsy gene” in 1995. Since then, she and her collaborators have discovered around half of the 40 or so genes involved in causing epilepsy.

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A summary of highlights from this Annual Report is available in print from Margit via email: margit.simondson@florey.edu.au or call +61 3 8344 9679.
As you get older, whether or not you’re a scientist, it’s exciting to understand what being human is. As a scientist, I’ve had a peculiar privilege in being able to see some aspects of life through chemistry. Maybe of all the things that fascinate me most, it’s to be able to look at the chemistry of ageing and in our case, we’ve opened up the field of metals and their role in human disease. We increasingly understand how much of ageing is actually related to good old-fashioned chemistry. That is mind-blowing sometimes.

Professor Ashley Bush, heads the Florey Institute’s Oxidation Biology Unit, researching Alzheimer’s disease and other neurological disorders of ageing. In 2014, Professor Bush was the winner of the Victoria Prize for Science and Innovation in Life Sciences.
The Florey Institute of Neuroscience and Mental Health is one of the largest and most highly respected brain research centres in the world. Neuroscience is an area of medical research attracting enormous attention as our understanding of the brain rapidly evolves. Internationally, populations are ageing and there is a sense of urgency to find causes, treatments and cures for conditions affecting the brain and mind. There is an urgent imperative to address these conditions to avoid suffering and to contain health-related expenditure.

The Florey provides scientists and students with world-class facilities and the opportunity to improve people’s lives through brain research and, ultimately, to influence global wellbeing and health economics. By the end of 2014, the Florey employed 482 staff, and worked with 157 postgraduate students throughout the year.

The Florey continues to be a world-leader in developing and applying imaging technology, and research into genetics, stroke rehabilitation, epidemiological studies, psychotic illnesses and neurodegenerative diseases.
WHY DO WE STUDY THE BRAIN?

“While much of the human body has been analysed and its machinations largely understood, the brain is still an enormous mystery waiting to be unravelled. The knowledge gained over the next 20 years, I believe, is set to be utterly fascinating and will transform the human condition.

We are at a crucial time in neuroscience with our understanding accelerating at a cracking pace. We are learning how the brain is vulnerable to addiction, how it stores and retrieves information, how it influences our appetite, heart function and breathing. We are delving down and isolating amino acids which may contribute to depression and asking whether particles of iron contribute to dementia. These are just a few of the many life-changing projects underway at the Florey.

As President Barack Obama recently declared, the neuroscience revolution has begun.”

Professor Geoffrey Donnan AO
Director
The Florey Institute of Neuroscience and Mental Health
MBBS MD FRACP FRCP (Edin)
FLOREY IN A FLASH

Outreach
The Florey hosts regular events at its Parkville campus, involving school children and members of the general public. Our researchers and medical practitioners share their knowledge of the brain in a variety of ways.

Severe epilepsy: small brain lesions
Neuroimaging is helping to explain why epilepsy can involve intellectual disability. Widespread abnormal electrical activity occurs, even when patients are not seizing. In some patients we have located a small brain lesion. After surgical removal, the abnormal activity is eliminated and the patients are seizure free.

Alzheimer's disease: Global players against a global scourge
In 2014 alone, Florey researchers published 47 papers on Alzheimer's disease and other dementias, which were cited 121 times by other researchers. These papers included classifying new real-time imaging agents for dementia proteins, using blood-based markers to predict Alzheimer's protein deposition in patients' brains, and looked at the levels of that protein in patient blood samples to accurately predict changes in patients' mental abilities.

Stroke by the numbers: small brain lesions
87% of the 12 million strokes worldwide are caused by a blocked vessel in the brain, causing hundreds of thousands of brain cells to die. Every minute that can be saved before the clot is ’busted’, can save up to 1.8 days of disability-free life meaning 1.5 minutes saved on the average 70 minute wait for treatment could equate to an extra month of healthy life.

FLOREY INSTITUTE OF NEUROSCIENCE & MENTAL HEALTH ANNUAL REPORT 2014

Citations
- 488: The number of Florey publications for 2014.
- 17.5: Average citation per publication, 2004-2014.

Outreach
- 2000 ADULTS visited to attend lectures about various diseases of the brain and our quest to improve lives through improved treatments and cures.
- 2500 STUDENTS from 24 schools learned about the life of a neuroscientist.
- 900 YEAR 12 STUDENTS visited to learn about mental illness.

Research highlights
- Alzheimer's disease: Global players against a global scourge
- Severe epilepsy: Small brain lesions
- Stroke by the numbers: Small brain lesions

Our team
- 482: All staff
- 49: Administrative and Scientific support staff
- 433: Researchers
- 28: Countries represented by our staff and students
- 157: Postgraduate students

COUNTRIES REPRESENTED BY OUR STAFF AND STUDENTS
Argentina | Australia | Austria | Belgium | Brazil | Canada | Chile | China | England | Finland | France | Germany | Hong Kong | Hungary | Ireland | Israel | Italy | Japan | Malaysia | Northern Ireland | Norway | Netherlands | New Zealand | Philippines | South Korea | Scotland | Singapore | Spain | Sweden | Switzerland | Taiwan | UK | USA | Wales

Scientific publications published over the 10 years, 2004-2014.
Average citation per publication, 2004-2014.
The Florey’s past year has been packed with scientific activity. There have been great advances in our knowledge of the brain - both at the laboratory bench and in the hospital setting.

Our superb facilities continue to provide new opportunities to collaborate - for colleagues within the buildings and with those who come from overseas to work as members of the world’s third most-cited neuroscience facility. It is heartening to witness casual scientific connections being made and robust discussions taking place in corridors and hubs.

The scientists have been publishing in high-ranking journals on a range of diseases from Alzheimer’s to autism. You will read about some of these in this report.

Outside of research, the Florey has taken great strides forward in terms of our financial security. Our budget situation has stabilised, and in 2015 the investment earnings on our investments of over $25 million is solely being applied to support and grow research for the future of the institute.

Once again, we have experienced overwhelming support from the community. Diseases of the brain and mind touch the lives of so many people and we have appreciated the passionate interest shown in our work. The scientists are invigorated by the opportunity to share their research - through the media, at public lectures and as part of our school program. We are so grateful for donations, bequests and financial support for fellowships which we direct to our important science initiatives. Our community fundraisers have exceeded all expectations this year by contributing significantly to the Florey through a range of innovative fundraising initiatives. We thank them most sincerely.

The last 12 months saw the retirement from the Board of Laureate Professor Colin Masters and Professor Graeme Jackson. We acknowledge them for their enormous contribution over the years as we have successfully amalgamated the Mental Health Research Institute and the Brain Research Institute with the Florey. Both are dynamic investigators who contribute significantly to global research of the brain. Professor Masters is a world leader in Alzheimer’s research. His work over the last 35 years has been widely acknowledged as having had a major influence on our understanding of amyloid plaques. He continues the search for novel therapeutic strategies to combat this terrible disease.

Professor Jackson is a neurologist and leader of a research team dedicated to curing epilepsy. His work in MRI technology has changed international practice and has led to improved understanding of the disease and more sophisticated surgical outcomes for some of the most serious forms of epilepsy.

Most recently, we accepted the resignation from the Florey Board of Professor Anne Kelso AO, who has become the chief executive officer of the National Health and Medical Research Council. This significant position, at the centre of national research funding and policy, is perfectly suited to this very wise and strategic professional. We wish Anne well in this new endeavour at a time of great change in the sector.

From a national perspective, 2014 was a year dominated by political campaigning for fairer federal funding through the proposed Medical Research Future Fund. The Florey has been cautious when commenting on funding sources but, rather, we have emphasised our strong support for the $20 billion initiative. There is no doubt it will be an absolute game changer for medical research in this country. It would provide a stable environment for Australian scientists who currently live year to year with the uncertainty around the likelihood of being able to continue their research.

It is well documented that the incidence of diseases of the brain and mind is continuing to grow, placing a huge burden on healthcare costs. During 2014, the Florey developed a long-term strategic approach to address this looming crisis by designing four key ‘working models’ for disease interventions. We aim to deliver major advances by 2035, improving lives so individuals across the nation can work, feel well and be unimpeded by diseases that can be avoided, treated or cured. We aim to:

- Diminish the scourge of dementia
- Prevent stroke and limit its impact when it does occur
- Reduce the incidence and devastation caused by mental illness
- Identify and help those genetically prone to epilepsy.

We believe this comprehensive program has the capacity to enable 175,000 people per annum to participate in the workforce. This translates to individuals living more independent lives, with less reliance on the health system and a capacity to contribute to the economy. We are on the brink of an exciting new era.

Finally, we would like to take this opportunity to thank our dedicated researchers and clinical partners who work together over many years to deliver discoveries. You are working for the good of humanity, improving lives and ensuring that children born today will enjoy healthier lives, free of some of the neurological conditions we face today. With National Health and Medical Research funding static, there has never been a more testing time to be a medical researcher in Australia.

Thank you again to our dedicated and generous supporters. Please enjoy reading this report and know you have helped make discoveries happen.
During 2014 the Florey entered a new era. With the 2012 amalgamation, the completion of the building project and the collapse of the group structure behind us, management is focused on the Florey’s prosperous future.

We are absolutely committed to building tightly managed operations in order to support our mission, to improve lives through brain research.

During 2014 the restructuring and streamlining of internal operations has enabled management to focus on extracting the best value for the Florey on every dollar spent, whilst at the same time improving service and support to researchers. New systems, automation and reporting have been implemented to make internal operations easier for researchers, and this will continue throughout 2015, particularly with regard to the Human Resources function.

Additionally arrangements with third parties have either been re-negotiated or not renewed, such as building agreements and information technology, in order to ensure internal operations are fully funded.

In recent years our Corporate Services department has operated multi-million dollar deficits. Corporate Services is budgeting a surplus for 2015. This will mean that all monies contributed to the Florey’s endowment will be used to directly fund vital world class research. The tremendous work of the Board via the Finance and Investment Committee, the Commercialisation Committee and the Audit Committee has been instrumental in this regard and is greatly appreciated.

The management team has also commenced implementing a framework for the long term financial sustainability of the Florey, including the adequate co-funding of all researchers as a matter of policy and practice. A big thanks to all those who have contributed to the Florey’s on-going success and I look forward to providing an even brighter report in 2016.

As a young scientist, I felt a real need to make a positive contribution to society and eventually I found my niche in genetic epilepsy.

Research by Professors Sam Berkovic and Ingrid Scheffer - who would become my most important and closest collaborators - helped me realise that genetic epilepsies demanded an urgent clinical response and a paradigm shift in our understanding of the fundamental causes of this “sacred” disease. We are trying to change the lives of children and adults with genetic epilepsy by discovering how genetic mutations lead to seizures and by developing new drugs and therapies to improve lives.

Professor Steven Petrou, Deputy Director and Head, Division of Epilepsy, Ion Channels and Disease.
Our methods for staving off and treating dementia have been increasing very slowly despite intense international focus. But according to Dr Noel Faux from the Florey Institute of Neuroscience and Mental Health, one of the main issues with dementia is that by the time a clinical diagnosis is made, a huge amount of brain damage has already occurred. And the damage caused by this progressive disease is not reversible.

The race is on to develop an inexpensive test that will enable far earlier diagnoses of dementia. As with most diseases, the earlier the diagnosis the sooner treatment can begin and the better the chance of a good outcome. Making the test affordable is also important as it will allow greater numbers of people to access it and act on the results.

Dr Faux is in the thick of this race and is using data from the ongoing Australian Imaging Biomarker and Lifestyle Study (AIBL), which began in 2006, to support his research into the most common form of dementia, Alzheimer’s disease.

“AIBL is a large scale population-based observational study with over 700 cognitively healthy participants, over 100 participants with mild cognitive impairment and over 200 participants with Alzheimer’s disease,” Noel explains.

“Using blood-based measurements from AIBL, we were able to identify two useful signatures. One was able to distinguish people with Alzheimer’s disease from cognitively healthy individuals. The other signature was able to distinguish people who have a biomarker identifiable through brain imaging from those who do not.”

Analysing blood avoids the need for expensive imaging and cerebrospinal fluid analyses, which are currently used. Potential distress and pain are also minimised using this method.

Other researchers have adapted the research approach Noel used to identify blood-based signatures for several other diseases and conditions such as schizophrenia and Parkinson’s disease.

Looking back, it’s apparent that Noel was well-placed for his line of research with his background in computer science and PhD in bioinformatics.

“During my PhD studies, I became very interested in neuroscience and how I could apply my bioinformatics knowledge to help understand neurodegenerative diseases and, in the instance of Alzheimer’s disease, how we could identify people at high risk of developing Alzheimer’s disease before clinical symptoms show,” he says.

With nearly 1 million Australians expected to be diagnosed with dementia by 2050, Noel’s research could not have come at a better time. Needless to say, the hopes of the nation hang on significant breakthroughs in dementia – and Noel could be just the person to deliver one of them.
Alexander Eastwood was determined to become a secondary school teacher when he was in the final year of his science degree at the University of Melbourne. Passionate about education, Alexander was a Campus Ambassador for Teach for Australia, an organisation that recruits outstanding young graduates and other professionals to work in disadvantaged schools. He previously campaigned on educational and youth matters.

But a third-year lecture in neuroscience offered by the Florey’s Dr Emma Burrows changed his mind – and the course of his life. The lecture was about the emerging fields of environmental enrichment and neuroplasticity.

“It was a career changer,” says Alexander. “Emma was among the most engaging lecturers I had ever had.”

Alexander approached the scientist after the lecture, and she later invited him to do research experience in the Neural Plasticity laboratory, led by Professor Anthony Hannan.

The following year he jumped at the chance to study an Honours year researching autism spectrum disorder with Emma and Anthony as his supervisors.

“I’d always had an interest in autism – two of my cousins have the condition.

“We were interested in how it developed in a mouse model and also, in better understanding how mice communicate. We looked at the high-pitched sounds produced when males ‘sing’ to females.

“We were collaborating with researchers from other faculties and unexpectedly learnt that mice also yodel and growl!”

For Alex, it was an enjoyable yet intense year and his project was an overall success.

The researchers found that mice with the mutation similar to that in some humans with autism used a completely different set of calls to those without it.

“The project provides interesting and novel findings and is a roadmap for future research,” says Alexander.

Tony Hannan describes Alexander as bright and motivated.

“He has exceptional promise as a neuroscience researcher – he’s meticulous, curious, he reads all the literature and picks up the techniques really quickly. He has all the makings of a really exceptional scientist.”

At the end of the year Alexander was awarded a Rhodes Scholarship to complete a Masters and PhD at the University of Oxford.

The honour was the latest in a long string of awards and scholarships, including Dux of school in 2008 and Bendigo Youth Citizen of the Year in 2010. He’s an all-rounder, active in sport, debating, theatre and volunteering, including working on environmental causes.

“The Florey is an incredible launching pad – it’s stimulating, social and cosmopolitan.”

He is continuing autism research with Emma and Tony, working towards a publication before he leaves for England in September – and hopes to collaborate with them while at Oxford.

And beyond his PhD? “Ideally, I’ll join the global effort to better understand autism and help improve the lives of people with the condition.”

“Teaching is something ‘I’ll come back to but I need to chase this interest for now.”

Alexander Eastwood is off to Oxford University on a coveted Rhodes Scholarship. The Florey will miss this extraordinary young man’s contribution to our research. We wish him well for what is sure to be a great career.

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Neuroscience is attracting massive community interest as we discover remarkable facts about this elusive organ, hidden away behind our bony skulls. There is still a lot to reveal – and the Florey’s Dr Henry De Aizpurua is helping to steer our scientists to new frontiers.

He’s watched it grow in global relevance to become among the top three or four leading neuroscience institutes in the world.

And, he says, there’s more to come – much more.

He says the Florey will be active in several neuroscientific frontiers in the next 20 years.

The first will involve mapping the connectivity of the brain. The aim? To create a 3D map of the brain known as a “connectome”.

“This has the ability, when achieved, to help us understand the brain and the consequences of damage and repairs to it,” he says.

“There’s a huge amount of excitement about where we could go with this.”

Creating a connectome would be like the advent of the human genome, which revolutionised medicine more than a decade ago.

Like the genome, building a connectome would be a huge, global effort of staggering complexity and requiring massive investment”, he says.

“Work at the Florey on all the diseases we research is being driven at a frenetic pace but often in medicine serendipity is the thing that gets you across the line.”

“It’s an achievable ambition.”

A breakthrough with one disease could also lead to lessons and shortcuts in developing treatments for other diseases, he says.

“Medicine always shows you that there are lessons to be learnt and shortcuts to be understood as you unravel one Gordian knot of a disease and flow through to other pathologies. You can’t guarantee that but the history of medicine shows that, as in infectious diseases.”

Florey scientists are ready to tackle another frontier – the development of a simple, safe biomarker for early detection of neurological disease.

“It’s super important because fewer of us are going to die from heart attacks or tumours – they’re already becoming manageable diseases – and so we’re going to have a population living to an age that biology hasn’t actually been programmed to plan for.

“We want to identify those people in the community who are susceptible to early progression into chronic degenerative disease. Then we will offer them interventions that avoid the catastrophic collapse of the cognitive neuro functions, their mental health or their physical ability to navigate daily life.”

Right now we’re relying on big bulky expensive tools like MRI and PET (molecular imaging devices) but we need to refine medications and other treatments so we can offer simple, safe, cheap effective tools for people around the world.”

Brain maintenance is a third theme demanding attention of Florey scientists and one offering an opportunity for a partnership with the public, says Henry.

“But it’s already begun.”

The Florey is linked into the Obama BRAIN Initiative, and large initiatives in the European Union, among other projects.

Another ambition of the Florey is to nail down safe and effective treatment for at least one of the most common neurological diseases – within the next decade.

“Any institution that sees itself as globally relevant wants to do this. We aim to develop a powerful treatment that is broadly applicable to the community at large – possibly for Parkinson’s or Alzheimer’s, depending on our progress in the next few years.

“Thirty or 40 years ago, it was thought the brain was static and its development set in concrete once you hit puberty. Now, of course, we know it can be moulded, shaped, exercised and driven. It’s the concept of the plastic brain.”

“Maintain the brain” is the catchcry but it is ultimately up to the public to make the lifestyle choices to do this, he says. The Florey has an obligation to educate the community.

“It’s a bit like the public education campaigns to quit smoking,” Henry says.

“The concept of maintaining brain health is going to explode over the next decade. People will begin to understand the direct benefits of healthy lifestyles so they maintain brain health.

“The baby boomers and the Gen-Xers are better educated than any generation before them. They have an enormous interest in maintaining brain health – and they will be empowered to do something about it.”

Establishing partnerships with clinical psychologists, commercial organisations that develop brain training tools and the media, (the Florey has already has a strong link with the ABC’s Active Memory), is going to be pivotal in giving the public the important needs and in rolling out brain activity tools developed by cognitive neuroscientists.

“And at the end of the day, it will be use it or lose it.”

The final frontier is developing the ability for the brain to regenerate itself.

“Now that is a long way off,” Henry says, “because the whole area of cellular regeneration is still finding its feet.

“But there’s a huge amount of fantastic stem cell biology and regenerative medicine happening at the Florey. Eventually good quality medicine and research is going to deliver approaches to regenerate various parts of the body and the brain as well, which will give patients and their doctors a new set of options as they approach particular problems with their brain health.”

Henry says he is buoyed by the possibilities for neuroscience in the next two decades.

“The brain is the most complex, the least understood major organ in the body. The opportunity for exploration and discovery, for new insights and interventions, are just all there.

“The Florey is, aspires to be, and will be, a global leader in delivering some of these life-changing opportunities.”

It will probably require the invention of tools and systems we don’t have right now. It’s enormously multidisciplinary – engineers, IT specialists, imagers, basic cellular scientists, clinicians, will all have to be part of big programs in that area.”
The Two of Us
Prof Ashley Bush & Dr Ya Hui Hung

Professor Ashley Bush heads the Florey Institute’s Oxidation Biology Unit, researching Alzheimer’s disease and other neurological disorders. He’s a psychiatrist and basic researcher. Senior researcher Ya Hui Hung is investigating a rare, genetic and fatal disease called Niemann-Pick Type C (NP-C) that is also known as ‘childhood Alzheimer’s’. The two researchers hope this work will lead to drugs to treat young people afflicted with the condition, and that it will have implications for a cure for Alzheimer’s, too.

PROFESSOR ASHLEY BUSH

I met Ya Hui when I was recruiting staff after returning from Harvard University in 2005. My main work has been on the role of metals in brain diseases and we know this has something to do with Alzheimer’s disease. I thought Ya Hui was very bright and recruited her to do a post-doc.

For the first few years she investigated whether there was a relationship between copper and cholesterol. In 2010 I was approached by a lady called Chris Hempel, whose twin daughters have NP-C, who’d set up a foundation in the US to encourage study of it. It was such a heart-rending story, I found it hard not to engage. Chris’s girls are 11 years of age and have lost the capacity to walk and speak as they have advanced dementia. Ya Hui was very moved by the story as well. She’s got a big heart. Once she saw what this disease was, it made the science seem very real.

Her mission is to find drugs that can reduce the accumulation of cholesterol, and help correct the loss of function that occurs in NP-C.

Ya Hui’s very smart and an excellent scientist but is modest and self-effacing. She gets disappointed in herself very easily. I mentor her about her career and try to keep her optimistic. It’s a tough world trying to be a career scientist in Australia.

A couple of times she thought she’d have to give it away and I did what I could to keep her going.

We’re both music buffs. A common friend has an orchestra and we found ourselves in the same recording studio once, surprised to see each other outside work!

I insisted that Ya-Hui present her findings at an international conference in Greece in 2012. She was terrified so I got her trained by a coach, an actor from Neighbours.

She did a great job. I think that was the watershed for her, when she blossomed into a mature scientist. She went on to become our public face for this research. She must be the leading scientist on NP-C in Australia.

DOCTOR YA HUI HUNG

When Chris Hempel contacted Ashley in 2010, she brought to us a question: is there something you can do to help my daughters?

Driven by Chris’s personal quest, we looked at the metal changes in NP-C disease patient skin cells, in blood samples and post-mortem brain cells. We published a paper last year that reported widespread metal changes in NP-C disease. This finding gives us confidence that by altering metal levels we may be able to treat NP-C.

We’re learning amazing things from talking to patients and their families, too. I’m a softie! It’s really heart-breaking to see these children suffering, and see their parents’ lives so affected by the disease too. Hopefully our drug screen will result in a treatment to help patients.

Ashley’s really good when I’ve got questions; his door is always open. He’s very knowledgeable, a lateral thinker, and he’s always encouraging and very supportive. I often thank him for putting up with it when I say ‘I can’t do this any more’. He’s a great boss and mentor. He lightens things up – he says ‘everything’s a lazy afternoon’s work’!

He’s very determined and persistent in pursuing science. I’ve learned from him to never give up.

If you would like to help this research to continue, please contact the Florey on 1800 063 693.
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While the act of philanthropy is yet to penetrate deeply within Australia, it is a discussion
Finkel Foundation gave its support to annual scholarships for three promising young scientists.
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plant the seeds of medical research, and that, in due course, will yield a vast harvest. The
people and families who see the importance of medical research and share our vision for a healthier
The success rate of scientists across Australia for NHMRC grants was the lowest since the current
selection process was adopted 15 years ago. While there is great excitement and hope about
In 2014 the Florey Foundation and its Council included Chairman Trevor Clark, Julian Clarke,
Andrew and Claire Heenan have also been great supporters in the face of tragedy. Andrew,
and Cure MND, all of whom work tirelessly to raise funds to support our research. These Florey
We appreciate these brave, determination and commitment to help us find answers.
In addition to these individuals, it is important to also recognise the wonderful, ongoing
support we receive from voluntary groups in the community such as One in Five, River’s Gift,
and others were regular supporters who used this opportunity to keep fit and raise money and
awareness at the same time.
A CHANGING WORLD
The Federal Government’s National Health and Medical Research Council (NHMRC) has traditionally
been the major provider of funds for medical research. It is a highly competitive
arena under the constant pressure of funding constraints and increasing demand. In 2014, the
success rate of scientists across Australia for NHMRC grants was the lowest since the current
selection process was adopted 15 years ago. While there is great excitement and hope about
the proposed Medical Research Future Fund, it remains exactly that: a fund in the future.
In the face of the changing models of government funding, the Florey’s capacity to fundraise
has become increasingly important.
Thanks to the generosity of many individuals and organisations, the Foundation had a productive
year. We have seen good growth in our philanthropic income and the support we have received
has been crucial to our research programs and our ability to recruit and retain the best researchers.
Philanthropic contributions have purchased some of the latest research technologies and
equipment, thus playing a vital role in our work to identify methods of early diagnosis and to
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As part of this program we are fortunate to attract funds from philanthropic trusts and
foundations that enable research projects which are focussed on exciting new findings to get
underway and become established. They also allow us to purchase the latest technologies
that can accelerate the progress of research or provide new insights into the illnesses we
study. They often fund work being done by promising young scientists as they establish their
research programs.
Many trusts and foundations were established decades ago by forward thinking philanthropists.
Today, it is heartening to see new foundations being established by generous individuals and
families who see the importance of medical research and share our vision for a healthier
community. The Dowd Foundation was a new donor to the Florey this year, providing a three-
year fellowship to support Associate Professor Chris Reid and his work on epilepsy whilst The
Finkel Foundation gave its support to annual scholarships for three promising young scientists.
While the act of philanthropy is yet to penetrate deeply within Australia, it is a discussion
that is occurring increasingly around family dinner tables, conference rooms and parliamentary
cabinets. We definitely need more Australians to declare their belief in an act of public
generosity and to help create a groundswell of funding support for medical research. Those
behind new and innovative initiatives need to step up publicly and share their belief in
philanthropic generosity. As we have seen in the United States, the impact can last a century
or more.
In 2014 the Florey Foundation and its Council included Chairman Trevor Clark, Julian Clarke,
Graeme Kelly, Ross Oakley and Stephen Spargo. Ex officio members were Geoffrey Donnan,
Henry De Aizpurua and Ross Johnstone. We are very grateful to these individuals who have
contributed to the organisations with their expertise.
COMMUNITY SUPPORT
This year has seen a great many people sweating for the Florey, fundraising in the City2Sea,
the Melbourne Marathon, and Surf Coast Century. Some people were running for the first time
and others were regular supporters who used this opportunity to keep fit and raise money and
awareness at the same time.
And there were others who did something a bit more out of the ordinary, like Kingsley Just who
broke the world record for consecutive spins in a plane. That was a hair-raising day. Not only
did he break the world record, he did 600 more rolls to reach a staggering 987 rolls altogether.
This was all to raise money for research that may one day help his son Kaelen who has a rare
mental illness.
Andrew and Claire, set off from Perth on a 4000km solo cycle trip across Australia to
the NSW Central Coast. Before his journey Andrew shared a thought with his supporters: “I
lost my son Ben after a long battle with mental illness. Despite being surrounded by a loving
family and intensive treatment from a team of mental health professionals Ben could no longer
cope with his illness and took his own life. Ben’s death was a complete tragedy for our family”.
Rather than feel helpless, Andrew and Claire saw the value in investing in mental health
research and decided to help the Florey in its quest to improve treatments for those suffering
mental illnesses.
The support of people like these families, and the individuals running their own fundraising
activities, is invaluable in funding research into illnesses of the brain. We appreciate their
bravery, determination and commitment to help us find answers.
In addition to these individuals, it is important to also recognise the wonderful, ongoing
support we receive from voluntary groups in the community such as One in Five, River’s Gift,
and Cure MND, all of whom work tirelessly to raise funds to support our research. These Florey
champions are motivated by tragedy and determination to help others who might one day face
an illness of the brain or mind. We are so grateful for their vision and generosity.
I would also like to acknowledge the wonderful work being done by the fundraising, media and
marketing teams who work tirelessly across a wide range of activities to raise funds to support
our scientists while keeping the community up-to-date with the research we are doing.
BOARD OF DIRECTORS
Mr Harold Mitchell is the founder of Mitchell & Partners and until August 2013 was the Executive Chairman of Aegis Media Australia and New Zealand. Mitchell & Partners is the largest media and communication group in Australia, with growing presence in New Zealand and across the Asia-Pacific region. Mr Mitchell holds a large number of community roles including Chairman of the Melbourne Symphony Orchestra, Chairman of TVS, University of Western Sydney’s television service for Greater Sydney, Chairman of Arts Exhibitions Australia; Chairman Free TV Australia, Vice President of Tennis Australia; Director of New York Philharmonic; and Director of Crown Ltd. He has also been Chairman of CARE Australia; Chairman of the National Gallery Australia; Chairman of the Melbourne International Festival of Arts; President of the Melbourne International Film Festival; President of the Museums Board of Victoria and a Board member of the Opera Australia Council. Mr Mitchell was appointed Companion of the Order of Australia in 2010 for eminent service to the community through leadership and philanthropic endeavours in the fields of art, health and education and as a supporter of humanitarian aid in Timor-Leste and Indigenous communities. In 2013 Mr Mitchell was awarded the Victorian of the Year.

James Angus is former Dean of the Faculty of Medicine, Dentistry and Health Science at the University of Melbourne. He is also a Fellow and former Member of Council at the Australian Academy of Science. He is currently Professor of Pharmacology at the University of Melbourne, a Director of The Peter MacCallum Cancer Institute and Chairs the Victorian Clinical Training Council. Professor Angus is the Vice Chancellor’s nominee for appointment in accordance with the Constitution and was previously a non-executive Director of The Mental Health Research Institute (appointed 2003). He was appointed an Officer of The Order of Australia in 2010 for distinguished service to biomedical research, particularly in the fields of pharmacology and cardiovascular disease, as a leading academic and medical educator, and as a contributor to a range of advisory boards and professional organisations, both nationally and internationally.

Craig joined the National Australia Bank in November 2013 as Group Executive, Finance & Strategy and appointed Chairman of JBWere Board in July 2014. Prior to joining NAB, Craig spent four years as Chief Executive and Country Head of Bank of America Merrill Lynch Australia. Prior to that, Craig joined Goldman Sachs JBWere in 1986 and held various roles including Chief Operating Officer, Chief Executive Officer and Executive Chairman. Craig is a Board member of The Geelong Football Club and a member of The Ian Potter Foundation Finance Committee. Craig is a Senior Fellow of FINSA and a Chartered Accountant.

Ian Potter is a founding partner of MBM Investment Management, and has been a significant figure in Australia’s financial services and media industries for over 40 years. He is a former Director of Fairfax Media, The Australian Financial Review and News Limited. Mr Potter Chairs the Independent Remuneration Committee at the Reserve Bank of Australia. He is the Co-founder of the Ian Potter Charitable Trust, an independent grant-making organisation that fosters and assists junior researchers in the fields of medical research, arts and culture, humanities, and social science. Mr Potter is President of the Melbourne Convention and Exhibition Centre and Chairs the Victorian Clinical Training Council. Professor Anne Kelso has recently been appointed the Chief Executive Officer of the National Medical Research Council (NMRC).
Dr Brendan Murphy was appointed Chief Executive Officer of Alfred Health in January 2005. Prior to that he was Professor/Chief Operating Officer at Alfred Health where he has worked for 10 years in various roles. He has worked across various settings in the health sector and Victorian State Government including Director Mental Health and has undertaken service and strategic reviews for a range of organizations across Australia.

MR ANDREW STRIPP
MBCh (Clinical Psychol) BBSc (Hons)

Andrew Stripp is the Deputy Chief Executive Officer and Chief Operating Officer at Alfred Health where he has worked for 10 years in various roles. He has worked across various settings in the health sector and Victorian State Government including Director Mental Health and has undertaken service and strategic reviews for a range of organizations across Australia.

MR MARK JONES
BA (Hons) (Sheff) MBA (MRS)

Mr Mark Jones is the Ethics and Independence Partner and the Chief Operating Officer of the Risk Management Group at KPMG. He also provides professional services in the areas of corporate governance and internal audit. Mr. Jones is a Fellow of both the Institute of Chartered Accountants in England and Wales, and the Institute of Chartered Accountants in Australia, and is a member of both CPA Australia and the Australian Institute of Company Directors.

MR ANDREW ABERCROMBIE
BEc LLb MBA (IMD)

Andrew Abercrombie is the founding Director of FlexiGroup Limited (FXL) and remains on the FlexiGroup Board continuing to work with the CEO and management team. FXL is now a top 150 company on the ASX. Formerly a commercial lawyer, he oversees a broad range of commercial interests. He is the Regional Chairman of the World Presidents’ Organisation and continues to participate in international education programs in various roles. Formerly a member of one of Victoria’s Alpine Resort Management Boards, he is also a Director of the Menzies Research Centre, the Melbourne Zoo Foundation and Treasurer of the Liberal Party of Australia (Victorian Division).

MRS JENNIFER LABOURNE
BBus, FCPA

Jennifer Labourne is the Director of Finance & Business Services at Colac Area Health for the past 5 years. She was previously a partner at Ernst & Young, Deputy Chair of Health Purchasing Victoria, Director of Parks Victoria and has been involved on various committees of the Australian Society of Certified Practicing Accountants (CPA).

DR BRENDAN MURPHY
MBBS PhD FRACP FAICD

Dr Brendan Murphy was appointed Chief Executive Officer of Austin Health in January 2005. Prior to that he was Professor/Director of Nephrology and Chief Medical Officer at St. Vincent’s Health. He is President of the Victorian Hospitals Industry Association and is also a Director of the Olivia Newton-John Cancer Research Institute and a Professional Fellow with the title of Professor at Melbourne University.

EMERITUS PROFESSOR ANDREA HULL AO
BA Dip Ed (Univ of Sydney)

Emeritus Professor Andrea Hull has had a distinguished career in CEO and executive roles, and also as a non-executive Board member in government and not-for-profit organisations. She is an Emeritus Professor at the University of Melbourne, and is Chair of ABC Advisory Council, Deputy Chair of the Breast Cancer Network of Australia and former Deputy Chair of the National Museum of Australia. She is also a Board member of The Melbourne Forum, the Melbourne Prize, The Melbourne Zoo Foundation and Treasurer of The Liberal Party of Australia (Victorian Division).

MR STEPHEN SPARGO AM
LLB LLM

Mr Stephen Spargo is a Partner practising in the Banking and Finance Practice Group of Allens. He is a director of Asia Society Australasia Centre, Chairman of The Royal Agricultural Society of Victoria Limited, a Vice-President of the Melbourne Cricket Club, Vice-President of Golf Victoria and a director of the Committee for the Economic Development of Australia.

MR ANDREW STRIPP
MBCh (Clinical Psychol) BBSc (Hons)
Neuroscience Trials Australia is a niche, not-for-profit, contract research organisation within The Florey Institute of Neuroscience and Mental Health. It offers an Australian approach to global clients seeking economical, smart and timely neuroscience clinical research.

Neuroscience Trials Australia is co-chaired by two of Australia’s most experienced clinicians and medical researchers, Professors Geoffrey Donnan and Stephen Davis. The General Manager, Dr Tina Souls, oversees all personnel and projects as well as driving business strategy and objectives. To date, the business has grown, on average, 39 per cent each year and continues to provide a sustainable, highly experienced environment for bringing clinical trials to Australian patients.

The team’s areas of expertise include stroke and stroke-related conditions, multiple sclerosis, epilepsy, Parkinson’s disease, spinal cord injuries, Huntington’s disease, neurosurgery, pain, neuromuscular disease, mental illness and migraine. The team has strategic alliances with many therapeutic disease groups and can provide access to key opinion leaders, sites and clinical trial expertise through a range of tailored services. Staff have global management experience in all phases (I to IV), of clinical research.

The services provided include study feasibility, project management, monitoring of studies to global regulatory standards, safety reporting throughout the clinical trial, data management and biostatistics and report writing. The relationship with services provided and key stakeholders are outlines in the following diagram.

“Many of the projects we undertake at Neuroscience Trials Australia assess new ways of treating strokes and their effects. Our trials involve developing new drug treatments as well as new devices.”
Dr Tina Souls

The division continues to expand and has a healthy pipeline of new and ongoing projects with multiple trials in various neuroscience therapeutic areas being conducted at any one time. These projects consist of investigator initiated studies as well as those initiated by commercial interests. Outlined, next, are examples of the many projects underway.

Mechanically retrieving clots that occur during strokes: the EXTEND-IA study
Stroke is Australia’s second biggest killer after coronary heart disease and a leading cause of disability. According to the National Stroke Foundation, one in six people will have a stroke in their lifetime. The total financial costs of stroke in Australia are estimated to be $5 billion (2012 figures).

A stroke occurs when a clot blocks one of the blood vessels to the brain. This causes poor blood supply and lack of oxygen to the brain tissue. If blood supply is not restored to the brain there is permanent brain damage. Currently there is only one treatment for stroke caused by a blocked blood vessel. This treatment is a medicine called tissue plasminogen activator (t-PA). t-PA works by dissolving the clot that is blocking blood supply to part of the brain and has been proven to reduce disability after stroke. However, tPA does not always succeed in opening the blocked artery and it should be given within the first 4.5 hours after stroke.

The aim of the EXTEND-IA study was to test whether mechanical clot retrieval (using a device called Solitaire) after standard intravenous tPA is more effective in opening the blocked blood vessel and improving recovery from stroke than just tPA alone.

This cutting edge multi-centre study examined the effectiveness of one of the latest clot retrieval devices available globally, the Solitaire FR clot retrieval device.

Results were published in the New England Journal of Medicine with concurrent presentation at the International Stroke Conference in Nashville, USA. It was found that early intra-arterial clot retrieval, in addition to giving tPA, improved neurological recovery and functional outcome.

Neuroscience Trials Australia was the program manager and was responsible for setting up the project, the data management systems and project management for this successful trial.

Stem cell hope for Parkinson’s disease patients
A therapy for Parkinson’s disease from International Stem Cell Corp. is expected to get imminent approval for testing in Australia.

The US-based publicly traded company has grown neural stem cells, which can mature into cells making the neurotransmitter dopamine, deficient in Parkinson’s. The company plans to implant these stem cells into the brains of Parkinson’s patients, restoring dopamine production and normal movement in the patients.

The trial will be the first test of therapy with the company’s cells, derived from unfertilised, or parthenogenetic, human egg cells. The cells, which in theory can produce nearly all types of cells found in the body, are grown into neural stem cells. These cells will be implanted and mature in place. The trial will primarily assess safety, but also look for evidence of efficacy.

International Stem Cell Corp. chose Australia as its first trial because its regulatory agency is more “interactive” than the U.S. Food and Drug Administration.

Neuroscience Trials Australia has assisted the company with all required submissions and interactions with the Australian Therapeutics Goods administration utilising the Clinical Trial Exemption (CTX) scheme. In addition, Neuroscience Trials Australia will be responsible for the project management of the entire trial process, including project management, importation of study stem cells and data management processes.

Ground-breaking Alzheimer disease treatments
Anavex Life Sciences Corp. is a US-based publicly traded biopharmaceutical company dedicated to the development of novel drug candidates to treat Alzheimer’s disease, other Central Nervous System (CNS) diseases, and various types of cancer.
Anavex’s lead drug candidate, ANAVEX 2-73, is currently in a Phase 2a clinical trial for Alzheimer’s disease in an Australian-only trial that is being managed by Neuroscience Trials Australia. ANAVEX 2-73 is an orally available drug candidate that targets sigma-1 and muscarinic receptors and successfully completed Phase 1 with a clean data profile. Preclinical studies demonstrated its potential to halt and/or reverse the course of Alzheimer’s disease.

With its adaptive design, the aim of this trial is to objectively measure all possible effects of the drug in patients, which serves to optimally design and reduce the risk for future pivotal trials. There is an urgent, unmet need in Alzheimer’s disease, with a new case developing every 67 seconds and 5.2 million Americans currently diagnosed.

The current multicentre Phase 2a adaptive clinical trial will enroll at least 32 mild to moderate Alzheimer’s patients and they will be able to receive the study drug for up to 26 weeks. The primary objective of the trial is to evaluate the maximum tolerated dose of ANAVEX 2-73 in these patients. Additional trial objectives include dose response, bioavailability, cognitive efficacy and the relationship of ANAVEX 2-73 as an add-on therapy to donepezil, the current standard of care.

Innovative new treatment hope for neuromuscular disorders

Flex Pharma is a US-based biopharmaceutical company dedicated to creating innovative, novel treatments for neuromuscular disorders.

Neuroscience Trials Australia will manage several clinical trials that will assess a new treatment as a solution for people suffering from nocturnal leg cramps, as well as muscle cramping and spasms resulting from a broad range of neuromuscular disorders, such as multiple sclerosis.

Flex Pharma’s proprietary treatment is based on research showing that cramps are caused by excessive firing of alpha-motor neurons in the spinal cord that control muscle contraction. The treatment is designed to stop the firing of the neurons by topically stimulating the transient receptor potential (TRP) ion channels located in the gastrointestinal tract. Physical properties of the TRP activators largely limit their action to sensory neurons in the mouth, esophagus and stomach, with minimal concentrations reaching the bloodstream and, consequently, fewer potential systemic side effects.

Previous studies have demonstrated that Flex Pharma’s treatment reduced electrically induced muscle cramps within 15 minutes, and its effect lasted between six and eight hours compared to subjects taking a vehicle control. When data from the three studies were aggregated, the treatment showed a statistically significant overall treatment effect, reducing cramp intensity by three-fold compared to subjects taking a vehicle control (ANOVA, p<0.0001).

Neuroscience Trials Australia is the program manager and is responsible for setting up the project, project and data management systems as well as sourcing and labelling of the study drug.

Making spinal cord injury less traumatic

Neuroscience Trials Australia is fortunate to play a leading role in this ground breaking set of studies. Our team is involved in setting up project and data management of a unique program which aims to address and change the way that patients who have a spinal cord injury are treated.

The main focus of the project is to offer urgent decompression of the injury as close as possible to the time of occurrence.

The main causes of traumatic spinal cord injuries (SCI) are road trauma, falls and water related accidents with most spinal cord injuries occurring to men under the age of 35. This type of injury impacts the majority of people at the prime of their lives and it is thought that Australia alone currently has 10,000 people living with spinal cord injury.

The total cost of spinal cord injury in Australia is estimated to be $2 billion annually which includes costs to patients and their families. If just 10 per cent of carers were able to return to the workforce because their family member with a disability had appropriate personal support, there would be a $3 billion boost into the economy.

Even more disheartening, physical injury to the spinal cord results not just from the initial impact, but also from compression of the spinal cord as a consequence of the displaced vertebra.

A multi-centre clinical trial of immediate cooling followed by emergency decompression (ICED) in patients with cervical SCIs is proposed. The current project aims to conduct the pilot as well as safety and feasibility studies necessary before commencing this trial. The contemporary timing of decompression is currently being established in key Australian states and areas of delay identified. Treatment protocols will then be streamlined and the feasibility of decompression within the 18h window established.

Because hypothermia is being initiated by paramedics, it is important that entry neurological assessment is carried out in the field prior to initiation of therapy. A key study is therefore to establish the reliability and validity of paramedic L3 and S1 motor and sensory scores in acute cervical SCI. Once these studies have been performed, it will be possible to proceed to a feasibility and safety study of immediate cooling followed by emergency decompression.

Getting to the POINT of the matter – The (POINT) Trial: Platelet-Oriented Inhibition in New TIA and minor ischemic strokes

Transient ischemic attack (TIA) is a transient episode of neurological dysfunction. TIAs are common events with an estimated 250,000–350,000 occurring each year in the US alone, an incidence about 30 to 40 per cent that of stroke. Rapid recovery is a defining characteristic of TIA and distinguishes it from a complete stroke.

This Phase III multi-centre trial will involve 4,150 participants from 250 centres around the world with either a confirmed high-risk TIA or a minor stroke. Treatment will be within 12 hours of symptom onset with either clopidogrel or placebo. This multi-centered clinical trial is sponsored by the University of California, San Francisco and funded by the National Institute of Neurological Disorders and Stroke in the US.

The purpose of the study is to determine whether clopidogrel is effective in improving survival free from major ischemic vascular events (ischemic stroke, myocardial infarction, and ischemic vascular death) at 90 days when initiated within 12 hours of TIA or minor ischemic stroke onset in patients who are already receiving aspirin.

Recruitment into the trial across all sites is currently at 45% or 2632 participants to date.

Neuroscience Trials Australia is responsible for setting up the trial and complete project management across 10 sites throughout Australia and New Zealand.
A FAIR WORKPLACE FOR ALL

The Florey forges ahead

At the Florey we are committed to harnessing the full complement of talent within the organisation. We believe that supporting and promoting diversity will help accelerate scientific discovery and cures. The Equality in Science Committee (EqIS) collaborates to create conditions in which diverse people can both operate to their full potential and also work together cohesively. This committee has broad representation from professional and academic staff of the Florey to ensure relevant equity and staff development issues are canvassed. Our working groups tackled important issues across the institute and this year’s report celebrates many achievements.

A highlight of the communications group was the successful Women in Neuroscience “Wikibomb” or Wikipedia edit-a-thon, led by Dr Michele Veldsman and Dr Katherine Jackman, pictured left. In partnership with Wikimedia Australia, women and men from the Florey and beyond came together to create Wikipedia pages to profile the achievements of prominent Australian women who have worked or are currently working in neuroscience. The aim? To overcome the poor representation of this group. On the day, the 20 participants created 20 new pages. Amongst these was one dedicated to the achievements of our own Professor Ingrid Scheffer who has won several awards for her ground-breaking achievements in the genetics of epilepsy, including the 2014 Prime Minister’s Prize for Science.

The parent group continued to work on issues important to staff with young families. A key achievement in 2014 was the creation of two family-friendly workspaces (parenting rooms) at each campus of the Florey. This is in addition to supporting new policies to help increase flexible work practices such as family-friendly meeting times, flexible working hours and part-time positions. The family-friendly workspaces will allow scientists with young children to bring them to work when necessary, meet with colleagues or conduct other business in an environment that is safe for children.

At the policy level we continue to work to gain more equitable representation of our female scientists on committees across the institute. We recognise that diversity in committees can change conversations and that opportunities to participate in decision-making groups builds skills and confidence. We have also been working to increase transparency of committee appointments to ensure that everyone at the Florey gets a chance to contribute to the life and culture of the organisation.

The value of mentoring is often underappreciated by scientists, yet mentoring can create enormous opportunities for growth for both the mentee and the mentor. In 2014 we relaunched our mentoring program with a view to creating an even stronger culture of mentorship for Florey staff.

Another exciting development this year was our successful partnership with the Baker Foundation, supported by Kerry Kornhauser from Women in Rotary, to develop a new Women in Science Fellowship. Following an unusual selection process which considered both the quality and potential impact of the candidate’s science (judged relative to opportunity), and their ability to communicate their science to a lay audience, we selected Dr Despina Ganella as the preferred Florey candidate for this award. An application for the Fellowship was then made to the Baker Foundation Board and we were delighted to have the Fellowship approved in December. This three-year fellowship will support Despina as she works to find new treatments for young people suffering from anxiety disorders.

Further progress was made with Women in Science Parkville Precinct (WISPP) collaboration throughout 2014. The Florey acts as the backbone (support) organisation for the collaboration of some 4000 researchers in the Parkville hub. Following a number of meetings, stakeholder interviews and workshops, we created the collective vision for the group: “To be the best at research and translation by providing an environment that allows more women to lead and excel.” We launched the initiative in November, which now includes researchers from some of the largest medical research institutes in Australia: The Florey, Walter and Eliza Hall Institute (WEHI), Peter Mac, Murdoch Children’s Research Institute and the Doherty Institute.

The work of the group will continue with the support of funds from the Trust Company Australia as we move to develop agreed ways of measuring institute performance and achievements. The challenge of supporting more women to excel in science and the work of our WISPP initiative was highlighted across the ABC network in late 2014.

It has been an extremely successful year for the EqIS committee and we thank the efforts of our committee and our very active subgroup members who have helped to develop and implement policies and practices that encourage diversity at all levels of our Institute. We’d also like to thank supporters from outside the organisation for their donations to the Women in Science corpus. At the end of year function we were delighted to have a young male scientist say “your committee is really helping to change the culture of the Florey for the better.” That kind of feedback is deeply gratifying and motivating.

We will continue to find new ways of building equity for all into the fabric of our Institute.

“"To be the best at research and translation by providing an environment that allows more women to lead and excel.” Parkville hub - collective vision

Picture: Dr Michele Veldsman and Dr Kath Jackman.
Professor Andrew Lawrence is the Co-Division Head of Behavioural Neuroscience, running the Addiction Neuroscience laboratory. His primary research interest is in understanding how the brain is assembled during development, and what mechanisms protect brain cells from death following brain injury such as trauma and stroke. Professor Lawrence is currently Senior Editor of The British Journal of Pharmacology and also sits on the editorial boards of Neurochemical Research, the Journal of Pharmacological Sciences & Addiction Biology. In 2009, Professor Lawrence was awarded the Australian Neuroscience Society medallion for services to the society. In his spare time, Andrew is a keen cyclist and a surf life guard.

Professor Seong-Seng Tan is the Head of the Division of Brain Development and Regeneration, NH&MRC Senior Principal Research Fellow, and Adjunct Professor at the Melbourne Neuroscience at The University of Melbourne, and University of Queensland Brain Institute. He is interested in understanding how the brain is assembled during development, and what mechanisms protect brain cells from death following brain injury such as trauma and stroke. Professor Tan has published over 100 papers and was awarded the Angus Australia Medical Research Award (1997). He is on the Editorial Boards of the Journal of Neuroscience (USA) and Experimental Neurology. Professor Tan is a keen swimmer and a member of the Brighton Icebergers. He recently gave a TEDx Brisbane talk on “Why women have different brains.”

Professor Graeme Jackson is the Deputy Director of the Florey, a practising clinical neurologist specialising in epilepsy at the Austin Hospital, and a Professorial Fellow of the University of Melbourne. He is recognised as an expert and world authority in understanding brain function and structure using new MRI technologies, particularly as they apply to understanding and treating epilepsy. The National Health and Medical Research Council of Australia (NH&MRC) awarded him the Outstanding Achievement Award for research excellence.

Professor Steven Petrou is the Co-Division Head of Epilepsy, and heads the Laboratory of Ion Channels and Human Disease, a multidisciplinary team of researchers with a focus on revealing fundamental mechanisms of disease genesis in the central nervous system. Current major areas of investigation centre on the development and characterisation of genetically engineered mouse models for the study of human familial epilepsy. He works closely with industry and has several patents for his discoveries. In addition, he is the Deputy Director of the Centre for Neural Engineering at University of Melbourne, serves on the editorial board of the Journal of Neuroscience of Disease and the Basic Science Committee for the International League Against Epilepsy and is Editor of the Australian and New Zealand Society for Neuroscience.

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President of the International Society for Neurochemistry (2011-13).

is currently Chair of the Scientific Promotions Committee and past
and has provided extensive service to the NH&MRC. Professor Beart
medical research, particularly neuroscience, in the wider community,
post-graduate students. He has a long-term commitment to promoting
Michael Rand Medal (2009). He has trained numerous honours and
positions at the Austin Hospital and Monash University. Professor
He worked at Cambridge and Harvard Universities, before holding
Florey and Adjunct Professor in Pharmacology, University of Melbourne.

Professor Philip Beart (PhD ANU, DSc Melbourne) has been a NH&MRC
outstanding leadership in medical research.

Multiple Sclerosis
Trevor Kiplpatrick leads the MS Division at the Florey Institute of
Neuroscience and Mental Health and is a neurologist and Head of
the MS Unit at the Royal Melbourne Hospital, in addition to being a
Professor of Neurology and Director of the Melbourne Neuroscience
Institute at The University of Melbourne. His research interests include
the neurobiology of multiple sclerosis, neural precursor cell biology and the study of genetic
and environmental factors that contribute to MS as well as the translation of basic research
discoveries to the clinic.

Professor Kiplpatrick has been the recipient of the
Sunderland Award (1994), AMRIAD Postdoctoral Award (1995), Inaugural Leonard Cox Award (2000), Bethlehem Griffiths Research Foundation Award for Research in Medical Research (2004), the Australian Museum's James Callacher Eureka Prize for Medical Research (2008), the Stephen C. Reingold Research Award by the US MS National Multiple Sclerosis Society (2010) and in 2013 Professor Kiplpatrick was awarded the Bethlehem Griffiths Research Foundation Medal for outstanding leadership in medical research.

Professor Ross Bathgate is the Head of the Division of Neuropeptides, an NH&MRC Senior Research Fellow (Level B) and Honorary Professional Fellow in the Department of Biochemistry and Molecular Biology at the University of Melbourne. His work focuses on understanding the interactions of peptide ligands with their G protein-coupled receptor (GPCR) targets for the development of peptide-based drugs and utilizing structure-based drug
design to develop novel therapeutics. One of the
peptide targets his lab is investigating is the peptide hormone relaxin which has recently
completed a successful Phase III clinical trial for the
management of acute heart failure. He works
closely with Novartis who are conducting the
clinical trial on relaxin as well as a number of other
corporate companies interested in the
clinical potential of drugs targeting peptide
GPCRs. He currently serves on the editorial boards
of Molecules and Cellular Endocrinology, Frontiers
in Molecular and Structural Endocrinology and Journal of Pharmacological Sciences.

Associate Professor David W. Howells is the Co-Division Head of the
Division of Stroke and began his career investigating the biochemical
and genetic basis of dopamine and serotonin deficits in children.
He went on to describe a new population of dopaminergic neurons,
demonstrated that BDNF depletion can cause parkinsonism and that
Parkinson's disease patients are deficient in
BDNF. His other research interest is in stroke: his studies of neuromodulation in stroke
have led to improved modelling of stroke in
animals, the development of new methods of imaging, and development of systematic
review and analysis as tools for rigorously
evaluating basic science literature. The
latter have led these leading stroke journals to publish guidelines for Good Laboratory
Practice.

Professor Richard MacDonell is Director of Neurology at Austin Health, a Co-Division Head of Systems Neurophysiology and an Honorary Professional Fellow. He trained in Neurology and Clinical Neurophysiology at Austin Health, Massachusetts General and the London Hospitals and has
been in charge of the Neurophysiology and Neuroimmunology services at Austin Health since 1991. His research interests include multiple sclerosis, peripheral nerve and muscle
disorders and using transcranial magnetic stimulation to
study the pathophysiology of epilepsy.
Our group is interested in the self-defence mechanisms that operate in the brain when something goes wrong. This may take the form of degenerative disease (Parkinson’s, Alzheimer’s) or cancer (brain tumours) due to gene mutations and aging. As a result, mutant or toxic proteins accumulate in brain cells, causing them to degenerate or proliferate. We have been working with one system of self-defence called protein ubiquitination which allows harmful proteins in brain cells to be removed and in the process, halt or reverse the disease process. We are particularly interested in finding how to accelerate beneficial ubiquitination in neurones using the Nedd4/Ndfip1 proteins. Our studies so far demonstrate that these proteins can halt cell death following injury and stroke, and slow down the division of brain cancer cells.

We have found that the longevity of brain cells is controlled much of our mental processing and sensory experience. Although they are in the minority, this class of neurones is strongly correlated with neurones affected by Parkinson’s disease. In animal models, we have shown that Ndfip1 is increased in surviving neurones after stroke. To study the consequences of removing Ndfip1 from neurones, we have deleted the Ndfip1 gene by mouse knockout technology. These animals demonstrate a greater sensitivity to brain damage from stroke, compared to normal animals that still carry the Ndfip1 gene.

We have found that Ndfip1 protects brain cells from death by hijacking an anti-cancer brain protein called PTEN. This protein is normally utilized as a defensive mechanism against tumour formation in brain cells. We found that after brain injury, this mechanism is activated to bolster the longevity of brain cells. The implication of this discovery exposes the PTEN anti-cancer pathway for therapeutic manipulation. In a separate discovery, we have shown that the anti-cancer protein PTEN can be secreted by cells and be carried in micro vesicles for transport to other cells. The secreted PTEN can then be internalised by recipient cells for physiological benefit, for example, for slowing down the proliferation of cancerous cells. This discovery opens up new ways of administering anti-cancer PTEN for the control of brain tumours.

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Our mission is to translate discoveries from our laboratory to help patients with brain diseases. Our experiments make use of a variety of modern techniques to study how brain cells are able to resist death in a hostile environment. Our experiments are framed around hypotheses that may be answerable using novel tools developed by our team. These tools include creation of new mouse strains with insertions in gene sequences, molecular cloning of brain genes and manipulation of brain proteins. We have a democratic team structure, where every scientist including students and technicians all have an equal voice.

In order for brain cells in the adult brain to function properly, it is important that they are first found in the correct locations. Failure of brain cells to migrate to their destinations is a frequent cause of many developmental disorders such as autism and schizophrenia. For many years, our group has performed experiments to understand how brain cells are able to correctly migrate to their final positions.

Research highlights for 2014
We recently focussed on a class of brain cells called interneurones. Although they are in the minority, this class of neurones controls much of our mental processing and sensory experience. Therefore studying the behaviour of interneurones holds the key to understanding a number of developmental brain disorders. Previously, we showed that interneurones are capable of migrating vast distances to reach their final positions in highly specific addresses. Over the last year, we have been tracking the migration of these neurones, using genetic mice engineered to paint brain cells with artificial colours. This technology allows us to follow the movements of different interneurone classes under a laser microscope. The information from these studies allows us to pinpoint which types of interneurones are most at risk when something goes wrong. Our work has showed that different interneurones destined for different layers have separate rules for movement, dispelling previous notions that all interneurones behave alike.

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Brain trauma directs the survival protein PTEN into the cell nucleus to keep neurones alive. Work performed by Jason Howitt and published in Journal of Molecular Cell Biology shows that this process requires Ndfip1.

AN IDEA LIKELY TO CHANGE LIVES BY 2035
We are working on using natural body transport vesicles called exosomes. We have discovered a way to load useful proteins into exosomes to bolster the survival of neurones under stress following injury. These exosomes can also be loaded with anti-cancer proteins to treated brain cancer.

BRAIN DEVELOPMENT GROUP
Leader: Joanne Britto
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RESEARCH HIGHLIGHT
We have made some progress in understanding how the natural brain protein Ndfip1 is capable of improving the survival of brain cells in stress environments which occur in traumatic brain injury and stroke. We have shown that artificially increasing the concentrations of Ndfip1 in brain cells can protect against metal poisoning. We found that Ndfip1 concentrations in human post-mortem brains is strongly correlated with neurones affected by Parkinson’s disease. In animal models, we have shown that Ndfip1 is increased in surviving neurones after stroke. To study the consequences of removing Ndfip1 from neurones, we have deleted the Ndfip1 gene by mouse knockout technology. These animals demonstrate a greater sensitivity to brain damage from stroke, compared to normal animals that still carry the Ndfip1 gene.

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BRAIN SURVIVAL GROUP
Leader: Jason Howitt

When the brain is injured, such as in an accident or in stroke, the main area of the brain injury is not recoverable due to massive bleeding and swelling. However, what is not commonly known is that dying brain cells (called neurones) can transmit death signals from the injured area into surrounding healthy tissues, this ripple effect causes death of neighbouring brain cells in large numbers. Right now, there is no drug treatment to reduce the rate of brain death after trauma. Therefore medical strategies to prevent neurones from succumbing to trauma-induced death is an unmet need.

Research highlights for 2014

Our brain survival team has identified a survival protein in human brain cells called Ndfip1. This survival protein is present in human brains following road trauma, and Ndfipi1 is massively increased in surviving cells, indicating its role as a protective agent. Ndfip1 behaves like a bar-coding tool by putting a mark on harmful proteins that are produced during injury. These bar-coded harmful proteins are then recognised by the waste disposal system called ubiquitination in the neurone for removal.

This protein is also able to wake up a survival mechanism in brain cells using cancer pathways in neurones without causing tumours, taking advantage of the survival mechanisms that cancer cells are famous for.

We have also discovered that Ndfip1 is an important defender against metal accumulation in brain cells. This is important for degenerative brain diseases such as Parkinson’s and Alzheimer’s disease. We showed that post-mortem brains from Parkinson’s disease contain deficient levels of Ndfip1. This deficiency is associated with increased iron accumulation in diseased brain cells. This work opens up the manipulation of Ndfip1 as a way of controlling onset and progress of Parkinson’s disease.

BRAIN COMMUNICATION GROUP
Leader: Ulrich Putz

This group is interested in studying ways of using natural vesicles called exosomes to behave as cargo systems. This comes on top of our discovery that the anti-cancer protein PTEN is exported by cells in exosomes, and the anti-cancer protein can be transferred into other cells with anti-cancer consequences. This group is excited to use this technology to try and target anti-cancer protein PTEN into brain tumour cells to arrest the disease.

Research highlights for 2014

Over the last year, we have identified a peptide that can be used to coat exosomes so that they specifically recognise and target brain tumour cells. In cell culture experiments, we showed that brain tumour cells with mutations in the epidermal growth factor receptor are targeted by our engineered exosomes. Realising the need for accurate and effective delivery of exosomes, we have invested our resources to understand how to more effectively transfer exosomes into recipient cells. We have discovered that centrifugation using special conditions and special media can increase the uptake of exosomes by recipient cells.

EDITORIAL POSITIONS
SEONG-SENG TAN
- Experimental Neurology (USA)
- Journal of Anatomy (UK)
- Journal of Cell Biology (Korea)
- Frontiers in Neuroscience

MAJOR NATIONAL AND INTERNATIONAL CONFERENCES 2014

INVITED SPEAKER
- Asian-Pacific Society Neurochemistry, Kaohsiung, Taiwan, August 2014. “Role of Ndfip1 during brain development.”
- Brain Disorders Institute, Beijing Capital Medical University, Beijing, China, August 2014. “Potential use of PTEN for therapy in gliomas.”
- Japan Neuroscience Society Annual Meeting, Yokohama, September 2014. “How PTEN can save neurones from death following stroke and brain injury.”
- Invited Speaker, TEDx Brisbane, October 2014. “Why women have different brains.”

The process of discovery is the most exciting, intellectually stimulating and challenging of activities. The painstaking and arduous work culminates in the pleasure of finding something new that no-one has known or understood before.

When this is applied to medical research then there is the added reward that it may improve the lives and reduce the suffering of people with illness. I am determined to discover better treatments for schizophrenia and related disorders and develop markers to better diagnose and manage people with these illnesses.

Associate Professor Suresh Sundram, head, Molecular psychopharmacology laboratory and Northern Psychiatry Research Centre.
It’s no secret that funding for medical research is critically short. So it was a ‘dream come true’ when the Florey’s Dr Brad Turner spoke to a community group and unwittingly attracted the attention of a ‘scout’ who would radically change his future – and hopefully the lives of people living with motor neurone disease.

Dr Bradley Turner is renowned for his community outreach activities and his unflagging quest to cure motor neurone disease (MND). As the head of the Florey’s MND group, Brad was recently speaking to an Inner Wheel Club in Pakenham 70km south east of Melbourne.

Brad enthusiastically described his work to the group, outlining a project he believed promised great hope for a new treatment. This alerted Rotary Pakenham and a short time later, a phone call arrived from a trustee of a philanthropic foundation, recommending he submit a research proposal as quickly as possible.

A few days later, Brad was told he would receive $3 million over five years, thanks to the Stafford Fox Medical Research Foundation, a fund that does not accept requests but, rather, seeks worthy projects and invites applications.

“This could change the course of MND. Until now, I haven’t had the funding to achieve it. It is truly, utterly amazing,” Brad says.

It is a relentless disease, with nerves controlling movement (motor neurones) degenerating and rapidly wasting muscles. It strips away the independence of people living with it, who lose their ability to walk, feed themselves, talk and breathe. The average lifespan from diagnosis is 27 months.

So the need to find effective treatment is urgent, Brad says.

The grant will allow Brad and his team to fast-track some significant findings they made last year, using a specially devised tool – a gene therapy – to deliver the SMA gene to motor neurones in the brains of mice.

For the next phase of research, Brad and his team will collaborate with Flinders University scientists using a specially devised tool – a gene therapy – to deliver the SMA gene to motor neurones in the brains of mice.

Children born with the condition are missing a gene and become weak at six months and die within two years. Significantly, Brad found the gene was also missing in MND mice and in tissue from patients.

He experimented by putting the gene back in the MND mice – with dramatic results: the lifespan of the mice increased by two months. MND mice usually only live for four months. The process of replacing the gene also noticeably saved motor neurones.

“The sad thing about MND is that by the time people are diagnosed with it, 50 per cent of motor neurones are gone so that they are already at crisis point,” he says.

“We want to prolong a person’s lifespan and save their motor neurones – they are the two key objectives for an effective treatment.”

“Conventionally, a clinical trial can take 10 to 15 years to happen but in the case of MND it can be sooner due to accelerated approval and fast track status of promising drug candidates. Within five years we could potentially have something.”

Dr Bradley Turner

Brad says the MND patients he talks to are heartened by the findings and particularly by a graph showing the prolonged lifespan of the mice.

“When people are diagnosed with MND they know precisely what it is, they know the course it will take and that they often have no or little hope. Part of their hope comes from the knowledge that people in lab coats are beavering away working on their disease, passionately, and as a fulltime commitment – and that actually lifts their spirits.”

Brad will continue to share his work with the public – going out to speak to interest groups and hosting an annual “Ask the Expert” day when patients and their families hear talks and see demonstrations of lab techniques.

“They love it!” he says, “and they ask some impressive questions.”

The 36-year-old has researched MND for more than a decade and has succumbed to the Ice Bucket Challenge four times.

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Brad Turner has a strong ally. Ian Davis, a medico living with MND, is driving a highprofile campaign to raise awareness and funds for research into a cure for the disease.

Ian was in his early thirties, engaged to be married to his now wife Mel, and researching childhood leukaemia as a lab researcher when he was diagnosed with MND – but only after recognising the symptoms himself. Since then Ian has made the most of his limited time. He has been skydiving, has been on stage in a wheelchair with Paul Jam (his favourite band), and completed an epic tandem bike ride from Brisbane to Sydney, raising money for MND research.

Last year he and Mel became parents to baby Archie. Ian has inspired public figures including cricketer Shane Watson, Masterchef winner Julie Goodwin, and Australian Open champion Serena Williams to speak out about the cause and to donate to it. He says medical research into MND is “absolutely crucial” because there is so little that can be done for people living with the disease.

TO DONATE, PLEASE VISIT FLOREY.EDU.AU
The Division of Behavioural Neuroscience focuses on the use and development of animal models that reflect aspects of human disorders such as addiction, anxiety, depression, schizophrenia, autism and neurodegenerative conditions such as Huntington’s disease. The Cognitive Neuroscience group additionally studies addiction-related disorders caused by diseases such as stroke (cerebrovascular disease), Alzheimer’s disease and other neurological conditions.

**RESEARCH HIGHLIGHT**

There have been a number of highlights within the Division during 2014. A long-term collaboration between Professor Andrew Lawrence and Professor Alon Chen (Max Planck Institute, Munich) came to fruition with the finding that CRF1 receptors within the ventral tegmental area are critically implicated in both cue- and stress-induced relapse to cocaine-seeking. This study was performed predominantly by a PhD student, Nicola Chen, and published in the prestigious Journal of Neuroscience.

**A QUICK SNAPSHOT**

By 2035, dementia will be a rare and treatable disease. Patients admitted with stroke will receive dementia risk assessments and be treated with therapies that will recover all functions, including cognition. People at risk of Alzheimer’s disease will be identified via online testing or following a sentinel risk event, and treated prior to the development of brain atrophy.

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**RESEARCH OVERVIEW**

2014 saw the Division strengthened by the addition of a new laboratory heads: Dr Brodtmann and Dr Lawrence. In 2014, 2015 and 2016, 11 new NHMRC project grants were awarded, and with half of these grants already published, we are seeing a significant increase in our research output. The Cognitomics team, led by Dr Brodtmann, has been awarded an NHMRC project grant to continue these important studies.

**COGNITIVE NEUROSCIENCE**

**Leaders:** Professor Andrew Lawrence and Dr Amy Brodtmann

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**ADDITIONAL NEUROSCIENCE GROUP**

**Leader:** Andrew Lawrence

The Addiction Neuroscience Group studies how alcohol and other drugs change the brain’s chemistry, structure and function. During 2014 we made a number of important findings, many of which are still being actively pursued. As part of her PhD, Hanna Kastman continues to unravel the circuitry implicated in stress-induced relapse to alcohol-seeking. In addition, she has also demonstrated for the first time that the neuropeptide, relaxin-3, interacts with both oestradiol and CRF to regulate relapse-like behaviour. This project has been expanded with the recruitment of two new PhD students (Sarah Sullam, O’Ctig and Leigh Walker) plus an overseas placement student (Jan Koelaman). Together, these students are interrogating how and where in the brain the neuropeptide systems interact to regulate reward-seeking. In parallel to this, Nicola Chen (co-supervised by Professor Andrew Lawrence & Dr Lee Hyun Kim) showed that CRF receptors within the ventral tegmental area are critically implicated in both cue- and stress-induced relapse to cocaine-seeking. Her studies are now concentrating on aversive learning paradigms. In 2014 Professor Andrew Lawrence was awarded an NHMRC project grant to continue these important studies.

We also continued with our longstanding project on mGlu5 receptors. The process of behavioural extinction is a form of inhibitory learning that can help to protect against relapse. Dr Christina Perry and Ms Felicia Reid are currently assessing the role of mGlu5 signalling in the extinction of drug cues and contexts. This is potentially translatable by using mGlu5 positive modulators to enhance the rehabilitation of addicts undergoing behavioural therapy.

Another project involves examining the link between salt appetite and opiate addiction. In collaboration with Professors Derek Denton and Michael McKinley, we have shown that opiate receptor antagonists increase sodium intake and that opiate withdrawal can affect salt appetite. Our studies are now in the process of establishing whether this social regulation occurs. Professor Andrew Lawrence received an NHMRC project grant to pursue these studies.

**NEURAL PLASTICITY GROUP**

**Leader:** Anthony Hannan

Many neurological and psychiatric disorders, including schizophrenia and autism spectrum disorders (ASD), involve abnormal development of the brain. We are interested in the mechanisms whereby specific genes regulate maturation of the brain and are determining how these genes interact with the environment in conditions like ASD and schizophrenia.

Autism spectrum disorders affect approximately one per cent of children. Dr Emma Burrows has discovered abnormalities in social interaction and communication in a mouse model of ASD carrying a human gene mutation. Ongoing investigations focus on identifying key molecules and cellular changes involved in ASD and testing new therapeutic approaches in this model. With collaborators at the University of Melbourne, we have new evidence that both the central and peripheral nervous system is disrupted in these mice, contributing to a broad array of ASD symptoms.

Schizophrenia is another neurodevelopmental disorder involving a complex combination of genetic and environmental factors which disrupt normal maturation and function of the brain. Using a mouse model of schizophrenia, Dr Emma Burrows has shown that enhanced functional connectivity can ameliorate cognitive deficits and other behavioural symptoms and benefit specific areas of the brain. Identifying molecules modulated by environmental stimulation has paved the way for future development of new therapeutic approaches. Furthermore, Dr Burrows and graduate student Faith Lamont have been the first researchers in Australia to generate data using our new automated touchscreen tests (which are directly translatable to human neuropsychological test batteries). They have identified specific aspects of cognitive dysfunction and are testing a therapeutic intervention in this model of schizophrenia.

Huntington’s disease (HD) is an inherited single-gene abnormality that involves a trinucleotide repeat expansion of a gene that disrupts normal function and leads to death. Using a mouse model of HD, Dr Emma Burrows has shown that enhanced functional connectivity can ameliorate cognitive deficits and other behavioural symptoms and benefit specific areas of the brain. Identifying molecules modulated by environmental stimulation has paved the way for future development of new therapeutic approaches. Furthermore, Dr Burrows and graduate student Faith Lamont have been the first researchers in Australia to generate data using our new automated touchscreen tests (which are directly translatable to human neuropsychological test batteries). They have identified specific aspects of cognitive dysfunction and are testing a therapeutic intervention in this model of schizophrenia.
implications not only for HD, but for depression and dementia in the wider community. Further study of gene-environment interactions and experience-dependent changes in the nervous system may lead to new therapeutic approaches for HD and other brain disorders. Another PhD student, Dean Wright, with Dr Renoir and Melbourne collaborators, has discovered a new treatment for HD, and shown that it works via mitochondrial, the cell’s ‘batteries’ that provide energy. Furthermore, their findings have implications not only for HD, but depression in the wider community.

These findings contributed to an NHMRC Project Grant won by Professor Harvey and Dr Nithianantharajah in collaboration with the University of Melbourne. Furthermore, another new NHMRC Project Grant exploring the effects of paternal lifestyle on the mental health of offspring was won by Professor Hannah, Dr Pang and a collaborator from University of Queensland.

DEVELOPMENTAL PSYCHOBIOLOGY GROUP

Leader: Jeen Hyun Kim

Our vision is to understand the role of memory and forgetting across development in mental disorders, namely anxiety and substance abuse. We believe the key to finding effective treatments lies in how we remember and forget emotionally significant events formed at various stages of our development. A number of important discoveries have been made in 2014. Dr Despina Ganelia showed that disruption of the communication between brain regions during inhibitory learning can permanently reduce the strength of a fear memory, during adulthood. In collaboration with Melbourne Neuropsychiatry Center, she also showed in humans that childhood maltreatment was significantly associated with accelerated rate of growth in pituitary gland volume across adolescence in females but not males.

Dr Despina Ganelia and Dr Heather Madsen, with PhD students Isabel Zlikovic and Sophia Lukina demonstrated that the popular bipolar medication, Arispiprazole, can lead to changes in dopamine signaling in the prefrontal cortex, inhibiting learning in adolescent animals. This finding explains why Arispiprazole may enhance inhibitory learning and reduce relapse in anxiety and drug seeking. Dr Heather Madsen is using transgenic mice that show green florescence in dopamine receptor 1 (D1) or D2, and PhD student Isabel Zlikovic is measuring changes in D1/D2 mRNA profile across adolescence to understand the mechanisms behind adolescence vulnerability to anxiety and addiction.

Lastly, PhD student Nicola Chen discovered that reduction of corticotropin releasing factor 1 receptor in the ventral tegmental area leads to a stronger fear memory formation in mice, which suggests reductions in the stress signaling during learning may be beneficial.

INHALANT ABUSE LABORATORY

Dr Jhodie Duncan

The abuse of inhalational chemical vapours to produce self-intoxication is a significant concern, especially among adolescent and Indigenous populations. In 2014 Dr Jhodie Duncan and Dr Alc Dick published work demonstrating that exposure to inhalants during adolescence results in specific impairments in aspects of instrumental learning, without altering motor function or response timing. Our data suggest that exposure to inhalants affects corticostratal processes specifically and does not involve global toxicity to white matter pathways in the brain as was originally thought.

Using this model we have also shown that exposure to inhalants during adolescence results in long-term metabolic dysfunction. This includes altering dietary preference and glycemic control. This novel finding suggests that adolescent inhalant abuse may increase the risk of adult onset disorders such as diabetes and has significant implications for our understanding of the long-term consequences, especially in Indigenous populations where there is a high degree of overlap between inhalant abuse and nutrition related illness. The next step in our studies is to determine the underlying mechanisms, including both changes to central or peripheral mediated processes that drive the adverse outcomes observed in human abusers.

SYNAPSE BIOLOGY AND COGNITION GROUP

Jeen Nithianantharajah

2014 saw the addition of the Synapse Biology and Cognition laboratory to the Division of Behavioural Neuroscience led by Dr. Jeen Nithianantharajah, who was recruited back to Melbourne after six years in the UK (Cambridge and Edinburgh). Dr. Nithianantharajah was awarded a highly competitive Australian Research Council Future Fellowship in 2014, the only application out of 150 successful proposals awarded under the theme of Neuroscience.

Sensory information from the environment is ultimately processed at the level of synapses, the connection between neurons that form the most fundamental information-processing units in the nervous system. A central research focus of the lab is to understand the role of synaptic genes in cognition and disease. Vertebrate synapses contain a large yet intrinsically organised signalling complex of proteins encompassing neurotransmitter receptors, scaffold proteins and cell adhesion proteins. In recent years, human genetic studies have increasingly highlighted that disruption of over 200 genes encode postsynaptic proteins result in over 130 brain diseases. While it is accepted that postsynaptic proteins are fundamental for synaptic function, plasticity and thus behaviour, very little is actually known about the impact of postsynaptic gene mutations in regulating complex cognition and higher order processing.

Moreover, modelling the complex cognitive processes that are routinely assessed in the clinical setting has been challenging in animal models. Towards bridging the gap between mouse and human cognition, the lab is using novel behavioural paradigms to probe both genetic and experience-dependent changes in the nervous system of synaptic genes in cognition and disease.

Furthermore, their findings have implications not only for HD, but for depression and dementia in the wider community.

OTHER ACADEMIC INVITATIONS

Neuropsychiatry Neurobehavioural Meeting, Frontotemporal Dementia Update, Melbourne.

Public Lecture Flinders University.

FTD support group: Update from the International FTD Meeting, Vancouver.

OTHER ACADEMIC INVITATIONS

Neurology Trainee lectures: Frontal lobe syndromes; Memory and HFA.
ANTHONY HANNAN

EDITORIAL POSITIONS

- Instructor in Huntington's Disease, Associate Editor
- European Journal of Neuroscience, Scientific Review Associate
- CNS & Neurological Disorders - Drug Targets, Editorial board member
- Neuro Plastics, Editorial board member
- Neuroscience Letters, Associate Editor
- Frontiers in Pharmacology, Review Editor
- Neuroepidemiology, Editorial board member

MAJOR NATIONAL AND INTERNATIONAL CONFERENCES 2014

INVITED SPEAKER

- Integrative Center for Learning and Memory, Brain Research Institute, UCLA, USA.
- Invited Symposium Introduction and Discussant, Behavioral manipulation and alcohol misuse, 37th Annual Research Society on Alcoholism (RSA) Scientific Meeting and 17th Congress of the International Society for Behavioral Research on Alcoholism (ISBRA), Bellevue, Washington, USA.
- Invited Lecturer, European Molecular Biology (EMBL) PhD Course, ANU, Canberra.
- Invited Speaker, 12th International Conference on Cognitive Neuroscience (ICON) satellite meeting, 'Mission MMN Workshop', Newcastle.
- Symposium Speaker, 12th International Conference on Cognitive Neuroscience (ICON), Brisbane.

OTHER ACADEMIC INVITATIONS

- Member, National Committee for Brain and Mind, Australian Academy of Science.
- State Representative for Victoria and Tasmania, National Association of Research Fellows (NARF).
- Scientific Committee Member, 12th International Conference on Cognitive Neuroscience (ICCN).
- Scientific Committee Member, 5th International Congress on Neurology and Epidemiology (ICNE).
- Monash Clinical Imaging Neuroscience, Monash Biomedical Imaging, Monash University – invited lecture.
- Leaders in Science Seminar, Garvan Institute of Medical Research, Sydney.
- Stroke Division Seminar Series, Melbourne Brain Centre, Austin Campus.

JEE HYUN KIM

EDITORIAL POSITIONS

- Frontiers in Behavioral Neuroscience, Review Editor
- International Scholarly Research Network: Neuroscience, Associate Editor
- Neurotransmitter, Associate Editor
- Pharmacology Research & Perspectives, Associate Editor

MAJOR NATIONAL AND INTERNATIONAL CONFERENCES 2014

INVITED SPEAKER

- “Extinction of fear and drug-seeking during adolescence”. 37th Annual meeting of the Japan Neuroscience Society (JNS), Yokohama, Japan.

OTHER ACADEMIC INVITATIONS

- Department of Psychology, Korea University, Seoul, South Korea – invited lecture.
- RIKEN Brain Science Institute, Tokyo, Japan – invited lecture.
- Department of Psychology, Australian Catholic University, Melbourne, Australia – invited lecture.
- School of Medical Sciences, The University of Sydney, Sydney, Australia – invited lecture.
- Department of Cell Biology and Neuroscience, Sapienza University of Rome, Italy – invited lecture.
- Academy of Sciences of the Czech Republic, Prague, Czech Republic – invited lecture.
- 12th meeting of Asian-Pacific Society for Neurochemistry, Kaohsiung, Taiwan – Symposium Chair.
- International Society for Developmental Psychobiology – Board Member.

JHODIE DUNCAN

EDITORIAL POSITIONS

- Journal of Rett Syndrome Disorder, Associate Editor
- Brain Pathology, Editorial board member
- Neurochemical Research, Editorial board member

MAJOR NATIONAL AND INTERNATIONAL CONFERENCES 2014

INVITED SPEAKER

- “Gluon sniffing suck! The long-term consequences of inhaling abuse during adolescence on the brain and body.” Department of Pharmacology, The University Of Melbourne, Vic., Aust.
- “Why you can’t sniff sucks! The long-term consequences of inhaling abuse during adolescence on the brain and body.” Monash Institute of Medical Research - Prince Henry’s Institute, Vic., Aust.

JESS NITHIANANTHARAJAH

MAJOR NATIONAL AND INTERNATIONAL CONFERENCES 2014

INVITED SPEAKER

- International Conference on Cognitive Neuroscience (ICCN), Brisbane Australia (Chair of workshop).
- Evolution Symposium, Victorian Department of Environment and Primary Industries, Melbourne Australia.

EXTERNAL COLLABORATIONS FOR ADDICTION NEUROSCIENCE GROUP

Professor Alan Chen (Weizmann Institute, Israel), Professor Jian-Hsiang Lang (NEDD, Beijing, China), Professor Bernard Balkin (University of Sydney), Professor Peter Kalivas (MUSE, USA), Professor Rainer Spanagel (ZIMH, Germany), Professor Caroline Rae (UNSW), Professor Sarah Dunlop (UWA), Assoc. Prof. Peter Dold (UQ), Dr. Kevin Pfuger (UWA), Dr. Amir Raviv (Duke, USA), Prof. Madhava Rama (National Institute of Mental Health, Kohnoda, Japan), Dr. Tim Bredy (The Queensland Brain Institute), Dr. Zane Andrews (Monash), Prof. Dan Lubman (Turning Point / Monash), Prof. Michael Cowley (Monash), Prof. Danny Widder (Vanderbilt, USA).

EXTERNAL COLLABORATIONS FOR COGNITIVE NEUROSCIENCE GROUP

AMY BRODMANN

Dr Marina Boccard and Dr Giovanni Frisini, LENTIER, Fidenza/Salerno, Italy, IRCSS, Brescia, Italy, Dr Marco Catani, King’s College, London, UK, Dr Charles CoCarr, University of California Davis, USA, Professor Trish Desmond, Royal Melbourne Hospital, Dr Martin Diligens, Institute for Stroke and Dementia Research (ISD), Ludwig-Maximilians-University, Munich, Professor Vladimir Hachinski, Case Western University, London, Ontario, Canada, Professor John Hodges, FRONTIER, Sydney, Cambridge, Dr Tobias Losticher (Finders University, Adelaide), Professor tennis O’Brien, Royal Melbourne Hospital, Professor John Michell, Monash University.

DAVID DARBY

Professor Kai Nombe, Oxford University, UK, Dr Maize Silva Neto, Brasilia, Brazil.

EXTERNAL COLLABORATIONS FOR INHALANT ABUSE LABORATORY

Professor Andrew Lawrence (Flinders), Professor Bernard Balkin (University of Sydney), Professor Caroline Rae (UNSW), Prof. Maasa Faudana (National Institute of Mental Health, Kohnoda, Japan), Dr. Tim Bredy (The Queensland Brain Institute), Dr. Zane Andrews (Monash), Prof. Dan Lubman (Turning Point / Monash), Mr. David Weight and Dr. Leigh Johnston (Flinders and Monash, Vic.), Dr. Joseph Nicaliozo (Monash University), Dr. Michael Mathias (Vic. Uni), Dr. Sarah MacLean (Turning Point Alcohol and Drug Center, Melbourne), Dr Tobias Losticher (Finders University, Adelaide), Drs. Marianne Garland, Michael Myers, William F. Filer, and Raymond Stark (Primate Center and Departments of Pediatrics and Psychiatry, Columbia University College of Physicians and Surgeons, New York).

EXTERNAL COLLABORATIONS FOR DEVELOPMENTAL PSYCHOLOGY GROUP

Professor Steven Collins (The University of Melbourne); Professor Anthony Paciotto (RMIT); Professor Terry Speed (Walker and Eliza Hall Institute); Dr Scott Whitle (Melbourne Neuropsychiatry Center).

EXTERNAL COLLABORATIONS FOR SYNAPSE BIOLOGY AND COGNITION GROUP

Prof. Seth Grant (Edinburgh University), Dr. Noboru Kiyama (Edinburgh University), Prof. Timothy Boxer (Cambridge University), Dr. Lisa Sakaida (Cambridge University), Dr. Eran Kleinerman (Pratick Wild Centre), Edinburgh University), Dr. Mandy Johnston (Royal Edinburgh Hospital), Prof. Douglas Blackwood (Royal Edinburgh Hospital), Prof. Chris Pankau (Melbourne Neuropsychiatry), Prof. Arthur Christopoulos (Monash Institute of Pharmaceutical Sciences), Dr. Chris Langmead (Monash Institute of Pharmaceutical Sciences).

2014 STUDENTS:

PhD: Nicola Chon, Alc Dick, Rose Chessworth, Hanna Kastman, Andrew Walker, Danny Baker-Andrews, Isabel Zhukov, Sophia Lukinga, Christina Mo, Annabel Short, Dean Wright, Jake Rogers, Shiloh Yashurin, Sarah Sulaiman Ch’ng, Leigh Walker, Jarrod Srisrikulysakul, Fiona Bright (Adelaide), Rebecca Norris, Matthew Poole, Kirby Rogers, Karen Borschmann (primary supervisor Julius Bernhardt, MASTERS), Shae Teacher, Fatimah Lamont, Emma Glass, Felis Reid, Katherine Borschman, HONOURS, Rosa Haller.

Ashleigh Qama, Katherine Drummond, Johnny Park.
FOUR KEY WAYS TO IMPROVE YOUR BRAIN HEALTH

By Professor Anthony Hannan

It’s time we all focused more on this most important organ, to improve brain health throughout our lives.

FIRST: STAY PHYSICALLY ACTIVE

This is an obvious idea, however not everyone realises that physical activity is not only good for the body, it also boosts brain health.

There are many ways this could occur, as the brain and body are in constant, dynamic communication. Muscles release beneficial molecules that reach the brain, and exercise also stimulates the heart and other body systems which can beneficially impact the brain. Enhanced physical activity may stimulate the generation of new brain cells and connections.

Evidence is growing that such healthy lifestyle choices may help protect against Alzheimer’s, depression and other brain disorders.

SECOND: STAY MENTALLY ACTIVE

Two cardinal rules of brain plasticity are “use it or lose it” and “neurones that fire together wire together”. People who maintain higher levels of cognitive activity may, in fact, be protected from Alzheimer’s and other forms of dementia.

Cognitive stimulation may help build a “brain reserve” to protect from, and compensate for, the brain ageing. So what mentally stimulating activities could you do? Each individual will know what cognitively challenges and interests them and making positive lifestyle choices that can be maintained for months and years are more likely to lead to long-term benefits.

THIRD: EAT A HEALTHY DIET

Did you realise a balanced nutritious diet is good for your brain?

Most of the nutrients from food circulate through your brain via the bloodstream. So a healthy diet can directly improve the health of brain cells and may even slow down brain ageing.

What’s more, by improving body health, the brain may benefit via the heart and cardiovascular system, as well as the immune system, that impact on the nervous system.

FOURTH: DON’T STRESS TOO MUCH!

Seldom do we need the stress response (“fight or flight”) that protected cave dwellers thousands of years ago.

Excessive chronic stress may be toxic for the brain which is loaded with sensitive “stress receptors.” Stress-reducing strategies such as “mindfulness” and meditation are increasingly popular. Other lifestyle choices, such as a good diet, plenty of physical activity, as well as healthy sleep patterns, may also contribute to resilience.

TAKE-HOME MESSAGE

The phrase “mens sana in corpore sano” (a sound mind in a sound body) is thousands of years old, so the concept is clearly not new. The good news is that we can all do something to improve the health of our brains and bodies.

Each of us is dealt a genetic deck of cards at conception that we can do nothing about. Through development and adulthood, our genes interact constantly with environmental factors to regulate how our brains and bodies function, as well as dysfunction when they put us at risk of specific diseases.

With a positive mental attitude supporting a healthy lifestyle, we may be able to maintain soundness of body and mind for as long as possible. And hopefully, brain research at the Florey and elsewhere will deliver new treatments for devastating disorders such as Alzheimer’s disease and other forms of dementia.

The human brain is the most extraordinary and complex object in the known universe, a kilogram and a half of soft tissue that, at its peak, leaves computers behind with its endless capacity for problem solving, innovation and invention.

If the body is a “temple”, then surely the brain must be the “high altar” as it generates all of our thoughts, feelings and movements. Indeed, it is fundamental to all of our conscious experience.

Brain diseases such as Huntington’s, Alzheimer’s and other forms of dementia demonstrate how devastating it is when the brain degenerates, dragging the mind and its many wonderful capacities down with it.
EPILEPSY

Leaders: Professor Graeme Jackson and Professor Steve Petrou

A QUICK SNAPSHOT

The Florey Epilepsy Division is a world-leading centre for epilepsy research. The division has major groups at both the Florey's Austin and Parkville campus. The group studies mechanisms that cause epilepsy from cells to the function of the whole brain. We use technologies including advanced MRI and cutting edge cellular physiology techniques to allow us to understand genetic and acquired mechanisms that give rise to epilepsy. Together with our colleagues from The University of Melbourne and across Australia, we are working towards finding a cure for epilepsy.

RESEARCH HIGHLIGHTS

Our neuroimaging studies of epilepsy, including Lennox-Gastaut Syndrome, a particularly severe form of epilepsy, are helping to explain why epilepsy can be associated with intellectual disability. Abnormal electrical activity has been detected in the brains of patients with this syndrome. It occurs frequently, even when the patients are not having a seizure and the activity is widespread, involving many of the brain's major functional networks, and is therefore likely disrupting normal cognition. Yet in some patients with these symptoms we have located a small brain lesion. After surgical removal of the lesion, the widespread abnormal activity is eliminated and the patients are seizure-free.

AN IDEA LIKELY TO CHANGE LIVES BY 2035

We have shown that abnormal activity involving much of the brain can be triggered by a small focal brain lesion. We have also shown that if such a lesion can be found and surgically removed, seizures can be stopped. We will continue to help drive neuroimaging advances and we hope in coming years this will enable us to routinely locate all such lesions, providing many more epilepsy patients a surgical option to stop their seizures.

MAIN AREAS OF RESEARCH

- Epilepsy genetics
- Epilepsy imaging
- Human brain structure and function
- Functional modelling of gene mutations in epilepsy
- Multimodal imaging in epilepsy disease models
- Purinergic signalling

SENIOR STAFF

EPILEPSY IMAGING
- Professor Graeme Jackson (Division Head)
- Dr David Abbott
- Associate Professor Peter Brotchie
- Dr Patrick Carney
- Associate Professor Paul McCrory
- Dr Saul Mullen
- Professor Ingrid Scheffer

ION CHANNELS AND EPILEPSY LAB
- Professor Steve Petrou
- Dr Alison Clarke
- Dr Carol Milligan
- Dr Elena Gazina
- Dr Kay Richards
- Dr Robert Richardson
- Dr Verena Wimmer

SYNAPTIC PHYSIOLOGY
- Dr Christopher Reid
- Dr Marie Phillips

PURINERGIC SIGNALLING
- Dr Ben Gu
- Professor James Wiley

EPILEPSY – ION CHANNELS AND HUMAN DISEASE

Leader: Steve Petrou

Our research focuses on understanding the pathology of ion channel disorders, in particular epilepsy, using in vitro and in vivo models to reveal opportunities for developing novel therapeutics. We use a multidisciplinary approach spanning ion channel biophysics, mouse transgenesis, genetic analysis, computational modelling and in vitro and in vivo electrophysiology.

Research highlights for 2014

In 2014 we have accelerated our efforts towards delivering precision medicine outcomes in genetic epilepsy. We showed that quinidine, a drug related to the quinine of tonic water, is effective in controlling the function of an aberrant gene in a severe epilepsy. Subsequent clinical trials showed efficacy of this treatment paving the way for disease mechanism specific therapies – the backbone of precision medicine approaches.

We continue to seek to find markers of the disease state in epilepsy, from fundamental biophysical changes in ion channel function, to structure of neurons and brains studied with light microscopy and MRI. This year alone contributed to the characterisation of four different epilepsy genes.

These markers of the disease state are critical for accurate diagnosis, but even more importantly can be used to track the efficacy of new therapeutics emerging from our disease mechanism targeted drug programs. We have fully embraced state-of-the-art optical imaging approaches for structure and function of neurons to enhance our ability to tease out disease mechanisms.

NEUROIMAGING

Leader: Graeme Jackson

Research highlights for 2014

This group undertakes activities across both the Imaging Division and the Epilepsy Division and has published over 50 peer reviewed papers in 2014. This is a reflection of its origins as an advanced imaging centre with methods development and application to the problems of epilepsy. Through the use of cutting-edge MRI methods such as functional connectivity, tractography, simultaneous electroencephalography and functional MRI (EEG/fMRI) and advanced imaging, we continue to achieve greater understanding of epilepsy mechanisms. The new knowledge is rapidly translated to improved patient care through the Victorian Epilepsy Centre’s comprehensive epilepsy program at the Austin Hospital in Heidelberg, and through Epilepsy Melbourne, which integrates centres across University of Melbourne teaching hospitals.

This group is primarily based at the Austin campus of the Florey. Our basic work is to understand brain development and function, particularly the disturbances in distributed networks that underlie epileptic disorders. We are using EEG/fMRI, advanced diffusion techniques including tractography, functional connectivity and network analysis to investigate the underlying brain mechanisms responsible for the clinical symptoms. This is done in a translational environment that is immediately relevant to patient care.

In addition to the obvious symptomatology of epilepsy (i.e. seizures), cognition, memory and language disturbances are key cognitive areas affected by the disease. For example, we recently studied language in a group of patients with focal epilepsy, some with and some without reading difficulty, in an attempt to identify brain regions that may have disturbed function. We imaged the brain using functional MRI in the patients and also in healthy control subjects.

With the recent advances in genetics and technology it is now possible to devise and deliver therapies based specifically on the fundamental disease mechanism in individual patients.”
We discovered a functional abnormality in the left frontal region of the brain in patients with and without reading difficulties, and a further functional abnormality specific to the reading difficulty group localized to right temporo-occipital cortex—a region previously implicated in lexicosemantic processing (figure 3). Our observations suggest a failure of left hemisphere specialization among focal epilepsy patients with reading difficulties, perhaps arising from abnormalities in brain development.

The epilepsy imaging group is also developing new neuroimaging analysis methods to improve sensitivity to detect abnormal brain activity. For example, we have developed a novel processing method to remove unwanted noise from functional MRI data. The algorithm, called “SOCK”, is an objective and fully automated procedure. An example of its effectiveness in a simultaneous EEG-fMRI study of Rolandic epilepsy is shown in figure 4. SOCK increases power to detect real effects in functional neuroimaging, providing a more complete picture of the brain networks of interest.

Brain activity during performance of a language task (thinking of words beginning with a given letter). Three brain slices are shown for each subject group, with significant activity associated with the task overlaid in colour (increases in warm colours, decreases in blue). Top row: healthy controls. Second row: focal epilepsy patients without reading difficulty. Bottom row: focal epilepsy patients with reading difficulty. Relative to healthy controls, both patient groups showed reduced activation in left inferior frontal cortex. However the reading difficulty group also exhibited greater activation in the right temporo-occipital cortex (see dashed ellipse), indicating a failure of normal specialization to the left hemisphere in this region. Adapted from Tailby C, Warntoft DL, Saling MM, Fitzgerald C, Jackson GD. Reading difficulty is associated with failure to lateralise temporo-occipital function. Epilepsia. 2014;55(5):746-753.

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Epilepsy - Ion Channels and Human Disease

EDITORIAL POSITIONS
- Neurobiology of Disease
- PIDS Genetics

MAJOR NATIONAL AND INTERNATIONAL CONFERENCES 2014
- Mechanism of proton modulation of neuronal excitability.
  International Biophysics Congress, Brisbane, Australia.
- Functional correlates of severity in Alternating Hemiplegia of Childhood. 3rd International Meeting of the AHC in Amsterdam, September.
- Clear thinking in epilepsy: CLARITY imaging of short and long-range neuronal networks. Hertie Institute, University of Tübingen.
- Direct and emergent pathologies reveal therapeutic opportunities in BINPS and Draw. Hertie Institute, University of Tübingen.
- pH modulation of neuronal excitability in epilepsy. Hertie Institute, University of Tübingen.
- Translational opportunities in the genetic epilepsies: something old, something new, something borrowed, something blue. Aikenhead medical research week. St Vincent's Hospital.
- Precision therapeutics in epilepsy. Epilepsy Genetics in the Era of Precision Medicine, San Francisco, USA.
- Translational opportunities in the epileptic encephalopathies. Hertie Institute, University of Tübingen.
- Biophysical consequences of SCN2A pathology in Epileptic Encephalopathies. Epilepsy Research Retreat, Yarra Valley Lodge.
- University of Newcastle, NSW: September.
- Multi-modal approaches to understand brain functions. Interactive Brain Function Workshop, Monash University.
- Modulation of neuronal excitability in health and disease. Pathway Grant Retreat, University of Queensland.
- CLARITY imaging in genetic epilepsy models. Epilepsy retreat, Austin Hospital.
- Novel peptide therapy in Dravet Syndrome. Draw round table meeting, Seattle, USA.
- Challenges and opportunities in delivering precision therapies in genetic epilepsy. The Epfeel annual meeting, Seattle, USA.
- Challenges and opportunities in delivering precision therapies in genetic epilepsy. The Epfeel annual meeting, Seattle, USA.

Epilepsy - Neuroimaging

EDITORIAL POSITIONS
- Annals of Neurology - Ingrid Scheffer
- Epileptic Disorders - Ingrid Scheffer
- Frontiers in Neuroscience - David Abbott, Patrick Carney, David Vaughan, Graeme Jackson

MAJOR AND INTERNATIONAL CONFERENCES 2014
- Invited speaker: "Malformations of cortical development" Center for Integrative Brain Research Seattle Children's Research Institute, Seattle, 9th Dec, 2014.
- Plenary speaker: "From the bedside to the bench and back" 3rd annual National Health and Medical Research Symposium Parkville, Melbourne 18th November 2014.
- Chair: UCB Educational meeting: "Management of epilepsy in women across the life cycle": Sydney, 28th August 2014.
- Plenary lecture: "EEG-MRI in Epilepsy", EEG-MRI forum 21, Keil, Germany 8th June 2014.
- Keynote lecture: "Finding epilepsy networks in functional magnetic imaging of the human brain" and participation in the mathematics Study Group Workshop (SCGW 2014), Kyoto University, Fukui, Japan & University of Tokyo, Tokyo, 30th July – 5th August 2014.
- Presentation: "Age-related structural changes to the human visual pathway determined using in vivo clinical imaging techniques". Annual Meeting of the Association for Research in Vision and Ophthalmology (ARVO), Denver, Colorado, USA (May 3-7, 2015).
- Presentations: 14 Officer of the Order of Australia (AO)
- Prime Minister's Prize for Science
- Awarded for distinguished service to medicine as a clinician, academic, and mentor, and for her research identifying new epilepsy syndromes and genes.
- Prime Minister’s Prize for Science
- Most prestigious science prize in Australia
- Officer of the Order of Australia (AO)
- Awarded for distinguished service to medicine as a clinician, academic, and mentor, and for her research identifying new epilepsy syndromes and genes.
- Australian Academy of Science Fellowship (FAA)
- Elected as a Fellow for paradigm-shifting research into the genetic causes of epilepsy and defining new epilepsy syndromes.
- Founding Fellow and Vice-President of the Australian Academy of Health and Medical Sciences (FAHMS)
- Australian Academy of Health and Medical Sciences (FAHMS)
- Founding Fellow and Vice-President of the Australian Academy of Health and Medical Sciences (FAHMS)
- British Medical Research Foundation Medal
- In recognition of outstanding leadership and international contribution to medical research.

MAJOR AWARDS
The seminal contributions to epilepsy research of Professor Ingrid Scheffer continue to be recognised with several new awards bestowed in 2014:
- 2014 Prime Minister’s Prize for Science
- Most prestigious science prize in Australia
- 2014 Officer of the Order of Australia (AO)
- Awarded for distinguished service to medicine as a clinician, academic, and mentor, and for her research identifying new epilepsy syndromes and genes.
- 2014 Australian Academy of Science Fellowship (FAA)
- Elected as a Fellow for paradigm-shifting research into the genetic causes of epilepsy and defining new epilepsy syndromes.
- 2014 British Medical Research Foundation Medal
- In recognition of outstanding leadership and international contribution to medical research.

Interested in testing in epilepsy: the key to precision medicine”, Dravet Syndrome Foundation Annual Meeting, Seattle, USA, 6 December, 2014.

Interested in testing in epilepsy: where does the ketogenic diet sit in practice”, Global symposium for the dietary therapies for epilepsy and other neurological disorders, Liverpool, UK, 7-10 October 2014.

Invited Chair: “Translation to the clinic”, Epilepsy Genetics in the new era of Precision Medicine, San Francisco, US, 29-30 September 2014.


EXTERNAL COLLABORATIONS FOR EPILEPSY IMAGING GROUP
Ann & Robert H. Lurie Children’s Hospital of Chicago, USA, Austin Health, Melbourne, Boston Children’s Hospital & Harvard Medical School, Boston, USA, Centre Hospitalier Universitaire Vaudois (CHUV), Lausanne, Columbia University, NY, USA, Department of Molecular Genetics and Cytopathology, Women’s and Children’s Hospital, North Adelaide, South Australia, PostHilts Medical Centre, Canada, Harvard Medical School, Boston, USA, Hospital Dr. Erasme Malakas, Paris, INSERM, France, Monash University, Melbourne, Murdoch Children’s Research Institute, Melbourne, New York University School of Medicine, USA, Northwestern University Feinberg School of Medicine, USA, Royal Children’s Hospital, Melbourne, Royal Children’s Hospital for Sick Children, Melbourne, Royal Children’s Hospital for Sick Children, Great Ormond Street, London, UK, The University of Melbourne, The University of Queensland, University of Antwerp, Belgium, University of Bologna, Italy, University of Calgary, Canada, University of California, San Francisco, University of Otago, Wellington, New Zealand, University of Washington, Seattle, Walter and Eliza Hall Institute of Medical Research, Melbourne.
were not previously possible, thus enabling new scientific research. In 2014 has continued to progress over a wide range of MRI methods, including diffusion MRI, perfusion MRI, functional MRI, and high resolution structural MRI. Much of this work involves the application of up to date MRI acquisition and analysis methods to disease related neuroscience issues, while the work of the Advanced MRI Development Group is at the forefront of developing novel methods to facilitate neuroscience investigations that were previously not possible.

RESEARCH HIGHLIGHT

The Advanced MRI Development team is a world leader in diffusion MRI innovation, and the methodological advances made at the Florey are being applied increasingly worldwide to further our understanding of the healthy brain and how network connectivity is affected in disease. Such advances in technique will also have a major influence on human connectome investigations.

A QUICK SNAPSHOT

The Florey Imaging Division encompasses the following research groups: Advanced Magnetic Resonance Imaging (MRI) Development, Brainway Imaging, and Small Animal MRI. These groups perform neuroscience related MRI research across a wide range of MRI methods, including diffusion MRI, perfusion MRI, functional MRI, and high resolution structural MRI. Much of this work involves the application of up to date MRI acquisition and analysis methods to disease related neuroscience issues, while the work of the Advanced MRI Development Group is at the forefront of developing novel methods to facilitate neuroscience investigations that were previously not possible.

AN IDEA LIKELY TO CHANGE LIVES BY 2035

Understanding how structural connections relate to brain function is the subject of a major international program of research (the human ‘connectome’ project). The Florey’s methods development achievements will contribute significantly to this effort to move towards a more complete understanding of how the brain works, which has the potential to revolutionise human neuroscience.

We achieved major advances during 2014 in developing world-leading methods to visualise fibre tracts within the brain, and introduced novel approaches to identify abnormalities in the densities of white matter fibre connections in the brain in disease states including epilepsy and Alzheimer’s disease.

ADVANCED MRI DEVELOPMENT GROUP

Leader: Alan Connelly

Research highlights for 2014

Major breakthroughs were achieved in 2014 in establishing improved methods to visualise fibre tracts within the brain, including advances that enable diffusion MRI data from multi-shell and multi-tissue to be acquired and processed. The latter is part of an international collaboration and has allowed significantly improved white matter fibre tracking (particularly in cortical regions - see example images). Application of our novel analysis methods to mouse models (see example images) is enabling in particular the study of genetic based epilepsies in conjunction with colleagues in neurophysiology at the Florey.

Also, such methods have been used in another international collaboration to study cerebello-thalamic-cortical pathways in the human brain (see example images), enabling an improved understanding of the connectivity network between functionally important areas of the brain.

Advantages of multi-shell diffusion weighted MRI acquisition for visualising white matter fibre tracts within the brain. The images show sagittal visualisation of a fibre tractogram obtained from white matter fibre orientation distributions estimated with single-shell single-tissue constrained spherical deconvolution (SSST-CSD) (left column) and multi-shell multi-tissue CSD (MSMT-CSD) (right column). The lower image in each case shows an expanded image of the region indicated by the yellow box in each of the upper images. MSMT-CSD is shown to directly benefit fibre tracking. The increased precision and reduced number of spurious peaks in the fibre orientation distributions result in less noisy tractograms near the WM–IEF and WM–GM interfaces, with better defined fine structures. (This work represents a collaboration involving the Florey and the Universities of Antwerp and Leuven, Belgium)

The development of novel network analysis methods have allowed us to use cerebral blood flow (CBF) not only to identify functional brain networks but also to identify quantitatively the CBF associated with important highly connected ‘hubs’ in order to better characterise functional networks within the brain (see example images). Given that network abnormalities are increasingly believed to be associated with a number of important disease states, the latter information opens up potentially new areas of neuroscientific inquiry.

Software

The Advanced MRI Development Group has created and made publicly available a number of software packages that have enabled research groups worldwide to be able to implement and use the technical advances that have been developed at the Florey. These software packages have been extensively downloaded and are widely used throughout the research community.
ADVANCED MRI DEVELOPMENT GROUP

EDITORIAL POSITIONS

ALAN CONNELLY

Member Editorial Board of Epilepsia

MAJOR NATIONAL AND INTERNATIONAL CONFERENCES 2014

INVITED PRESENTATIONS


Alan Connolly - Diffusion MRI at ultra-high field strength. Ultra High Field MRI Symposium, Centre for Advanced Imaging, University of Queensland, Brisbane 2014.


COLLABORATIONS

In addition to a range of collaborations within the Florey, the Advanced MRI Development group has both national and international collaborations with a wide range of institutions, including:

- University College London
- Kings College London
- Stanford University, USA
- Karolinska Institute, Stockholm, Sweden
- Leiden University, Germany
- George Mason University, Washington DC
- Neuroscience Research Institute, Incheon, S Korea
- Max Planck Institute, Leipzig, Germany
- University of Antwerp, Belgium
- KU Leuven, Belgium

ANIMAL MRI

MAJOR NATIONAL AND INTERNATIONAL CONFERENCES 2014

INVITED PRESENTATIONS

- Leigh Johnston - Compressed Sensing for Mouse Imaging. Sick Kids Hospital, Toronto, 2014.

COLLABORATIONS

- CSIRO
- Monash ARMII
- Monash Institute of Medical Research
- Royal Women's Hospital
- University of Melbourne
- Neurological Institute of Radiological Science, Japan
- University of Freiburg, Germany
- University of Toronto, Canada

There are experienced groups doing it in Montreal, UCL in London and in Seattle but when I heard about Graeme Jackson and the team in Melbourne, it was an easy decision to come. They have been successfully using these methods to study epilepsy for about 15 years.”

“I want to uncover the complex changes in brain networks that enable seizures to start, as well as those networks that prevent seizures from happening. If we could understand how these brain networks behave in individual patients, we could better cater treatments for each of them.”

Contralateral cerebello-thalamo-cortical pathways: images show a 3 dimensional view of the average cerebellum-thalamo-cortical pathway across 15 subjects in MNI space. Cerebral (4), cerebellar (5) and deep grey matter (6) streamlines are overlaid to assist visualisation of cerebellar connections. A) Distribution of left (red) and right (blue) tracts in the cerebral cortex; the reconstructed tracts reach the prefrontal (yellow), frontal (fuchsia) and temporal (violet) cortices with greater density of streamlines. (b) Streamlines distribution in the cerebellar cortex; the lateral Crus I–II (fuchsia) and the lateral lobules VIII–VIII (green) are showing the greatest density of tracts. (c) Streamlines distribution of deep grey matter nuclei: the thalamus (violet), the caudate (light blue) and the putamen (fuchsia) show the greatest proportion of the overall tract grey matter belonging to specific cortical regions of interest. (This work represents a collaboration involving the Florey, University of Pavia (Italy) and UCL Institute of Neurology, London.)

Introducing

Dr Jennifer Walz has been with the Florey for a few months having completed her PhD in New York at Columbia University, specialising in biomedical engineering.

She brings a unique perspective of epilepsy to Graeme Jackson’s team of researchers. “I have deep insight from a patient’s perspective and as an engineer but until now, I haven’t had access to the clinical research side of the disease,” Jen says.

“The work I do involves simultaneous EEG and functional magnetic resonance imaging, which is a challenging and relatively new technique that most researchers still struggle to use.

Pictured: Dr Jennifer Walz.
A

ssociate Professors Suresh Sundram and Elizabeth Scarr are researching one of the toughest mental illnesses to treat: schizophrenia. They hope to develop blood tests to identify those with mental illnesses to treat: schizophrenia. They are trying to discover markers in the blood that identify people with schizophrenia who are at risk of suicide.

The brain bank is a huge resource – unparalleled in Australia – and the Florey also has access to technology platforms difficult to find elsewhere,” Suresh says.

Their investigations into a drug called clozapine are causing excitement. Clozapine, first synthesised in 1959, is an anti-psychotic drug used to treat the 30 to 40 per cent of people with schizophrenia who don’t respond to other anti-psychotic medication. It also markedly reduces the rate of suicide among this group.

But clozapine, while highly effective, has potentially fatal side effects, including agranulocytosis, which severely reduces white blood cells, so is used only as a last resort.

The drugs work by blocking receptors in the brain for several neurotransmitters including acetylcholine. Acetylcholine is thought to play a significant role in cognition – in learning, memory, understanding and in interpreting the outside world – factors that are profoundly changed in people with schizophrenia, Elizabeth explains.

The pair has investigated the neurotransmitter, and a receptor responsible for attracting it into cells, since 2000.

“Whatever you are developing, you always hope to go to market in a couple of years, but that’s not the case,” says Elizabeth.

These drugs have the potential to improve cognitive impairment, helping with memory, attention and planning, among other things.

Suresh and Elizabeth are currently exploring several new strands of research. They are trying to tease out the properties that make clozapine so effective and investigate how these could be used in other medications – without the harmful side effects. Such medication would improve the overall symptoms of schizophrenia, enhancing the individual’s quality of life, says Elizabeth.

The researchers are also using clozapine as a tool to try to discover what’s wrong with the brains of people with schizophrenia.

“The bottom line with psychiatric disorders is there’s no objective test that says ‘this means you have this or that disorder’,” says Suresh. “There’s no abnormality in blood tests or lesions in the brain that can point to a disorder,” he says.

“What that means is that we’re all essentially floating around in the dark trying to identify the pathology.”

“But now we’re shining a little flashlight!” says Elizabeth.

Using post-mortem brain tissue, they are trying to discover markers in the blood that identify people with schizophrenia who are at risk of suicide.

“If we can actually identify this abnormality when people first become sick with this disease, we can treat them better and potentially prevent them from killing themselves, which would be a sensational step forward.”

“We’re certainly hot on the lead of something we think is potentially important.”

Associate Professor Suresh Sundram

Blood tests might also identify the patients who are not going to respond to standard medications.

“If these people could be introduced to clozapine early in their illness then a lot of the complications we see – the homelessness, the loss of jobs and relationships, crime, the drug use – all those problems could be ameliorated,” says Suresh.

The tests may later be useful for patients living with bipolar disorder or depression.

Suresh says research, and the constant concerns about funding that go with it, can be a struggle and that scientific outcomes are always uncertain.

“But the findings we’re taking forward have very strong grounding,” he says. “For me, I look at the lives of these people and I’m going to keep on trying.”

I think that as a lab scientist you do get locked into your ivory tower, focusing on your little molecule of interest and you don’t have the opportunity to put it into context,” she says.

It is perhaps little wonder then that Elizabeth later teamed up with psychiatrist Suresh Sundram, who heads the Northern Psychiatry Research Centre and who is also a scientific researcher.

The pair, who have collaborated on projects since the late ’90s, are now working closely together at the Florey in a synergy they say gives them much greater capacity.

According to Suresh, 50 per cent of people with schizophrenia will attempt to commit suicide and 12 per cent will succeed. That’s fifteen times the general rate of suicide in the population.

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MENTAL HEALTH
Leader: Professor Colin Masters

A QUICK SNAPSHOT
The Mental Health division encompasses research into the aetiology (Alzheimer’s disease, Parkinson’s disease and other related conditions) and the psychoses (including schizophrenia and mood disorders). Research also extends into discovering biomarkers using longitudinal cohorts of volunteers who are prepared to be followed up over many years. This creates an environment rich in opportunities for drug discovery and development.

RESEARCH HIGHLIGHT

Why is one antipsychotic drug, clozapine, effective in people for whom other antipsychotic drugs are not? Our novel finding that clozapine activated the epidermal growth factor receptor (EGFR) system in the brain has led us to investigate if this system is dysregulated in people with psychotic disorders. From this we hope to gain insight into the pathology of psychotic disorders and develop more effective ways of treating them.

PEOPLE LIKELY TO CHANGE LIVES BY 2035

Professor Ashley Bush won the prestigious 2014 Victoria Prize for Science and Innovation in recognition of his outstanding contribution to translational neuroscience. He is the most cited scientist in Australia and is credited with discovering the importance of metals in degenerative diseases, particularly Alzheimer’s. He is actively working to develop improved disease-modifying drugs, as well as being a practising psychiatrist.

Professor Everall at the University of Melbourne, to form the Parkville Psychoses group. This grouping ensures we have a coordinated approach to understanding changes in gene expression that contribute to the onset of schizophrenia, bipolar disorder, major depressive disorder and suicide. Our approach is based on the understanding that clinically definable psychiatric disorders occur in people with a genetic predisposition who have encountered as yet unknown environmental factors. This interaction between genes and environment is then known to affect gene expression by a variety of epigenetic mechanisms. As psychiatric disorders primarily affect the human CNS we have a strong focus on studying gene expression in the CNS of people with psychiatric disorders and those who have died by suicide. On identifying changes in gene expression we then use an array of animal and cellular models to better understand the mechanisms that have brought about such a change in expression in the human CNS.

Clinical research unit (DIAN and A4)
Translation of our research findings into clinical practice will become more important over the next five years, as we move from a series of failed or equivocal phase 3 drug trials sponsored by the pharmaceutical industry. There is now general agreement that these drug trials need to be based at the earliest possible stage of Alzheimer’s disease, hence our participation in the Dominantly Inherited Alzheimer Network (DIAN) and the Anti-Amyloid Treatment in Asymptomatic Alzheimer’s disease (the A4 study). These two pre-clinical trials are designed to administer drugs in the preclinical phases of both familial and sporadic Alzheimer’s disease. They are being coordinated by Dr Manees Mastyk and Ms Lesley Vidaure and are currently recruiting.

THE NEHRG program in neurodegenerative disease
Also involves collaborators at the University of Melbourne: Prof Andrew Hill (Biochemistry and Molecular Biology), Prof Roberto Cappai (Pathology), Prof Steven Collins (Pathology) and Prof Anthony White (Pathology).

MOLECULAR PSYCHIATRY GROUP
Leader: Brian Dean
Our group seeks to identify new changes in gene expression that contribute to the onset of schizophrenia, bipolar disorder, major depressive disorder and suicide. Our approach is based on the understanding that clinically definable psychiatric disorders occur in people with a genetic predisposition who have encountered as yet unknown environmental factors. This interaction between genes and environment is then known to affect gene expression by a variety of epigenetic mechanisms. As psychiatric disorders primarily affect the human CNS we have a strong focus on studying gene expression in the CNS of people with psychiatric disorders and those who have died by suicide. On identifying changes in gene expression we then use an array of animal and cellular models to better understand the mechanisms that have brought about such a change in expression in the human CNS.

Unlike some neurodegenerative disorders, some drugs have been developed that can be used to treat the symptoms in some people with psychiatric disorders, albeit with varying success. Therefore our group also seeks to understand the mechanisms of action of such drugs, which in the main remain obscure.

The major goal of the group, through the study of the pathophysiology of psychiatric disorders and suicide, as well as the mechanisms of action of psychiatric drugs, is to generate new ideas that may lead to new potential drug targets that will either improve outcomes in currently treatment responsive treatment and/or lead to the development of drugs that will be effective in currently treatment resistant people.

Importantly, our group has formed a seamless collaboration with the psychiatric neuropathology laboratory headed by Associate Professor Elizabeth Scar and with the laboratory of Professor Ian Everall, both at the University of Melbourne, to form the Parkville Psychoses group. This group aims to develop a coordinated approach to understanding changes in gene expression in human can cause psychiatric disorders.

MOLECULAR PSYCHOPHARMACOLOGY AND NORTHERN PSYCHIATRY RESEARCH CENTRE
Leader: Suresh Sundram
The Molecular Psychopharmacology laboratory is dedicated to understanding the molecular pathology of psychiatric disorders such as schizophrenia, bipolar disorder and major depression. It aims to develop better and more effective markers and interventions for these illnesses. We do this by investigating how psychotropic
medications and drugs interact with receptors and intracellular signaling mechanisms in nerve cells (neurons).

The understanding gained from this work can then be tested in clinical populations through the Northern Psychiatry Research Centre (NPRC) leading to the development of new treatments and markers. Moreover, the NPRC can collect clinical material and biological samples that can be examined in the laboratory to better understand these disorders.

CLINICAL RESEARCH GROUP
Leader: Dr Alan Rombach (until November 20, 2014) and Dr Christopher Fowler

The Clinical Research Group (CRG) collects research data and stores biospecimens from human participants involved in neurodegeneration and healthy aging studies.

The multi-disciplinary team includes biomarker researchers, neuropsychologists, research nurses, neuro imaging specialists and bioinformaticians.

The group is currently involved in:
- Australian Imaging, Biomarkers and Lifestyle (AIBL) Flagship Study of Ageing;
- AIBL Active (exercise intervention trial);
- the CRC for Mental Health;
- the Dementia Collaborative Research Centre (DCRC) - Early Risk Diagnosis and Prevention;
- the Dominantly Inherited Alzheimer’s Network’s (DIAN) study;
- the Rates of Change in Cognition (ROCS) study;
- the Older Australian Twin Study (OATS);
- the Woman’s Healthy Aging Project (WHAP);
- the A4 study.

Translation of our research findings into clinical practice will become more important over the next five years, as we move from a series of failed or equivocal phase III drug trials sponsored by the pharmaceutical industry.

There is now general agreement that these drug trials need to be based at the earliest possible stage of Alzheimer’s disease, hence our participation in the Dominantly Inherited Alzheimer Network (DIAN) and the Anti-Amyloid Treatment in Asymptomatic Alzheimer’s disease (the A4 study). These two pre-clinical trials are designed to administer drugs in the preclinical phases of both familial and sporadic Alzheimer’s disease.

NORTHERN PSYCHIATRY RESEARCH CENTRE

PERSONNEL AND COLLABORATIONS
- Head: Associate Professor Sudhir Sundaram MBBS, MMed, FRANZCP, PhD
- Senior research physician: Dr Russell D’Souza MPM, MD
- Research coordinator: Fiona Bole RN
- Research nurses: Sumathy Sathiyamoorthy RN (Div II)
- Research physicians: Dr Rohit Lodhi MD, MRCPsych, FRANZCP and Dr Manish Sharma MD
- PhD student: Jody Stanley
- Postgraduate students: Daniel Bennett and Amy Dzuzniak
- Advanced medical sciences (AMS) student: Zexi Allan

COLLABORATIONS
- Professor Michael Berk (The University of Melbourne)
- Dr Olivia Carter (The University of Melbourne)
- Dr Gursh Chana (The University of Melbourne)
- Dr Peter Conach (The University of Melbourne)
- Professor Brian Dean (Mental Health Research Institute)
- Dr Swati Dodd (The University of Melbourne)
- Professor Ian Ewal (The University of Melbourne)
- Dr John Farhall (La Trobe University)
- Ms Marine Grasso (Northern Hospital)
- Professor Brenda Haddad (Central Queensland University)
- Ms Alison Harrington (Northern Area Mental Health Service)
- Dr Alexander Holmes (The University of Melbourne)
- Dr Ana Hutchinson (Northern Clinical Research Centre)
- Dr Nigel Jones (The University of Melbourne)
- A/Professor Gerard Kennedy (Victoria University)
- Dr Ken McAnulty (Defence Science Technology Organization)
- Professor Ralph Martin (Edith Cowan University)
- Professor Terence O’Brien (The University of Melbourne)
- Dr Meaghan O’Donnell (The University of Melbourne)
- Dr Elizabeth Sear (The University of Melbourne)
- Dr Elizabeth Thomas (Scripps Institute, USA)
- Professor Cynthia Shannon-Weickert (Neurosciences Australia)
- Dr Anthony White (The University of Melbourne)

2014 was another productive year for the partnership between the Clinical Discovery Unit and the IMPACT Strategic Research Centre at Deakin University. The quality and quantity of our research output continues to grow with 145 (plus potentially more to be added) publications in 2014 including a number of high impact publications in the top journals in the field, including Molecular Psychiatry, Lancet Psychiatry, The American Journal of Psychiatry and The British Journal of Psychiatry.

A QUICK SNAPSHOT

The unit is supported by a number of funding bodies. These include a NHMRC senior principal research fellowship, three NHMRC project grants, NHMRC Targeted Call for Research grant, NHMRC CRE, CRC grant, one NIH R34 grant, two Stanley Medical Research Institute grants; a Simons Autism Foundation grant, two Rotary Health Grants and a National Natural Science Foundation of China grant.

RESEARCH HIGHLIGHTS

The principal research focus of the unit is the discovery and implementation of novel therapies. The enduring partnership between the Florey and the IMPACT Strategic research centre continues actively. Following on our early projects showing the efficacy of N-acetyl cysteine in schizophrenia and bipolar disorder, we have recently published two studies showing the efficacy of N-acetyl cysteine in depression, as well as in smoking cessation. A large number of follow-on studies of N-acetyl cysteine are planned and will be submitted to the current NHMRC funding round. Together with the CRC for Mental Health we continue to leverage the new understanding that bipolar disorder is associated with fundamental dysregulation in mitochondrial energy generation. We are completing a first-in-kind study of mitochondrial agents in the treatment of bipolar depression. In all of these studies, we aim to look at biomarker mediation and moderation to explore target engagement. This approach is concordant with the NIH mandated RDoC philosophy.

The SRC continues to develop strong collaborative links with health service providers including: Barwon Health research centres within Deakin including PRADA, Centre for Molecular and Medical Research, Centre for Mental Health and Wellbeing, Centre for Science, Engineering and Built Environment and Deakin Population Health; and multiple international partners in countries including the US, Brazil, Denmark, Portugal, Canada, Thailand, Spain and China. We would like to thank Deakin University and Barwon Health for their continuing support.
The Psychotropic Drug Advisory Service (PDAS) is an independent source for information on medicines used to treat mental illnesses and other drugs that affect the way we think, feel and behave. Service users include public mental health services, individuals, medical practitioners, health care professionals, mental health care support organisations and their staff, carers and consumers. Though predominantly telephone based, the service is also accessed via email and facsimile. The service responds to approximately 2000 enquiries each year. Associate Professor Suresh Sundram heads the unit and provides clinical support to pharmacist Christine Culhane who manages the service. We would like to take the opportunity to thank Professor Nicholas Keks for his long involvement as head of the unit and as an ongoing clinical support. Funding is provided by the Department of Human Services Victoria, Mental Health Division and is auspiced to the Mental Health Research Institute.

PRESENTATIONS

Presentations to both professional and consumer groups are also part of the work undertaken by the service. Presentations have been requested by and provided to a number of professional and lay audiences. Christine has ongoing involvement with The Delmont Hospital Psychopharmacology Master classes with Professor Nicholas Keks and Dr. Judy Hope. These forums are held twice each year to update the knowledge of practicing psychiatrists and trainees. Tutorials and online discussions for undergraduate and post graduate pharmacists have also been provided. Christine has also been to a number of carer and consumer support organisations to provide information on medications in a patient sensitive forum.

PROFESSIONAL DEVELOPMENT

The Psychotropic Drug Advisory Services provides a much needed source of specialised information to the broader mental health community in Victoria. Its value is measured by consistency of enquiry numbers and timeliness of responses. In order to provide the best available information, professional development activities are undertaken including the requirements for continued registration as a pharmacist as well as attending psychiatry and pharmacy specific congresses and symposia.

HIGHLIGHTS

Each year many people, young and old, are diagnosed with a mental illness. For some, psychosocial interventions adequately control their symptoms. Others will require biological treatments which include medications. Many do not fully understand the implications of the treatments or their role in managing their disorder despite the provision of this information by their prescriber or other healthcare professionals. Others wonder about what to expect from their medication: their benefits, side effects and the possibility of interactions with other medications they may be taking. This service provides a forum for discussion of prescribed medication that is timely and tailored to the needs of the caller. People have the opportunity to talk about their medication concerns in a confidential setting and receive current information. This is also an important service for carers of people with a mental illness who are concerned about the effects of these drugs on the person with the illness. The service can answer the questions of carers regarding the potential benefits of medications, adverse effects, safety and tolerability and possible interactions with other medications. Enquiries from the general public are nearly half of those recorded by the service. A range of health care professionals also utilise this service: psychiatrists, other medical practitioners, health care professionals including nurses, pharmacists, psychologists and dentists, as well as researchers. Electronic databases allow many professionals to research some of their own queries making their calls to PDAS when the clinical situation is complex or to gain extra insights when there are new medications or other complications involved. The provision of this information to service providers allows them to best manage the changing needs of their clients. This service also provides vital information for practitioners and consumers who reside or practice in rural or remote communities as they may not have the immediate resources to provide this extra information.

The Victorian Brain Bank Network collects, processes and stores post-mortem human brains and related samples from individuals who have had neurological diseases (e.g. Alzheimer’s disease, motor neurone disease and Parkinson’s disease), psychiatric disorders (e.g. bipolar mood disorder, depression and schizophrenia) as well as normal control cases. We facilitate research into the study of brain diseases by providing tissue to researchers who aim to unlock our understanding of how brain diseases occur. This will lead to improvements in diagnosis, early diagnostic tests, therapeutic interventions and ways to prevent brain disease. We provide a vital and unique neuropathological diagnostic service that confirms a ante-mortem clinical diagnosis, increases clinicians’ awareness and understanding of atypical presentations of certain brain diseases, confirms a diagnosis for donor families, in whom neurological disease may have hereditary or familial association and may be at risk of developing the disease, generates pathological description of brain diseases and advances knowledge of some brain pathologies, thus providing a powerful tool for education and research and importantly, this service is relied on for the validation of research studies.

We would like to acknowledge the generosity shown by the donor and donor families in donating tissue to the brain bank. It is an act of great foresight and kindness to give at a time of loss, so that others may be helped in the future. The clinicians and researchers who benefit from these donations are very grateful to the donors and their families who support them in these decisions. We would like to acknowledge the support of the following funeral directors: Bethel, Jensen, Allison Monkhouse, Fink, Nelson Brothers, Tobin Brothers and WD Rose & Joseph Allison who provide metropolitan transfers for tissue retrieval at no cost to the brain bank.

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Multiple Sclerosis is the commonest neurodegenerative disease affecting young adults in our community. It is a complex disease, characterised by disrupted interactions between the immune and nervous system, resulting in the demyelination and loss of nerve cells. Our division focuses on novel ways to manipulate immune activation and to protect the nervous system to limit this damage as well as to develop new ways to repair damage.

A major highlight of our work in 2014 was the discovery by Dr Toby Merson and his team that different types of nervous system precursor cells remyelinate the brain in different ways in response to a demyelinating insult. This result indicates that it is now critically important to interrogate the functional consequences of these differences and therefore how the differences influence the extent of recovery and to determine how these differences can be exploited for therapeutic benefit.

We aim to identify and use novel treatments to prevent patients from developing progressive multiple sclerosis.

Our work has identified novel ways to reduce the burden of MS by either protecting the nervous system from damage or by promoting its repair.

Dr Holly Cate • Dr Simon Murray • Dr Junhua Xiao

Dr Scott Kelbie • A/Prof Helmut Budkaunen

Dr Tomas Kilianik • A/Prof Olivia White •

A QUICK SNAPSHOT

Multiple sclerosis has a variable course, with outcomes ranging from negligible to severe disability. Both the cause of the disease and the determinants of disease severity remain uncertain. The MS division, with strong collaborative interaction extending into the University of Melbourne and the Royal Melbourne Hospital, is adopting a multifaceted approach to researching the disease. Our approach focuses on understanding the genetic determinants and molecular drivers of MS. Our laboratory work has provided novel and important insights into how to promote nervous system repair, in particular remyelination; this understanding has been assisted via our research that has focussed on how myelinating cells and their precursors behave during both development and in the healthy adult, as well as in disease. Our work has also provided important insights into how the immune cells in the brain interact with the myelinating cells during disease, thereby identifying approaches that have therapeutic potential.

We continue to focus on how our preclinical work can be translated into the clinical environment for it to directly benefit people with MS. With this in mind, we continue to collaborate actively with colleagues throughout Australia to interrogate the genetics, epidemiology and pathogenesis of MS, in this way clarifying that our laboratory results are directly pertinent to the human disease. During 2014 we have also developed a collaborative interaction with the Monash Institute of Pharmaceutical Sciences in order to scope the feasibility of developing therapeutic approaches targeting the activity of key molecular drivers of demyelinating disease that we have identified. Our collaborative work focusing on patients at the Royal Melbourne and Box Hill hospitals has also allowed us to develop new paradigms by which to assess the severity of the disease, which includes approaches focusing on imaging, eye movements and novel biomarkers in blood. These developments are important preambles to approaches that will ultimately focus on assessing the efficacy of new treatment paradigms involving either neuroprotection or remyelination.

A RESEARCH HIGHLIGHT

Multiple sclerosis is a chronic and progressive neurodegenerative disease with a great impact on the quality of life of the affected individuals. The disease is characterised by demyelination and axonal damage leading to functional impairment and disability. While the disease is characterized by a variable course, the majority of patients present with a relapsing-remitting form of the disease.

The therapeutic strategy for the treatment of multiple sclerosis (MS) remains largely symptomatic. Treatments are largely focused on the reduction of new lesion formation and reduction of relapses. However, the advent of secondary progressive MS makes it evident that there is a need for new therapeutic strategies focusing on remyelination. Our laboratory has focused on developing therapeutic strategies focusing on remyelination.

Research conducted by PhD student Philipp Röth has further clarified the mechanisms underlying the generation and organisation of oligodendrocytes in white matter. Developmental analyses have revealed that postnatal myelination is preceded by the emergence of linear array of oligodendrocytes whose cell bodies align with the axis of nerve fibre tracts. In these tracts, we have shown that postnatal oligodendrocytes are generated from neural progenitor cells (NPCs) that migrate to the target area and differentiate into oligodendrocytes. Our work has also provided important insights into how the immune cells in the brain interact with the myelinating cells during disease, thereby identifying approaches that have therapeutic potential.

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of the activated transcription factor to the genome, thus identifying the genes that it targets to promote myelination. These findings were published in the prestigious journal Plos Biology, back-to-back with the complementary findings of another group. Another 2014 highlight was a collaboration with Prof Bill Richardson’s laboratory at University College London, who have used our mice as a tool to demonstrate that ongoing myelination in the adult brain is required for types of motor learning (published in Science). Our current research is focussing on trying to understand how to stimulate both the expression and activity of Myrf to promote myelin repair in human diseases.

**NEUROIMMUNOLOGY GROUP**

**Leader:** Trevor Kilpatrick, Michele Binder and Judith Field

We continue to study an important set of three receptors (the TAM family) that is expressed on both immune cells and oligodendrocytes in the brain and which influence both the susceptibility to and the severity of demyelinating disease. We are currently exploring how these receptors and their ligands influence cellular behaviour in order to both limit the extent of demyelination and enhance the capacity for remyelination.

Research highlights for 2014

We recently published the finding that Myrf is a novel example of a membrane-associated transcription factor, require a clearance event to free it from the membrane and enable it to function as a transcription factor. Using ChIP-Seq techniques we were able to map the binding of the activated transcription factor to the genome, thus identifying the genes that it targets to promote myelination. These findings were published in the prestigious journal Plos Biology. Our prior research in this area identified that animals deficient in one of the TAM ligands (Gas6) exhibit worse disease when demyelination within the nervous system is induced.

Work currently being undertaken by PhD students, Gerry Ma and Rainer Akkermann is exploring how this occurs; in particular, whether TAMs exert their beneficial effects by influencing immune cell activation in the periphery or within the central nervous system, and which of the three receptors is predominantly responsible for exerting each of these effects. We have found that one of these receptors influences cells that are critical regulators of antigen presentation and, in consequence that it is an important regulator of autoimmune inflammatory demyelination. A second receptor in this family has been shown to directly influence the capacity of oligodendrocytes to myelinate neurons. We have shown that the expression of one of the key ligands of these receptors is suppressed in a subset of patients with multiple sclerosis and that it could serve as a severity marker of the disease. We are currently also exploring strategies that involve modulation of TAM receptor activity to determine whether this might be a viable strategy to limit disease severity.

**MS GENETICS GROUP**

**Leader:** Judith Field

Dr Judith Field and colleagues continue to focus on key genes that have recently been implicated in the susceptibility to multiple sclerosis. Particular areas of interest include understanding how these genes function, whether perturbations in particular genes might define subsets of people with MS and whether these or other genes are also important determinants of disease severity. In 2014 the work has also extended, in collaboration with Dr Andrew Fox, to establishment of ways to identify the signatures of gene methylation that are expressed by particular subsets of immune cells isolated from whole blood which are key determinants of molecular expression and to determine how these signatures are influenced by MS.

Research highlights for 2014

Research into the genetic contribution to the development of MS within the Multiple Sclerosis Division continues in collaboration with the ANZGene Consortium. Our work also continues to refine the genetic risk association within the TAM receptor gene MERTK, and also the role that the TAM genes play in demyelinating disease. Importantly, the genetic changes in MERTK that lead to increased risk of developing MS have also been shown to influence the level of the MERK gene in key immune cells in the blood.

This work has allowed us to identify gene expression and protein expression changes of potential functional significance, including the CD40 costimulatory molecule, which is expressed on both lymphocytes and monocytes as well as their progeny and which is likely to be key to the pathogenesis of MS.

Promotion of myelination in cell culture. Dorsal root ganglion neurons were isolated from one day-old Sprague-Dawley rats and cultured for 14-21 days. Oligodendrocyte precursor cells were then isolated from 5-day-old C57BL/6 mice and grown on top of the neurons for 14 days to allow these cells to differentiate into mature oligodendrocytes and produce myelin sheaths that wrap the axons of the neurons. The cells were fixed and subsequently stained for Myelin Basic Protein (red) and Neurofilament (green) to highlight the myelin sheaths and axons, respectively.

**OLIGODENDROCYTE BIOLOGY AND NEURONAL-GLIAL INTERACTIONS GROUP**

**EDITORIAL POSITIONS**


**MAJOR NATIONAL AND INTERNATIONAL CONFERENCES 2014**

**PRESENTER**

- Merloni TD. “The role of remyelination in progressive MS”. 7th Congress of the Pan-Asian Committee for Treatment and Research in Multiple Sclerosis (PACTRIMS). Nov 6-8, 2014, Taipei, Taiwan. (Invited platform presentation)
- Merloni TD. “Stem Cells in Multiple Sclerosis and Neurological Disease”. MS Research Australia/NSW Stem Cell Networking workshop, May 28, 2014, Sydney, NSW. (Invited oral presentation)
- Xing YL, Rith PT, Stratton JAS, Ellis SL, Chuang BHA, Ng SW, Kilpatrick TJ and Marson TD. “Myelin regeneration by precursor cells in the adult central nervous system” ComBio Meeting, 28th Sept – 2nd Oct 2014, Canberra, Australia. (Invited symposium presentation)
- Xing YL, Rith PT, Stratton JAS, Chuang BHA, Ng SW, Kilpatrick TJ, Merloni TD. “Adult neural precursor cells from the subventricular zone contribute significantly to oligodendrocyte regeneration and remyelination”. 34th Annual Meeting of the Australian Neuroimmunology Society, 28th-31st January 2014, Adelaide, Australia. (Invited symposium presentation)
- Merloni TD, Chuang BHA, Kilpatrick TJ, Rith PT. “Cellular dynamics underlying the generation of linear arrays of oligodendrocytes in CNS white matter”. 44th Annual Meeting of the Society for Neuroimmunology, 15th-19th November 2014, Washington, DC, USA. (Poster presentation)
- Xing YL, Rith PT, Stratton JAS, Ellis SL, Chuang BHA, Ng SW, Kilpatrick TJ, Marson TD. “Neural precursor cells osteomorphogenic oligodendrocyte precursor cells to remyelinate broad regions of the rostral corpus callosum” Ola in Health & Disease - Cold Spring Harbor Laboratory, July 17-21, 2014, New York, USA. (Selected for oral presentation)
- Rith PT, Stratton JAS, Xing YL, Chuang BHA, Kilpatrick TJ, Marson TD. “The cellular mechanisms underlying the generation of oligodendrocyte linear arrays in white matter”. 9th FENS Forum of Neuroscience, July 5-9, 2014, Milan, Italy. (Poster presentation).

**COLLABORATIONS**

- Assoc Prof Helmut Butzkueven, Department of Medicine, University of Melbourne.
- Assoc Prof David Booth, University of Sydney.
- Prof Jim Wiley, Florey Institute of Neuroscience and Mental Health.
- ANZGene Consortium.
- The International Multiple Sclerosis Genetics Consortium.
- Phil Hodgkin, The Walter and Eliza Hall Institute of Medical Research.

**NEUROIMMUNOLOGY GROUP**

**EDITORIAL POSITIONS**

- Therapeutic Advances in Neurological Disorders (International Journal) (2008-)
- Experimental Neurology (International Journal) (2011-)

**MAJOR NATIONAL AND INTERNATIONAL CONFERENCES 2014**

- TREvor KilpatRiCK

  - Invited speaker at the 11th World Congress of the Society for Brain Mapping and Therapeutics, 2014, Sydney, March 2014.
  - Invited speaker at the endMS Research and Training Network, Alberta, Canada, April 2014.
  - Invited speaker at Department of Clinical Neurosciences, University of Calgary, Canada, April 2014.
  - Invited speaker at 20th Stem Cell Network Workshop, “Stem Cells in Multiple Sclerosis and Neurological Disease”, Sydney, May 2014.
  - Invited keynote speaker at the University of Queensland, Advanced Imaging in MS Meeting, Brisbane June 2014.
  - Invited speaker at the Neuropsychiatric Diseases Symposium 2014, Monash Institute of Pharmaceutical Sciences, Monash University, Melbourne, August 2014.
  - Invited speaker at John Curtin School of Medical Research Seminar Series, ANU, October 2014.
  - Invited Chair of MS Genetics’ session at PACTRIMS Taiwan, November 2014.

**COLLABORATIONS**

- Greg Lemke, The Salk Institute for Biological Studies.

**MS GENETICS GROUP**

**COLLABORATIONS**

- Assoc Prof Helmut Butzkueven, Department of Medicine, University of Melbourne.
- Assoc Prof David Booth, University of Sydney.
- Prof Jim Wiley, Florey Institute of Neuroscience and Mental Health.
- ANZGene Consortium.
- The International Multiple Sclerosis Genetics Consortium.
- Phil Hodgkin, The Walter and Eliza Hall Institute of Medical Research.
"I’m driven by a lifelong curiosity to understand how the nervous system works. Designing experiments to uncover the brain’s hidden mechanisms is a gratifyingly creative process. Then there’s the thrill of seeing your hypothesis finally come to light. Sometimes months of work culminate in the blazing reality of seeing something down the microscope for the first time. This always brings a sense of excitement and anticipation. Sometimes this stirs delight, sometimes surprise and, at other times, angst. Sharing this process of discovery with a team of likeminded students and colleagues is wonderfully motivating. I consider it a great privilege to be able to make this my career."

Dr Tobias Merson
Lab Head, Multiple Sclerosis Division.
Scientists in the Neurodegeneration division interrogate how neurons live, die and can be rescued to improve brain function in degenerative conditions such as Parkinson’s and Motor Neuron Disease. There is no effective treatment for Motor Neuron Disease (MND) and the incidence of Parkinson’s disease (PD) is rising alarmingly in our aging community. Gene abnormalities, energy deprivation, toxic rubbish accumulation and inflammation all contribute to a toxic environment for brain cells. Our teams study these events in animal models and cultured cells, with a view to translating knowledge into new therapies for human patients.

RESEARCH HIGHLIGHT

Neurodegeneration

The brain contains much more than neurones and injury is followed by an inflammatory response that involves a population of glial cells, astrocytes, which proliferate locally and becoming reactive. This process is defensive and subsequently the astrocytic response supports repair and reconstruction of circuits. Persistence of astrocytes in the “defensive” mode, often called glial scarring, limiting functional recovery. Scientists in our team have exciting signposts on how astrocytes can be persuaded to adopt a healthy phenotype supportive of the regenerative phase. Mature astrocytes maintained on injury models. The ultimate goal is a safe, bio-injectable scaffold to prevent untoward glial scarring and to promote regeneration.

Highlights for 2014

Lachlan Thompson and Clare Parish continue to advance their impressive work on stem cell-based therapies for brain repair and recently have been investigating the capacity of neurones generated from human stem cells to survive and integrate after transplantation into the stroke-damaged brain. Not only do these neurones survive, but they are capable of an extensive degree of growth, including the re-formation of long-distance pathways related to motor circuitry. Furthermore, the stem cell grafts also protect the host brain against the progressive degeneration that can result from an acute injury such as stroke. Thus the therapeutic strategy of stem cell grafting may have a neuro-protective benefit in addition to regenerative value by replacing pathways lost in injury.

Brain plasticity remains a topic of great interest and Tim Aumann and his team have continued their work on the plasticity of neurones and its relevance to the human brain. They have recently analysed adult human brains of people who died in mid-summer (long days) or mid-winter (short days) and found four times more dopamine neurones in summer than winter in the human midbrain. Clearly the adult human brain is more adaptable than previously thought, and our environment can alter the amount of dopamine in our brains.

These findings support their hypothesis that the number of neurones exhibiting a particular neurochemistry is changing constantly depending upon our environment. Environmental enrichment works in many animal models of human neuropathology, so this new insight supports efforts to understand how neuronal chemistry can be manipulated to benefit function in various disorders, including Parkinson’s disease.

Sex hormones such as oestrogens and androgens also exert local effects by modulating neuronal function and Wah Chin Boon has shown the key enzyme, aromatase, is discretely localized in limbic brain regions involved in overt behaviours. Malcolm Horne continues his traditional success with the Parkinson’s Kinetigraph system for measuring the motor symptoms, and disorders of sleep and impulse control in Parkinson’s disease. This development is now in routine clinical use in some 40 major Parkinson’s centres in Europe, Asia and Australia.

Dysfunctional energetics happens in most brain pathologies, and Brad Turner’s laboratory has unique insights into energetic stress occurring early in motor neurones of genetic mouse models of motor neurone disease (MND). An important energy sensing kinase called AMPK is abnormal. Importantly, blocking an enzyme that controls AMPK activation called PTPA can restore AMPK function in cells. This evidence suggests that therapeutic targeting of PP2A and AMPK could help correct defective energy metabolism in MND. Intracellular debris, be it damaged molecules, organelles or toxic aggregates, accumulates in all neurones during stress. Autophagy has a key mechanism for debris removal, is a key focus in the laboratory of Philip Beart. The focus is not only on its fundamental mechanistic aspects, but also on its therapeutic potential. Philip Beart, Brad Turner and Malcolm Horne, in a wide-ranging collaboration with interstate and international colleagues, are currently harnessing autophagy to combat motor neurone pathology in mouse models to evaluate its therapeutic potential in MND. This wide-ranging study has also revealed activation of various components of the brain’s inflammatory response in both astrocytes and microglia.

Molecular Neuropharmacology Group

Leader: Phil Beart

Pathological mechanisms affecting neurones and astrocytes, which have an interdependent relationship, essential to brain health, are the focus of our laboratory. Diverse experimental approaches provide insights into how new strategies may be targeted to rescue threatened neurones and to establish a supportive environment near an injury zone.

Aging or injured neurones accumulate damaged molecules and aggregates which affect their function. This process is termed autophagy (“self-eating”) and represents one of the cellular rubbish removal mechanisms. If the load becomes too extreme or if the autophagic mechanisms become compromised, the process can become a form of programmed cell death. Most research into the controlling mechanisms has been performed in non-mammalian cells, so our work in primary neurones is groundbreaking. Damaged mitochondria also enter the autophagic cascade through a process termed mitophagy. We have found that disturbed energy generation causes mitochondria to lose their membrane potential with a concomitant drop in ATP production and entry into mitophagy. Since disturbed energetics underpins various forms of neurodegeneration, we believe that this cascade contributes to many degenerative conditions. We are currently investigating autophagy in other brain injury models.

Over many years our team has studied the neurobiology of astrocytes and made impressive advances in defining “good” or “bad” responses which relate to the state of inflammation in brain pathologies. By culturing mature astrocytes in 3D on bio scaffolds, we find a hormetic (dose dependent) increase in glial scarring, increased G-actin, glutamate transport, brain-derived trophic factor (BDNF) and anti-oxidant activity. These “signposts” guide current studies where a novel and potentially superimposable mouse has shown promise in minimising inflammation in studies performed in cultured astrocytes and in vivo in a model of traumatic brain injury. The ultimate goal is a safe, bio-injective scaffold to prevent untreated glial scarring and to promote regeneration.

Molecular Neuropharmacology Group

Leader: Tim Aumann

In 2014 we furthered our research into plasticity of adult midbrain dopaminergic neurones. We had earlier shown that the number of these cells increases or decreases following drug administration and environmental stimulation in adult mice. New work with post-mortem human brains of people who died in mid-summer (long days) or mid-winter (short days) shows there are appreciably more dopamine neurones in summer than winter in the human midbrain. The adult human brain is far more adaptable than previously thought, and given that dopamine is a “feel good” chemical, this might explain why our mood is elevated during summer. Environmental stimulation offers a unique way of keeping our brain healthy.

Our research has identified the putative “infectious particle” in MND, and we have imaged for the first time microscopic particles released by motor neurones, called exosomes, which may be responsible for intercellular spread of misfolded, toxic proteins in MND. Importantly, blocking these particles with antibodies halts the spread of misfolded proteins between cells, raising hope that this approach could potentially halt MND in its tracks.

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Neurodegeneration Group

Leader: Tim Aumann

In 2014 we furthered our research into plasticity of adult midbrain dopaminergic neurones. We had earlier shown that the number of these cells increases or decreases following drug administration and environmental stimulation in adult mice. This year we compiled the first evidence that this might occur also in the adult human brain. To test this we obtained human brains from the Edinburgh Brain Bank in Scotland of people who died in mid-summer (long days) or mid-winter (short days). Research from our collaborators overseas had shown that adult rats exposed to long days have fewer hypothalamic dopaminergic neurones than those exposed to short days, and we thought this might extend to midbrain in humans (although the other way around because rats are nocturnal and humans diurnal). Indeed we did find there were four times more dopamine neurones in summer than winter in the human midbrain. This indicates that the adult human brain is far more adaptable than previously thought, and that our environment can alter the amount of dopamine in our human brains of people who died in mid-summer (long days) or mid-winter (short days) we had earlier shown that the number of these cells increases or decreases following drug administration and environmental stimulation. Summer. Environmental stimulation offers a unique way of keeping our brain healthy.

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Regenerative therapies for brain and spinal cord repair are a key focus of our efforts. We share the view that success in this area will be closely aligned with a deeper understanding of the complex processes that underlie brain development. Our particular interests involve the molecular mechanisms that trigger neurogenesis as well as neuritic outgrowth and connectivity in the developing brain. Our goal is to adapt key concepts in this area to the development of stem cell-based therapies for brain repair; a central focus is the generation of midbrain dopamine neurones from pluripotent stem cells for use in transplantation-based procedures for Parkinson’s disease. We are also working on similar approaches for other neurological conditions including MND and Huntington’s disease. In the stroke-damaged brain we have found these neurones are capable of an extensive degree of growth, including the re-formation of long-distance pathways related to motor circuitry. In addition to transplantation-based strategies, we are also exploring other novel avenues for brain repair including the use of viral vectors to deliver trophic factors that can protect neurones from injury or even promote ‘self-repair’ from the brain’s own stem cells.

The Parish laboratory has also developed a successful programme in neural engineering. The team is developing and testing bioengineered scaffolds with recent success focusing on GDNF tethered to a biocraft, which holds significant potential to enhance brain repair.

Figure 1: Cartoon illustrating the various sources of stem cells and their potential application in Parkinson’s disease. Stem cells, differentiated into dopaminergic progenitors, can be used for transplantation, in vitro modeling of the disease, screening compound libraries in the identification of new drug targets and development. Alternatively, it is the potential to stimulation of quiescent stem cell populations in the adult brain to promote self-repair.

MOTOR NEUROGENESIS

Leader: Claire Parish

The Parish laboratory has a broad interest in repairing the injured brain and places a strong emphasis on understanding neural development, with the idea that repairing the injured brain will require recapitulation of these early events. Major research themes running within the laboratory include: understanding the neural development (notably wnt signalling), directed differentiation of pluripotent stem cells, molecular mechanisms underlying axial targeting and synaptogenesis and improving cell-replacement therapy for neural injuries. While historically the major focus of the group has been on understanding dopamine development and developing cell replacement therapies for Parkinson’s, more recently the team has expanded its interests to apply similar approaches to Huntington’s disease and stroke. Much of this work is done in close collaboration with the laboratory of Dr Lachlan Thompson, based at the Florey Institute.

There are more dopamine neurones in the human midbrain in summer than in winter. Shown are sections through the human midbrain (at two different locations; rostral and caudal) that have been processed to colour dopamine neurones black (using two different markers of dopamine neurones: tyrosine hydroxylase (TH) and dopamine transporter (DAT). The 1st and 3rd rows are low-power images in summer and winter, respectively, and the 2nd and 4th rows are high-power images of the areas outlined in rows 1 and 3, respectively. Note the many more black ‘dopamine neurones’ in summer compared with winter. All ∆ = dopaminergic group; A8 ∆ = dopaminergic group A8; cp = cerebral peduncle; DBC = decussation of the brachium complexum; M = medial dopaminergic group; Mv = medioventral dopaminergic group; RN = red nucleus; SNc = substantia nigra pars compacta.

STEROID NEUROPATHOLOGY GROUP

Leader: Phil Beart

Steroid hormones such as oestrogens and androgens (e.g. testosterone) affect human behaviour. Oestrogens are produced in the brain from androgens (e.g. testosterone) that are converted to oestrogens by the enzyme aromatase, neuronal functions and provide neuroprotection. The conversion of androgens to oestrogens from androgens is catalysed by the enzyme aromatase, neurones. Furthermore, we noticed that oestrogen receptors are of many brain regions under normal physiological conditions, and oestrogens from androgens is catalysed by the enzyme aromatase, pathways related to motor circuitry. In addition to transplantation-based strategies, we are also exploring other novel avenues for brain repair including the use of viral vectors to deliver trophic factors that can protect neurones from injury or even promote ‘self-repair’ from the brain’s own stem cells.

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NEUROGENESIS AND NEURAL TRANSPLANTATION GROUP

Leader: Lachlan Thompson

Regenerative therapies for brain and spinal cord repair are a key focus of our efforts. We share the view that success in this area will be closely aligned with a deeper understanding of the complex processes that underlie brain development. Our particular interests involve the molecular mechanisms that trigger neurogenesis as well as neuritic outgrowth and connectivity in the developing brain. Our goal is to adapt key concepts in this area to the development of stem cell-based therapies for brain repair; a central focus is the generation of midbrain dopamine neurones from pluripotent stem cells for use in transplantation-based procedures for Parkinson’s disease. We are also working on similar approaches for other neurological conditions including MND and Huntington’s disease. In the stroke-damaged brain we have found these neurones are capable of an extensive degree of growth, including the re-formation of long-distance pathways related to motor circuitry. In addition to transplantation-based strategies, we are also exploring other novel avenues for brain repair including the use of viral vectors to deliver trophic factors that can protect neurones from injury or even promote ‘self-repair’ from the brain’s own stem cells.

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DRUG TARGETS IN SIGHT

Diseases including Alzheimer’s, Parkinson’s disease, and epilepsy in the firing line.

N March 2011, Daniel Scott was working on what he describes as a risky line of research - new technologies in receptor engineering.

If successful, his plan was to solve a big problem in modern drug discovery - the instability of membrane proteins - and to enable the design of vital new medications.

“In general, diseases are caused when the natural signalling networks such as hormones or neurotransmitters become corrupted. Drugs are then prescribed to act on receptors and restore the signalling balance,” Daniel explains.

One way to do this is to analyse the molecular structure of the target receptors and design drugs that can “fit” into the target. But most receptors are very unstable and “fall apart” during the experiments needed to perform “structure-based drug design”.

Daniel, who was researching in a renowned protein-engineering laboratory at the University of Zurich, Switzerland, had already spent three-and-a-half years trying to solve this problem and had started to worry about whether his ideas would work.

The project was using a molecular biology technique called “directed evolution” to select receptor genes that exhibited enhanced stability, cycling them through evolutionary rounds until the receptors were very stable.

His supervisor liked the idea for the new technology but had doubts. Daniel’s wife Melissa was expecting their first child.

“The challenge is to discover drugs that can modulate specific receptors associated with this aberrant signalling in disease without disrupting normal signals and causing side effects.”

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“I was starting to stress out because I’d taken a big risk to go to Switzerland and was doing this crazy work. I thought that as a family we had to start thinking about stability,” he says.

But then the breakthrough came. Daniel’s son Hamish was born and the research results were validated soon after. “At last I could relax and enjoy Hamish,” he says.

Daniel returned to the Florey in late 2011 with his innovative technology, CHESS, or Cellular High-throughput Encapsulation Solubilisation and Screening, which allows researchers to engineer very stable receptors for drug discovery.

CHESS had been patented, and publication of Daniel’s work in 2012 received international recognition.

The Florey is only one of two places in the world using CHESS.

Daniel has used the technology to stabilise several G protein-coupled receptors (GPCR) that are key drug targets for central nervous system disorders.

Some of these GPCRs are currently untargeted by drugs.

His work has attracted two prestigious awards – the Australasian Society of Clinical and Experimental Pharmacologists and Toxicologists (ASCEPT) Denis Wade Johnson & Johnson New Investigator Award, and the BPS/ASCEPT Outstanding Young Investigator Prize.

Daniel’s next challenge is to work with others at the Florey to mass-produce these engineered receptors, for which he needs new equipment.

“We hope that by opening new avenues to GPCR drug discovery, our technology will ultimately lead to new drugs to help people living with diseases such as Alzheimer’s disease, Parkinson’s disease, epilepsy and schizophrenia.”

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The Neuropeptide Division primarily conducts multi-disciplinary studies on the role of neuropeptides in the control of complex behaviours including arousal, stress, mood, motivation and reward, and associated memory processes, under normal and pathophysiological conditions. These studies are coupled with fundamental drug discovery research on both these physiological and disease states. These studies are coupled with fundamental drug discovery research on both these neurobiology of the peptide transmitter, relaxin-3. We and others have demonstrated that relaxin-3 and its neural receptor RXFP3 modulate the activity of nucleus incertus neurones in adult rats using viral vector-delivered ‘designer’ receptors (DREADDs) and observed strong effects on brain activity (EEG, physiology, stress-induced cardiovascular responses) and behaviour (locomotor activity, spatial memory). This research has been assisted by the development of advanced software for the automated analysis of EEG and EMG activities. Planned studies will help us model similar changes that occur in stress- and trauma-induced clinical anxiety and mood disorders. Ongoing studies will also better define the projections of nucleus incertus neurones into key brain areas and their effects on brain activity and behaviour.

These and related studies will continue in 2015 with ongoing support from NHMRC (Australia), Brain & Behavior Research Foundation (USA), Australian Alzheimer’s Australia Dementia Research Foundation and The University of Melbourne.

Other research highlights include:

- Dr Sharon Ma, a senior research officer, undertook a four-month Commonwealth Endeavour Fellowship at the Department of Neurobiology, University of California, Berkeley, USA, where she trained in the use of optogenetics to dissect neural pathways and their effects on behaviour.

**NEUROPEPTIDE RECEPTOR GROUP**

**Leader: Ross Bathgate**

The Neuropeptide receptor laboratory studies G protein-coupled receptors (GPCRs) which represent the most important class of biomolecules for pharmaceutical development, being targeted by ~30 per cent of current drugs. Our studies on the structure and function of novel neuropeptide GPCRs will enable the development of new drugs to specifically target neurological and other diseases.

**Research highlights for 2014**

Studies by the group continue to demonstrate the unique mechanism by which the hormone relaxin binds to and activates its receptor, RXFP3. Two recent publications (one in the prestigious journal of Biological Chemistry) have furthered our understanding of the mechanism of interaction between relaxin and RXFP1 to enable the design of new drugs. Relaxin was recently demonstrated to be an effective treatment for acute heart failure in Phase III clinical trials and will soon be used clinically to treat this disease. However, the patients must be treated by continuous intravenous infusion of relaxin which is not an ideal method to deliver the drug. Studies by our group, which are concentrating on determining the precise mode of interaction of relaxin with RXFP3, will lead to the development of smaller drugs that can be taken orally for the treatment of heart failure and other diseases.

**PEPTIDE NEUROBIOLOGY GROUP**

**Leader: Andrew Gundlach**

Dementia and psychiatric illnesses remain major clinical, scientific, societal, and economic problems. A better understanding of how the brain controls physiology and behaviour and how this becomes dysregulated in disease is currently required. Basic research studies are therefore needed to identify new structural and molecular neural targets that may form the basis of novel therapeutic approaches in the future. In this regard, our laboratory conducts ‘systems neuroscience’ research and a primary interest is to understand the role of neuropeptide signalling in the control of complex behaviours including arousal, stress-induced motivation and reward, and associated memory processes, under normal and pathophysiological conditions. We conduct experimental studies in animal models of normal physiology and psychiatric disorders, using a range of biomolecular tools including receptor-selective peptides, ‘viral-vector’ delivered designer receptors, and a range of transgenic mouse strains.

**Research highlights for 2014**

Since its discovery at the Florey in 2002, we have been studying the neurobiology of the peptide transmitter, relaxin-3. We and others have demonstrated that relaxin-3 and its neural receptor RXFP3 appear to play a role in anxiety, cognition, motivation, and the modalities in rodents that are commonly aberrant in humans suffering from interactions with specific brain serotonin systems. These findings improve our understanding of state-dependent, modulating the INSL5 axis presents a new strategy for the treatment of acute heart failure by the Swiss Pharmaceutical Company Novartis. A Phase IIIb trial is ongoing and the relaxin drug, serelaxin, has been approved in Russia to treat patients with acute heart failure. Hence fundamental research on the mechanism of action of a hormone, in the case of relaxin pioneered at the Florey by the former Neuropeptides Division Head, Prof Geoffrey Trogan, can ultimately lead to its use to treat disease in patients.

**A QUICK SNAPSHOT**

- Expertise is obtained by ‘systems neuroscience’ analysis, using sophisticated optogenetic and pharmacogenetic manipulation of neural circuits and advanced complementary methods to record their impact. Combined with a greater knowledge of brain peptide and hormone neuroendocrine systems, these studies will allow the improved design of drugs that target ‘receptor states’ or ‘receptor combinations’ present in specific brain regions/circuits under pathological conditions.

**SENIOR STAFF**

- **Professor Ross Bathgate**
- **Associate Professor Andrew Gundlach**
- **Dr Muhammad Aliker Hussain**
- **Dr Daniel Scott**
- **Professor John Wade**

**POWERFUL INSIGHTS INTO HOW THE BRAIN CONTROLS BEHAVIOUR**

Powerful insights into how the brain controls behaviour can be obtained by ‘systems neuroscience’ analysis, using sophisticated optogenetic and pharmacogenetic manipulation of neural circuits and advanced complementary methods to record their impact. Combined with a greater knowledge of brain peptide and hormone neuroendocrine systems, these studies will allow the improved design of drugs that target ‘receptor states’ or ‘receptor combinations’ present in specific brain regions/circuits under pathological conditions.

We received four NHMRC project grants for our researchers during 2014, in a very competitive funding environment, and two key publications in the prestigious journal, the Proceedings of the National Academy of Sciences USA (see details below).

Together with collaborators at Cambridge University and the pharmaceutical company Takeda Cambridge, we identified insulin-like peptide 5 (INSL5) as a product of colonic endocrine L-cells, and demonstrated that INSL5 levels were elevated in calorie-restricted mice and reduced after feeding. Consistent with this profile, INSL5 administration were elevated in calorie-restricted mice and reduced after feeding. Consistent with this profile, INSL5 administration stimulated food intake in mice, making it only the second demonstrated that relaxin-3 and its neural receptor RXFP3 modulate the activity of nucleus incertus neurones in adult rats using viral vector-delivered ‘designer’ receptors (DREADDs) and observed strong effects on brain activity (EEG, physiology, stress-induced cardiovascular responses) and behaviour (locomotor activity, spatial memory). This research has been assisted by the development of advanced software for the automated analysis of EEG and EMG activities. Planned studies will help us model similar changes that occur in stress- and trauma-induced clinical anxiety and mood disorders. Ongoing studies will also better define the projections of nucleus incertus neurones into key brain areas and their effects on brain activity and behaviour.

These and related studies will continue in 2015 with ongoing support from NHMRC (Australia), Brain & Behavior Research Foundation (USA), Australian Alzheimer’s Australia Dementia Research Foundation and The University of Melbourne. Other research highlights include:

- Dr Sharon Ma, a senior research officer, undertook a four-month Commonwealth Endeavour Fellowship at the Department of Neurobiology, University of California, Berkeley, USA, where she trained in the use of optogenetics to dissect neural pathways and their effects on behaviour.
Insulin is one of the most clinically important peptide drugs on the market. It still represents the only treatment for diabetes (particularly for type 1). There are seven other insulin-like peptides (also called insulin family of peptides): H1, H2 and H3 relaxins, INSIL1, 4, 5 and 6 which have similar structures to insulin (2 chains, 3 disulfide bonds), but have a diverse range of physiological functions. H3 relaxin is the most studied peptide in our laboratory and has recently passed phase III clinical trials for the treatment of acute heart failure.

**MEMBRANE PROTEIN ENGINEERING GROUP**

**Leader: Daniel Scott**

Protein instability poses a major barrier to the characterisation and deployment of many proteins into industrial and biotechnological applications. Membrane proteins are a class of proteins that are particularly unstable, yet are highly important as they are the main targets for most prescription drugs. Membrane proteins are located on the surface of all types of cells and are involved in processes such as sensing neurotransmitters, driving neural impulses and responding to drug treatment. The instability of membrane proteins, however, makes them difficult to study. We use novel technology (CHESS) to engineer stabilised membrane proteins, particularly neuropeptide-binding G protein-coupled receptors (GPCRs), to aid in elucidating the atomic level mechanisms that govern their function and to facilitate novel drug discovery.

A particular focus of the laboratory is engineering members of the relaxin receptor family to enable greater understanding of how these receptors work at the molecular level and in turn enable the design of drugs targeting these important receptors. We also use this technology to engineer highly stable versions of other protein classes, such as fluorescent proteins and enzymes, for biotechnological and industrial applications.

**Research highlights for 2014**

Specific research highlights include:

- A critical proof-of-principle study was published in the prestigious journal, PNAS (USA), describing several X-ray crystal structures of GPCRs engineered with CHESS (Egloff P et al., PNAS (USA), 2014).

- We successfully demonstrated that CHESS could be applied to non-membrane protein classes, by using CHESS to engineer ultra-stable fluorescent proteins. These proteins are useful tools for next generation imaging methods (Yong KJ & Scott DJ, Biotech Bioeng, 2014).

- Kelvon Yong, a PhD Candidate, achieved a “special mention” in the poster prize section of the Australasian Society of Clinical and Experimental Pharmacology and Toxicology (ASCEPT) annual scientific meeting, 2014.

- Nicholas Smith, an Honours student, won the undergraduate poster prize at the Australasian Society of Clinical and Experimental Pharmacology and Toxicology (ASCEPT) annual scientific meeting, 2014.

- Awarded three NHMRC project grants for applications submitted in 2014 totaling $1M.

**PEPTIDE AND PROTEIN CHEMISTRY GROUP**

**Leader: Prof John Wade**

We employ modern chemical peptide synthesis methods together with structure-based drug design and development to produce novel peptidomimetics with improved receptor selectivity, potency and pharmacokinetics. Our primary research focus is on complex insulin-like peptides including the peptide hormone, relaxin, and the neuropeptide, relaxin-3.

**Research highlights for 2014**

Relaxin is principally an ovarian hormone that has a number of physiological roles, one of which is to regulate the level of collagen throughout the body. Relaxin-3 is a neuropeptide expressed in the brain which has an important role in regulating mood and stress systems. Because of their similar chemical structures, relaxin-3 can cross react with the receptor for relaxin, which is also present in high levels in the brain and this can complicate our understanding of whether relaxin-3 better understand the biological role of relaxin-3.

However, in addition to our ability to chemically produce relaxin and relaxin-3, we have prepared a series of progressively truncated relaxin and relaxin-3 analogues and identified the minimum size that endows near full biological activity at the distinct receptors. Unexpectedly, we discovered that relaxin’s activity could be maintained within a single small peptide chain, which promises considerable savings in both cost and effort of production and biological insights.

The peptide has been patented and is the subject of significant interest from major pharma to determine if it fully replicates all the known beneficial actions of native relaxin. A similar minimization strategy has been applied to relaxin-3 and together with the chemical conformation-constraining approach, a single chain peptide has been identified that mimics the agonist actions of the native relaxin-3. This peptide is now under further investigation within the Neuropeptides Division to better determine the clinical potential of relaxin-3 receptor-related drugs for treating psychiatric disorders such as anxiety and depression.

We have also continued our studies on antimicrobial peptides (AMPs), a novel class of antibiotic that displays clinical promise in bypassing the vexing problem of resistance development by bacteria. In particular, we have examined a novel insect-derived AMP called A3-P0 and shown that a dimer of this compound is a powerful antibacterial against Gram-negative bacteria as well as an immunostimulant which does not induce resistance. Studies are underway to determine if this efficacy can be further increased in combination therapy with conventional antibiotics.
NEUROPEPTIDE RECEPTOR GROUP

EDITORIAL POSITIONS
- Ross Ballgute
- Associate Editor of Frontiers in Molecular and Structural Endocrinology
- Editorial Board Member of Journal of Pharmacological Sciences
- Associate Editor of Molecular and Cellular Endocrinology
- Member - IUPHAR subcommittee on relaxin receptors

COLLABORATIONS
- Department of Biochemistry and Molecular Biology, University of Melbourne
- School of Biomedical Sciences, University of Queensland
- Monash Institute of Pharmaceutical Sciences, Monash University
- Baker Heart Research Institute, Melbourne
- Department of Pharmacology, University of Melbourne
- Department of Human and Molecular Genetics, Herbert Wertheim College of Medicine, Florida International University, USA
- Corthera (owned by Novartis), San Mateo, USA
- Chinese National Compound Library, Shanghai, China
- Department of Pharmacology, University of Pittsburgh, USA

PEPTIDE NEUROBIOLOGY GROUP

EDITORIAL POSITIONS
- Andrew Gurditch
- Editorial Board Member, Journal of Chemical Neuroanatomy
- Editorial Board Member, Neuropeptides
- Editorial Board Member, Frontiers in Molecular Neurosciences
- Editorial Board Member, Frontiers in Neuroanatomy
- Editorial Board Member, Neurosignals
- Editorial Board Member, Scientific Reports
- Chair, IUPHAR Database Committee on Galanin Receptors
- Guest Editor, Neurochemical Research

MAJOR NATIONAL AND INTERNATIONAL CONFERENCES 2014
- Australasian Neuroscience Society Annual Scientific Meeting, Adelaide, Australia
- European Molecular and Cellular Cognition Society Meeting, Milan, Italy
- Mediterranean Neuroscience Society, FENS Satellite Meeting, Milan, Italy
- FENS Congress of Neuroscience, Milan, Italy
- Associated Professional Sleep Societies, Sleep 2014, Minnepolis, USA
- Endocrine Society of Australia Annual Scientific Meeting, Neuroneuroendocrinology Symposium, Melbourne, Australia
- Congress of European Sleep Research Society, Tallinn, Estonia
- Cardiovascular and Respiratory Control Meeting, Melbourne, Australia
- Society for Neuroscience-Annual Scientific Meeting, Washington, DC, USA

COLLABORATIONS
- Florey Behavioral Neuroscience and Neurophysiology Division
- School of Biomedical Sciences, University of Queensland
- Monash Institute of Pharmaceutical Sciences, Monash University

INSULIN PEPTIDES GROUP

EDITORIAL POSITIONS
- Mohammed Akhter Hossain
- Review Editor of Frontiers in Chemical Endocrinology
- Editorial Board Member of Modern Chemistry

MAJOR NATIONAL AND INTERNATIONAL CONFERENCES 2014

COLLABORATIONS
- School of Chemistry, University of Melbourne
- Department of Biochemistry and Molecular Biology, University of Melbourne
- Department of Pharmacology, University of Melbourne
- School of Biomedical Sciences, University of Queensland
- Department of Pharmacology, Monash University
- Department of Chemistry, Monash University
- Monash Institute of Pharmaceutical Sciences, Monash University
- School of Medicine, Flinders University
- Department of Chemistry, Osaka University, Japan
- Takeda Cambridge Ltd, United Kingdom

MEMBRANE PROTEIN ENGINEERING GROUP

MAJOR NATIONAL AND INTERNATIONAL CONFERENCES 2014
- Keystone Meeting on GPCRs, 2014, Snowbird (International), Utah, USA
- GPCR Forum, Monash Institute of Pharmaceutical Sciences [Daniel Scott, invited speaker]
- Endocrine Society of Australia ASM Neuroendocrinology Symposium, 2014 [Daniel Scott, invited speaker]
- Pharmacology 2014, London, UK [Daniel Scott attended as the 2013 British Pharmacological Society/ASCEPT Outstanding Young Investigator Prize winner]

COLLABORATIONS
- The University of Melbourne, Australia
- University of Zurich, Switzerland
- Monash Institute of Pharmaceutical Sciences

PEPTIDE AND PROTEIN CHEMISTRY GROUP

EDITORIAL POSITIONS
- John Wade
- Editorial Board, Frontiers in Chemical Biology
- Editor-in-Chief, International Journal of Peptide Research & Therapeutics
- Editor-in-Chief, Biochemical Compounds
- Editor, Journal of Peptide Science
- Editor, Protein & Peptide Letters
- Editor, Amino Acids
- Editorial Board Member, Chemical Biology & Drug Design
- Editorial Board Member, BioMed Research International
- Editorial Board Member, International Journal of Peptides
- Editorial Board Member, Frontiers in Endocrinology - Molecular and Structural Endocrinology

MAJOR NATIONAL AND INTERNATIONAL CONFERENCES 2014
- 10th International Chinese Peptide Symposium, Daotong, China, July 2014 [John Wade, plenary speaker]
- 50th Anniversary Symposium of the IARC Laboratory of Molecular Biology, Cambridge, UK, 2014
- 33rd European Peptide Symposium, Sofia, Bulgaria, September 2014
- 4th MipTec Symposium, Basel, Switzerland, September 2014 [John Wade, plenary speaker]

COLLABORATIONS
- Bio21 Institute, University of Melbourne
- School of Chemistry, University of Melbourne
- Department of Pharmacology, University of Melbourne
- Department of Pharmacology, Monash University
- Department of Biology, Temple University, USA
- Institute of Bioanalytical Chemistry, Leipzig University, Germany
- Faculty of Medicine, Semmelweis University, Budapest, Hungary
- Ludwig Institute for Farm Animal Biology, Dummerstorf, Germany
- Sanofi-Aventis, Frankfurt, Germany
- Cooperative Research Center of Life Sciences, Kobe Gakuen University, Japan
- Novartis Institutes for Biomedical Research, Basel, Switzerland
- Institute of Protein Research, Tongji University, Shanghai, China

Monash University, Australia
- University of Queensland, Australia
- CSIRO, Australia
- IBM Research Collaboratory in Life Sciences & IBM Australia Research Laboratory
SLIPPING FROM STROKE INTO DEMENTIA

Fitness could be a key to recovery and ongoing health after stroke

Dr. Amy Brodtmann is a stroke and cognitive neurologist and is co-head of the Florey’s Behavioural Neuroscience division.

Amy Brodtmann is on a quest. She wants to solve a conundrum in neuroscience. The puzzle: why does it seem that one in three stroke victims will go on to develop dementia?

The scientific literature on the topic has been described as “scant” and “confusing” and that is enough to take Amy out of the consulting room and into the research space at the Florey’s campus next to Austin Health.

Typically people who experience a stroke have problems with speech, memory and thinking, but most are fortunate to recover many of these skills following drug treatment and rehabilitation. But Amy is searching for an answer – does stroke cause ongoing neurodegeneration?

She and her team are immersed in a world-first longitudinal study, the early findings of which have been remarkable.

Since 2011, Florey researchers have approached 135 people who had just had a stroke and who were admitted to the Austin. They are members of the CANVAS study, (Cognition And Neocortical Volume After Stroke), undergoing three-years of cognitive testing and a series of brain scans.

“We’ve been looking at how their brain volumes change over time and we have given them cognitive tests for memory, reason, judgement, how they visually process information and how well they pay attention,” Amy explains.

Amy is working closely with Dr. Michele Veldsman, a post-doctoral research fellow who joined the Florey in late 2013 from Cambridge University, and who has a strong neuro imaging background. She had heard about Amy’s work at Cambridge and was interested in its clinical direction.

Michele looks at the connections in the brain using 3D imaging of blood flow.

The study is still underway but Amy and her team have already had some significant results:

“We’ve found that certain parts of the brain are very sensitive to deterioration following stroke, including the hippocampus and the thalamus, which are structures deep in the brain important for many cognitive processes,” she says.

“The changes occur in many, but not all, the patients so our next step is to ask ‘why those people and why not others?’”

Michele says: “Ultimately, we want to use the network changes we see in the brain to predict if someone will go on to develop dementia.”

The research also shows the baseline brain volumes of the stroke survivors in the first scan are smaller than expected, causing Amy to wonder if long term high blood pressure and hypertension have caused earlier shrinking of the brain.

Another striking finding has been that there is an improvement in the brain connectivity of participants who are physically active: exercise helps “preserve” their brain networks.

“We know that in certain dementia syndromes, some brain networks are affected. We’ve looked at some of those networks and found that if you’re more active during the day, you preserve them,” says Amy.

“And that’s very exciting!”

Amy has presented the findings internationally and is publishing her results.

She is also incorporating her findings into advice she gives patients following a stroke.

“I gave a talk to Alzheimer’s Australia yesterday and they’re working it into their advice for this group of patients as well.

“I advise people to get as fit as they can be. If they can’t run then they should walk. If they can’t walk they should ride a bike. If they can’t do that they should swim – just keep moving!”

She also urges patients to have checks to ensure their blood pressure, cholesterol levels and diabetes blood sugar levels are “perfect”, and to “get lean”.

Kel Glare AO, former Victorian Police Commissioner, says he is taking part in CANVAS to do his bit towards helping future stroke victims.

Kel had a stroke in August 2011 but recovered with only some loss of vision. It’s a real pain when he’s playing golf and going for a putt, he quips, but he is otherwise “lucky”.

He is a keen supporter of the Florey, where he’s a Governor, and an advocate of the new Medical Research Future Fund.

“In my background, you can’t solve crime by building more prisons, and in medicine you can’t solve medical problems by building more hospitals – it takes medical research.

“The Florey’s great but needs more funding from government,” he says. Amy, whose future research into stroke and neurodegeneration depends on securing further funding, says that while curiosity compels her to investigate, she is also driven by concern for better outcomes for the people she treats in hospital.

“What I want to eventually be able to do when I’m on a ward with a stroke patient who’s just been admitted, is not only give them information about what’s going to happen in the next few weeks as they recover, but also information on what they can do in the days, months and years after that to make sure they have good brain health.”
STROKE PRECLINICAL SCIENCE

Leader: David Howells

The 17 member preclinical stroke laboratories comprise Australia’s leading translational stroke research team with expertise in therapeutic and diagnostic assessment in animal models of stroke, the use of human stem cell derived neurons and glia to explore stroke biology and identify novel drugs and the use of systematic review and meta-analysis to understand why translation to the clinic is so difficult and to provide evidence based selection of agents for clinical trial.

Research highlights for 2014

In both Stroke and Sci our analyses show that stem cell therapies improve outcome. However, in both clinical stereotypes facets of the disease modelling account for more of detected effect size than stem cell biology. This led us to concentrate on using stem cells as a source of human neurons for drug testing rather than implantation and the demonstration that hypothermia protects human neurons against ischemia with an exogenous and glucose dependent mechanism. This has led to a new collaboration to expand the use of human stem cell derived neurons and glia to explore stroke biology (Dr Cooper-Wheeler, UQ; Dr Dottori, UniM; Dr Wilson, CSIRO).

Evidence from meta analysis of the impact of hypothermia and hypertension on outcome in animal models of stroke contributed to the design of experiments which confirm that hypothermia is effective in animal models of stroke and that pethidine, used to express pain in human clinical trials of hypothermia, does not interfere in provision of this benefit.

Cumulative evidence from our analyses of the stroke literature and experimentation in co-morbid animals have contributed to the launch of the Stroke (multi-centre Preclinical Animal Research Team; www.multi-part.org), an international in vivo collaboration designed to develop the capacity to undertake international multi-centre animal studies to improve the validity, and generalizability of current preclinical research to improve the prospects of success for translation of efficacy to human clinical trials. The internal validity of experiments designed to examine candidates prioritized for clinical trials of efficacy in animal models of stroke, and that pethidine, used to express pain in human clinical trials of hypothermia, does not interfere in provision of this benefit.

Key research projects and staff

Julie Bernhardt: Dose escalation study for stroke survivors with impaired mobility. In partnership with Royal Talbot Rehabilitation Centre, Austin Health, we conducted a dose escalation study of exercise in stroke survivors with significant difficulty with walking. In clinical practice and clinical trials the selection of treatment dose (amount, frequency, intensity) is rarely based on solid data. We aimed to challenge this approach and develop a new way of identifying the best dose of training to get the best results.

Another highlight for 2014 was the development of our new acute exercise laboratory at the Austin Campus. This lab will support our acute interventions for the first 24 hours after stroke, with much of the equipment making bedside assessment and testing a possibility. We are now uniquely positioned to interrogate and develop treatments to help the profound deconditioning that occurs quickly after stroke.

Optimising health environments forum

We held our second optimising health environments forum in 2014, which brings together clinicians, architects, researchers and consumers of health care. The forum is to build strong linkages across the different sectors to improve the science that underpins decisions about the environments in which health care is delivered. Julie has the view that hospitals are expensive to build and the built environment (as well as the care services within) influence outcomes. If we can improve the evidence base for decision making about the health care environment itself, everyone benefits. This is an emerging area of interest in Australia and the Florey is taking a role in advancing the science of design and building strong collaborative partnerships. Julie’s vision is to design the best rehabilitation building and service model in the world, and then one day see that design become a reality.

Key research projects and staff

Toby Cunningham: The energy cost of walking in the first week after stroke. Stroke can have a major impact on walking ability, fitness and muscle strength, and these impairments may make being physically active more demanding. We are measuring the energy used by patients during steady-paced walking in the first week after stroke, and comparing this to energy used by healthy controls. Data from an unobtrusive electronic activity monitor are compared to ‘gold standard’ measurement of energy expenditure, which involves wearing a mask to measure oxygen intake. We are finding how hard patients can work early after stroke will inform treatment and rehabilitation programs.

Julie Bernhardt: Dose escalation study for stroke survivors with impaired mobility. In partnership with Royal Talbot Rehabilitation Centre, Austin Health, we conducted a dose escalation study of exercise in stroke survivors with significant difficulty with walking. In clinical practice and clinical trials the selection of treatment dose (amount, frequency, intensity) is rarely based on solid data. We aimed to challenge this approach and develop a new way of identifying the best dose of training to get the best results.

A QUICK SNAPSHOT

15 million strokes and six million stroke deaths occur each year leaving 55 million survivors suffering the consequences of stroke. Stroke Division provides a service through the Stroke Clinical Registry that offers a team of clinical and non-clinical staff whose aim is to understand the pathophysiology of stroke, optimise existing therapies and develop new treatments and techniques to both prevent and reduce the impact of stroke.

The division has five research teams: Stroke Preclinical Science, the AVERT Early Intervention Research Program, the Neurorehabilitation and Recovery group, Public Health and Epidemiology including the Stroke Telemedicine program and the Australian Stroke Clinical Registry, and Clinical Trials.

Recruitment to the AVERT trial, an international, 16 multicentre, randomised controlled trial of very early rehabilitation, completed in October 2014. Participants were recruited from five countries. This single blind, Phase III trial, tests whether starting out-of-bed mobility training within 24 hours of stroke is superior to current care. The results are eagerly awaited by the international stroke community and the first results of the trial will be reported at the European Stroke Organisation Conference in Glasgow, April 2015.

A IDEAS LIKELY TO CHANGE LIVES BY 2035

Our Stroke Telemedicine program is improving equity of access to the best available care for Victorians, whether they live in the city or country. It is the most comprehensive program of its kind that has been developed for acute stroke care in Australia. By 2035, we’d like to see the program used across Australia.

A RESEARCH HIGHLIGHT

The Florey Public Health and Epidemiology group is responsible for the integrity of the Australian Stroke Clinical Registry. This important national infrastructure provides the ability for hospitals across Australia to enter standardised data about their patients and compare their clinical performance and save lives. Currently, 51 hospitals are approved to use AuSCR. The registry is about to provide information on how many patients are receiving clot-busting thrombolysis medication within the first 4.5 hours of stroke and receiving access to stroke units. Both these treatment offer patients the best opportunity for a good outcome after stroke, however not all hospitals provide these treatments consistently for a variety of reasons. Through use of AuSCR, for the first time in Australia, we will be able to compare these aspects of treatment and have the impacts on longer term outcomes within 180 days of stroke.
The potential to drive adaptive neural plastic changes through rehabilitation is enormous and likely to lead to changes in rehabilitation practice and better outcomes for stroke survivors. However, we do not have effective means of identifying individuals who may benefit from these approaches, and it is important to develop effective rehabilitation therapy for an individual. The Neurorehabilitation and Recovery research program focuses on stroke recovery: in particular how the brain adapts after stroke to help survivors relearn functions, and the research involves development of new approaches to reposition learning that is supported by neuroscience. MRI is used to investigate how changes in the brain can help target rehabilitation most optimally to individual stroke survivors. Our research also explores whether changes in cognition, and that impact on stroke recovery. An important focus is to translate these discoveries into clinical practice and better outcomes for stroke survivors.

Research highlights for 2014
In 2014 the Neurorehabilitation and Recovery group achieved a milestone in forward planning its research of focused on harnessing real world drivers of neuroplasticity. The major objective of our group is to translate knowledge from neuroscience into evidence-based clinical practice protocols and better outcomes for stroke survivors. This goal represents a paradigm shift for stroke rehabilitation and better outcomes for the one in six people who experience a stroke. Our research is focused on: targeting rehabilitation to the individual based on viable brain networks; Neurobiology of recovery and impact of depression on outcomes; and implementation of evidence-based practice, as outlined below.

In 2014, we achieved 100% recruitment to the START longitudinal stroke cohort study and completed the implementation of evidence-based rehabilitation in clinical practice settings. Our team developed a national neuroscience and stroke rehabilitation, and scope for accelerated influence in the field, has been affirmed by our success in 2014 as lead site and Principal Investigator of an international James S. McConnell Collaborative Award to Translate Neuroscience to Rehabilitation and Everyday Life (a consortium of 70 researchers worldwide) and lead of the clinical discovery and neuroimaging stream on the NHMRC Centre for Stroke Recovery and Brain Recovery (2015-2019, $5,000,000).

Targeting rehabilitation to the individual based on viable brain networks
Few rehabilitation interventions are based on robust principles of neuroscience. With a rare combination of expertise in clinical rehabilitation and neuroscience, we have designed to build stroke rehabilitation evidence from clinical discovery to implementation. Our group has demonstrated changes in the brain associated with rehabilitation and how therapy may be used to drive neuroplastic changes. However, while we do not have effective means of identifying individuals who may benefit from these approaches, it is important to develop effective rehabilitation for an individual. In our current studies, we examine the first time, how different training conditions (task-specific vs transfer-enhanced) and different lesion sites (cortical vs subcortical) impact on reorganization of brain networks involved in sensory motor recovery. This project, Effective sensory rehabilitation after stroke: Targeting viable brain networks is funded by an NHMRC Project grant (2012-2015; CUA Care). In 2015, we expanded our recruitment to our study. We continue to collaborate with expert neurologists in Germany and Newcastle (AUS) and with the Advanced MRI Development team at the Florey. We are also involved in the program of research into neuroimaging outcomes of motor recovery after stroke conducted in Newcastle at the Hunter Medical Research Institute. Our findings will guide therapists in choosing the best therapy for the individual and to target interventions on key brain networks that have capacity to adapt. Translation: We developed a video animation to depict the translation of neuroscience to an evidence-based strategy: i.e. Connect: Neurangies to Neurorehabilitation. The video is available at: http://youtu.be/ GW7E_DqVjFw and has been sought after by therapists and stroke survivors alike. Our systematic approach to development of the SENSe neuroscience-based intervention now provides a template for further evidence-based approaches, and will be the subject of keynote presentations (see below). Expected outcomes include: (i) Improved outcomes for stroke patients receiving evidence-based SENSe rehabilitation; (ii) A community of ‘up-skilled’ health practitioners; (iii) A framework of success of knowledge-transfer methodologies in stroke rehabilitation; and (iv) Dissemination of the implementation template, with application to interventions for other groups.

Research highlights for 2014
In 2014, our team continued to lead the expansion of the Australian Stroke Clinical Registry and the Victorian Stroke Telemedicine Program. In addition, we received a competitive scholarship from the NHMRC partnership project whereby AU$159,000 data were linked to the National Death Index and the acute hospital quality improvement intervention, facilitated by the Stroke Foundation, was delivered across 20 hospitals in Queensland. These are our major flagship projects. We also continued to provide research support for the Research Excellence in Stroke Rehabilitation and Brain Recovery (2014-2017; $528,000 USD; a S. McDonnell Collaborative Award to Assoc Prof Dominique Cadilhac, Principal Investigator). Our research includes: (i) First-ever knowledge of how brain networks change, improve and stabilize post-stroke imaging (AUS) and Treatment, is funded by a CSIRO preventative health flagship (2010-2015). START PrePare (Prevention and Prevention to Achieve optimal Recovery Endpoints), the longitudinal cohort arm with advanced imaging and clinical outcomes is led by Professor Dominique Cadilhac. In 2014, the sampling was recruited as of 2014 and the final data will be collected in Autumn 2015. The imaging and sensory loss after stroke. Our national survey of current evidence-based practice guidelines and clinical practice guidelines, received competitive scholarships to support their work in this field. Three experienced therapists who have been awarded a PhD and Masters research program. All have now received competitive scholarships to support their work in this field. The team also continues to work with the Stroke and Therapist 5-10 stroke therapists at each pilot. Professor Marilyn Walker (Brain and Stroke Foundation) and Professor Andrew Jackson (Southland District Health Board) are involved. Expected outcomes include: (i) Improved outcomes for stroke patients receiving evidence-based SENSe rehabilitation; (ii) A community of ‘up-skilled’ health practitioners; (iii) A framework of success of knowledge-transfer methodologies in stroke rehabilitation; and (iv) Dissemination of the implementation template, with application to interventions for other groups.

Application of SENSe in children
The SENSe intervention is also being applied to children with cerebral palsy using randomised controlled methodology. A research group (n=8) comprising a paediatrician, therapists and PhD students are conducting this research in Perth in collaboration with us.

Stroke Telemedicine
Leaders: Professor Chris Bladin and Associate Professor Dominique Cadilhac.
Our group conducts various projects related to improving the clinical management of stroke and improving access to stroke care in public hospitals continues to be a major objective, as well as designing and implementing systems to improve the quality of evidence-based care and achieve better health outcomes after stroke.

Research highlights for 2014
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Our group conducts various projects related to improving the clinical management of stroke and improving access to stroke care in public hospitals continues to be a major objective, as well as designing and implementing systems to improve the quality of evidence-based care and achieve better health outcomes after stroke.

Research highlights for 2014
In 2014, our team continued to lead the expansion of the Australian Stroke Clinical Registry and the Victorian Stroke Telemedicine Program. In addition, we received a competitive scholarship from the NHMRC partnership project whereby AU$159,000 data were linked to the National Death Index and the acute hospital quality improvement intervention, facilitated by the Stroke Foundation, was delivered across 20 hospitals in Queensland. These are our major flagship projects. We also continued to provide research support for the Research Excellence in Stroke Rehabilitation and Brain Recovery (2014-2017; $528,000 USD; a S. McDonnell Collaborative Award to Assoc Prof Dominique Cadilhac, Principal Investigator). Our research includes: (i) First-ever knowledge of how brain networks change, improve and stabilize post-stroke imaging (AUS) and Treatment, is funded by a CSIRO preventative health flagship (2010-2015). START PrePare (Prevention and Prevention to Achieve optimal Recovery Endpoints), the longitudinal cohort arm with advanced imaging and clinical outcomes is led by Professor Dominique Cadilhac. In 2014, the sampling was recruited as of 2014 and the final data will be collected in Autumn 2015. The imaging and sensory loss after stroke. Our national survey of current evidence-based practice guidelines and clinical practice guidelines, received competitive scholarships to support their work in this field. Three experienced therapists who have been awarded a PhD and Masters research program. All have now received competitive scholarships to support their work in this field. The team also continues to work with the Stroke and Therapist 5-10 stroke therapists at each pilot. Professor Marilyn Walker (Brain and Stroke Foundation) and Professor Andrew Jackson (Southland District Health Board) are involved. Expected outcomes include: (i) Improved outcomes for stroke patients receiving evidence-based SENSe rehabilitation; (ii) A community of ‘up-skilled’ health practitioners; (iii) A framework of success of knowledge-transfer methodologies in stroke rehabilitation; and (iv) Dissemination of the implementation template, with application to interventions for other groups.
The objective of the program is to improve the care of acute stroke patients across Victoria through the use of cutting-edge technology. We aim to do this by implementing a seamless videoconference service to 16 regionally based hospitals providing 24-hour access to a stroke neurologist roster. Professor Chris Bladin and Assoc Prof Cadilhac, who co-lead this work, have secured over $8.96 million in funding for this program with an additional $474K for a more complete cost-effectiveness analysis with project funding from the NHMRC.

The Victorian Stroke Telemedicine Program includes three projects.

The initial project was the VST – Bendigo, a successful single site telemedicine project undertaken at Bendigo Health which concluded in 2013. The VST - Loddon Mallee project was commenced in 2013 and is funded by the Victorian Government under the Broadband Enabled Innovation Program (BEIP) grant. This project was the basis for expanding a team model to include Echuca Regional Health, Swan Hill District Health and Mildura Base Hospital in 2014. This work has been project managed by Michelle Vu who joined our team in 2014 as the conclusion of the two-year BEIP funding, Loddon Mallee health services will continue to receive support under the VStStroke Project. The VStStroke Project is funded by the Australian Government Health and Hospital Fund and will continue to support the VST Loddon Mallee project whilst increasing the scope to include a further 12 hospitals across the other regions of Victoria. This will enable state wide coverage of the teleradiology service and which is funded until 2018. These projects form the largest acute stroke telemedicine program in Australia. Our project partners include Victorian Stroke Clinical Network (Victorian Department of Health), Monash University, Telstra, Polyclinic, Ambulance Victoria, National Stroke Foundation and the Loddon Mallee Rural Health Alliance. Boehringer Ingelheim has also provided the hypothesis that will support adaptations to the AuSCR web-tool and education.

In the Victorian Stroke Telemedicine program there are three key research themes: i) clinical ii) implementation science, and iii) health economics. The platform has been developed to use the infrastructure available through the Australian Stroke Clinical Registry (AuSCR) (they are national data custodians) which has been expanded to include stroke telemedicine variables. In this way, ongoing benefits of the program can be captured to measure sustainability impacts beyond 2018.

Australian Stroke Clinical Registry and Stroke12 NHMRC partnership project (Leader Assoc Professor Dominique Cadilhac)

Our team leads expansion of the Australian Stroke Clinical Registry (AuSCR) in 2014. At the end of 2014, the team were informed that the Victorian Department of Health, through the Victorian Stroke Clinical Network, had committed about $785,000 to support greater establishment of AuSCR within Victorian hospitals. The Victorian government has provided, to date, the largest commitment we have received from government to support this initiative.

CLINICAL LEADER
Professor Geoffrey Donn

The Clinical Trials Platform crosses an array of clinical trial initiatives in stroke. The platform services of Neuroscience Trials Australia (NTA), housed within the Florey, are utilised. These include project management, regulatory and monitoring issues, statistical and data storage.

Research highlights for 2014

The main focus of clinical trial activity continues to be around the extended time window for neurological deficits (EXTEND) series of trials. This is in partnership with Professor Stephen Davis at the Melbourne Brain Centre/RHH and his colleagues. This family of trials is designed to extend the time window for the most commonly used stroke intervention, thrombolysis (clot dissolving). We are testing the hypotheses that the time window may be extended out to nine hours from 4.5 hours and that clot removal with the SOLITAIRE device may improve outcomes. This trial has now been completed and the results will be presented at the International Stroke Congress in the US in February 2015. A further hypothesis that administration of tranexamic acid (a clot promoting agent) may improve outcomes in patients with intracranial haemorrhage is currently being further studied in a phase III trial. Analysis has been completed on an earlier trial (ARCH trial - prevention of second stroke events in patients with stroke caused by clots coming from the main artery to the heart). Although the trial was stopped early because of the inability of the European arm to continue, the combination of the anticoagulant apixaban and clopidogrel were found to be safe and as effective as the antiagulant warfarin. Given the simplicity of the use of anticoagulant and antiplatelet agents, these would be the obvious ones to use in clinical practice. The results were published in the journal Stroke.

Clinical trial activity is built upon national and international collaborations and connections. Of the numerous clinical trials conducted, the majority are conducted by collaborating with numerous academic colleagues throughout Australia and commonly with those in other international locations. These collaborations occur with Professor Stephen Davis at the Royal Melbourne Hospital, Christopher Levi and Mark Parson at A NHMRC Partnership, Shane Graham at the Melbourne Brain Centre/RHH, Christopher Levi and Mark Parson at the University of Melbourne, Professor Steve Bladin and Associate Professor Dominique Cadilhac.

Commercial projects conducted through Neuroscience Trials Australia (NTA)

Clinical trial activity in stroke also includes very important partnerships and collaborations with pharmaceutical and biotechnology companies (both local and international). Trials range from phase III trials to phase IV trials, and include drug as well as devices. One of the products assessed aims to assist in dissolving clots that cause stroke. Another trial is assessing the use of aspirin compared to another agent in the prevention of TIA.

STROKE PRECLINICAL SCIENCE

COLLABORATIONS

International collaboration in preclinical stroke research: Corroborating the problems of bias, lack of statistical power and lack of generalizability in preclinical research requires larger, more rigorously controlled and replicated experiments. Our approach to achieve this establishment of the Multi-PART (mentioned above). This platform has the potential to transform preclinical animal research across the life sciences, similar to the tremendous improvements in clinical research that occurred through the introduction of multi-center clinical trials. This program is now being geared up for the stroke research, as well as the multi-center clinical studies.

NHMRC Program (Dorrow, Davis, Hankey, Parsons & Howells). Our NHMRC program (AppId’s 2013525, 454447, 1118621) established a scientifically integrated program with basic and clinical science elements to select neuroprotectors for clinical trials. We then expanded our basic science so that we had the capacity to develop novel targets for therapy and study the role of long term plasticity and are now exploring the use of cell derived human neurons as a drug screening tool and the use of blood biomarkers to select stroke patients for treatment.

Stroke on a chip: Since our understanding of human stroke pathophysiology is incomplete, we may have neglected the right cells or the right molecular processes within these cells in our attempts to develop drugs for stroke. A new collaboration with colleagues from University of Queensland (Prof Justin Cooper White, A/Prof Ernst Wohlgemuth), University of Melbourne (Dr Merlina Dottino) and CSIRO (Dr William Wilson, Dr Diadong Wang) will use human neurons, astroglia and oligodendroglia derived from embryonic stem cells grown on and microbead array, to better define the human ischemic cascade. The multipotent capacity of the MBAs will allow rapid and reproducible examination of complex interactions between the cells and the effects of isoflurane and other clinical injuries previously used to identify the key steps in the rodent ischemic cascade, on the biology of these cells. This data will allow us to build the first quantitative and statistically robust map of the human ischemic cascade. The nodes of the map are most easily disrupted by ischemia and related insults and those that are left for the greatest degree of normalization when treated will be identified as therapeutic targets for future drug testing.

Eng Li, Harvard, USA, Novo Hypozone inhibitors to reduce oxidative stress after stroke (US Patent 2012/0053536/D); the

Dave Lambeth, Emory University, USA, Novel NOX inhibitors to treat heart diseases. Professor David Lambeth, Emory University, USA, who co-lead this work, has also provided an educational grant to support adaptations to the AuSCR web-tool and education.


EDITORIAL POSITIONS

Evidence based preclinical medicine (Editor in chief)

International Journal of Stroke (Associate Editor)

International Journal of Stroke, Section editor Rehabilitation

Neurological Research (Editor in chief)

International Journal of Therapy and Rehabilitation

Neuroscience Briefs and Structured Stakeholder Dialogues to address challenges in earlier stages of clinical trials.

Clinical Researcher, Paradise in the Hills Rehabilitation Centre, University of Haifa, Israel.

Dr Julie Laker

Dr Lian Johnson

Karen Bormberich

Sharon Kramer

Anne Hokstad

Nat Frit

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University of Nottingham, UK  
Department of Psychological and Brain Sciences, Indiana Univ, USA  
Department of OT Education, Kansas Medical Centre, USA  
A/Prof Thomas Linden, Neurologist/psychiatrist, Gothenburg, Sweden  
Dept. of Occupational Science and Occupational Therapy and Gradute Dept. of Rehabilitation Science, University of Toronto, Canada  
Dept. of Clinical and Biological Neurosciences, University, Hospital, Grenoble, France  
International Post Stroke Upper Extremity Working Group  
National Institute of Health (NIH) Toolbox: Assessment of Neurological and Behavioral Function group.

NATIONAL  
CSIRO preventative Health Flagship, STF program of research.  
Hunter Medical Research Institute, Newcastle, Centre for Brain and Mental Health Research  
University of Newcastle, NSW  
Advanced MRI: Development, Florey Institute  
La Trobe University: School of Allied Health, Research Focus Area, Sport Exercise and Rehabilitation; and Living with Disability research group, (LDS)  
La Trobe Institute of Molecular Sciences (LIMS)  
School of Paediatric and Child Health, University of Western Australia  
Australian National University, Canberra  
Allied and Public Health, Australian Catholic University, Melbourne.  
Neurology, Austin Health  

EDITORIAL POSITIONS  
Neuromodulation and Neural Repair  
Occupational Therapy International  
Australian Occupational Therapy Journal  
Brain Impairment.

MAJOR NATIONAL AND INTERNATIONAL CONFERENCES 2014

INTERNATIONAL – KEYNOTE AND INVITED  
Cross-cultural issues in Stroke Policy, Population and Clinical Comparisons, Global Ageing Research Network Meeting, McDonnell International Scholars Academy 5th International Symposium: The Role of Research Universities in Addressing Global Challenges, St Louis, MO.  
Neuroscience makes Sense for Occupational Therapy, Washington University at St Louis, St Louis, 8th October 2014  
A learning based model of recovery and rehabilitation post-stroke: in the Symposium: Rehabilitation of Neurological Vision Impairment.  
Imaging associates of post-stroke depression and functional outcome: A longitudinal cohort study, 12th International Conference on Cognitive Neuroscience: Symposia, Brindavan.  
The Six Mile Bridge Recovery Journey: Across Countries and Over time. McDonnell International Scholars Academy 5th International Symposium, St Louis, MO.  
Health indicators, incidence, prevalence and mortality rates, temporal trends and gender differences in stroke between United States, Australia and Singapore: An in-depth cross-country comparison, McDonnell International Scholars Academy 5th International Symposium, St Louis, MO.  
Stroke rehabilitation and services in late stages of recovery and return to the community: Comparisons from three corners of the globe, McDonnell International Scholars Academy 5th International Symposium, St Louis, MO.  
Same intervention-Different reorganisation: Impact of lesion location on training touch after stroke. 2014 Organisation of Human Brain Mapping, Hamburg, Germany.  
Functional and structural connectivity in the brain associated with depression after stroke. 8th World Congress for Neurorehabilitation, Istanbul, Turkey.  
SENSE: Individual patient characteristics that predict favorable outcomes for sensory rehabilitation after stroke. 8th World Congress for Neurorehabilitation, Istanbul, Turkey.  
The Path through life project: ICNE 2014. International Conference of Neurology and Epidemiology.  
Automated detection of brain regions associated with post-stroke depression: A hypothesis, ISMRM 2014, Milan, Italy.  
Automated lesion detection from multimodal brain MRI using Markov random fields and random forest. ISMRM 2014, Milan, Italy.  
Fish-oil diet associated with acute-repulsion related haemorrhage, and with reduced stroke-related sickness behaviours and motor impairment. Modulating the Brain: Facts, Future Conference, Belgian Brain Council.  
Sensory discrimination training in children with hemiplegic cerebral palsy: 2 case studies. 8th World Congress (for Neurorehabilitation), Istanbul, Turkey.  
Advancing the Science of Rehabilitation: Translating Neuroscience and Rehabilitation into Everyday Life. 16th World Federation of Occupational Therapy Congress, Yokohama, Japan.  
Understanding occupational activity participation after stroke. 16th World Federation of Occupational Therapy Congress, Yokohama, Japan.  

PUBLIC HEALTH AND EPIDEMIOLOGY

COLLABORATIONS  
Stroke and Aging Research, School of Clinical Sciences at Monash Health, Monash University; The George Institute for Global Health; Stroke Society of Australia (SSA); School of Health, University of Newcastle, NSW; Nursing Research Institute, NSW; Population Health Research Network, Eastern Health, Monash University; Health Outcomes Institute, Arthritis Australia; National Institute of Health (NIH) Toolbox: Assessment of Neurological and Behavioral Function group.

MAJOR NATIONAL AND INTERNATIONAL CONFERENCES

CADIHAC  
CADIHAC International Journal of Stroke, Clinical Audit, Dose Medical Press and World Journal of Hypertension  
Dewey: Stroke journal and International Journal of Stroke  
Bladin, Current Neurology and Neuroscience Reports and British Journal of Sports Medicine

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Dr Adele Gibbs  
Akshon Das  
Brenda Graboch  
Prof Christopher Blied  
Erena Salama  
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Gary Eaton  
Prof Helen Dewey (honorary)  
Karen Moos  
Keesey Walks  
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Dr Kate Bagot  
Linda Francis  
Michelle Vu  
Morique Kilkenny (honorary)  
Nancy Captanico  
Sally Berger  
Tara Puns (honorary)  

MAJOR NATIONAL AND INTERNATIONAL CONFERENCES

CADIHAC  
Reviewing the options for performance benchmarks for acute stroke care in Australia NHMRC Research Translation Faculty conference, Melbourne, November 2014  
Update on the Victorian Stroke Telemedicine (VST) Project. Smart Strokes, Sydney, August 2014  
Stroke data collection in the Australian Stroke Clinical Registry – Progress with a purpose, Smart Strokes, Sydney August 2014  
Introduction to Research Principles, Smart Strokes, Sydney August 2014 (Invited)  
Variances in hospital mortality: Experiences from the Australian Stroke Clinical Registry (ASCERT). Stroke Society of Australia, Hamilton Island, August 2014  
NSW Stroke Services Clinical Network, panel discussion with Agency for Clinical Innovation on stroke data May 2014 (Invited)  
The economic implications of practice gaps in stroke care: an Australian case study. European Stroke Conference, Nice, France, May 2014  
Co-convenor National Stroke Data, Quality and Telemedicine workshop, Flinders, Melbourne March 2014

BIADON  
Co-convenor National Stroke Data, Quality and Telemedicine workshop, Flinders, Melbourne March 2014

DEWEY  
Generalisability of imaging selection for intra-arterial therapy in ischemic stroke – up to 30% of IIA eligible patients are potentially eligible. European Stroke Conference, Nice, France May 2014.  
Early mobilisation after thrombolysis (t-PA) in acute stroke: are it/it+ treatment patients enrolled in a trial of early mobilisation (AVERT) different from those that are not? International Stroke Conference, San Diego, USA, February 2014

VU  
Experiences with scaling up the Victorian Stroke Telemedicine Programme, Successes and Failures in Telehealth (SFT-14), Adelaide November 2014

GRABCH  
Australian Stroke Clinical Registry; progress and future plans. Registry Special Interest Group, Melbourne, September, 2014.
In Systems Neurophysiology we seek to learn how the nervous system controls various bodily functions and how that control is altered in disease. Our disease focus includes not only neurological disorders such as epilepsy and multiple sclerosis, but also systemic conditions that have a significant impact on neurological diseases such as heart failure and inflammatory disease. A clear understanding of basic mechanisms is crucial in developing better treatments and reducing the impacts of illness.

AN IDEA LIKELY TO CHANGE LIVES BY 2035

We have shown that a key area for upper airway control can be identified by a single gene-marker. This maker will allow us to investigate critical cell populations in animals, but importantly also in the human brain. These finding will significantly help us understand and treat neurodegenerative upper airway disorders.

A QUICK SNAPSHOT

The brain controls basic bodily functions such as blood pressure, body temperature, body fluids and breathing.

AUTONOMIC NEUROPHYSIOLOGY GROUP

Leader: Robin McAllen

We investigate the central nervous pathways that regulate basic bodily functions such as blood pressure and body temperature, as well as their transmission to bodily targets via autonomic nerves.

Research highlights for 2014

It has long been known that, to control body temperature and maintain it within a narrow range, the brain uses temperature signals from the skin and from deep body structures as well as from the brain itself. Tony Shafston, Michael McKinnely and Robin McAllen are tracking down the brain’s intrinsic temperature sensors but in order to do this, we need to eliminate temperature signals arising from the brain itself. Others have shown that skin temperature signals relay in brainstem nuclei called the parabrachial nuclei eliminating those structures prevents the influence of skin temperature on thermoregulatory responses such as increasing or decreasing blood flow to the skin. We hypothesised that temperatures signals from deep body structures, such as the stomach and abdomen, are transmitted to the brain by the splanchnic sympathetic nerves, similar to those that transmit skin temperature signals. In anaesthetised rats, we first showed that the nerves to blood vessels in the tail (the major organ of heat exchange) respond to temperature changes in the abdomen, and so did independently of brain or skin temperatures. Next, we made lesions of the parabrachial nuclei, and confirmed that they blocked any influence of skin temperature on the thermoregulatory response of the tail’s tail nerves. Finally, we showed that these same lesions also blocked the effects of temperature changes in the abdomen. But the influence of brain temperature was preserved. Now we can remove the influence of temperature signals from the rest of the body and investigate the actions and neural pathways of the brain temperature sensors acting alone.

The research focus of the team has changed over the last 12 months and most of the time has been used to investigate the neural control of immune function. During 2014, we published a study (Martelli D., Yao S.T., McKinnely M.I., McAllen R.M. Reflex control of inflammation by sympathetic nerves, not the vagus. J Physiol. 592, 2014/167-1686). This was recommended in faculty of 1000 and as the editor’s choice of the published issue, where we described a neural reflex, termed the inflammatory reflex, that controls inflammation. This study contrasts the current dogma, that considers the vagus nerve as the main player of the inflammatory reflex, and shows how inflammation is controlled by the splanchnic sympathetic nerves. We also published a paper through investigation of the target organ of the inflammatory reflex. Our results (still unpublished) once again, contradict the common view that it’s the spleen the principal organ where nerves physiologically interact with white cells to inhibit inflammation. We now have data that demonstrate how this interaction is generalised to all the organs innervated by the greater splanchnic nerves (spleen, adrenal glands, liver, stomach and intestine).

Professor Michael McKinnely has been investigating the relationship between fat and hydration. When fat is broken down by metabolism, it generates water as well as energy. We wondered whether the body uses this process to generate water when it is needed to offset dehydration. We tested this idea in rats. Using an MRI instrument designed for the purpose, we measured their total body fat and total body water before and after 24 hours of water deprivation. After this, their total body water fell by eight per cent and their body fat by 16 per cent. The fat levels returned to normal within 48 hours of restoring access to water. Although dehydrated rats ate less food, reducing the food intake of normally hydrated rats by the same amount had only a very small effect on their body fat levels. These findings show that fat can be mobilised in dehydrated animals to produce water. We suspect that this process is controlled by osmoreceptors in the brain.

RESPIRATORY NEUROBIOLOGY LAB

Leader: Matthias Dutschmann

We study the basic neural mechanisms underlying breathing, how these patterns of nerve activity adjust to accommodate other behaviours such as swallowing, and how they are modified during development and in neurodegenerative disease.

Research highlights for 2014

Our main research focus is how the central nervous system controls upper airway muscles to modulate respiratory airflow during normal breathing. The neural pathways that control these muscle are different in the newborn and the adult, but they converge in response to changes in the environment in the form of breathing patterns. This hypothesis was tested in a novel study that used ultra-high resolution non-invasive imaging techniques to track electrical activity of the respiratory muscles in response to experimental conditions. These findings provide new insights into the way breathing control is established during development and how this control is modified by disease.

Heart Failure

Heart failure is a complex syndrome resulting from structural changes in the heart that reduce cardiac output and thus perfusion of tissues. It is a major public health problem in all Western countries where, in addition to the human cost in terms of morbidity and mortality, it is estimated to cost more than five per cent of health budgets. Disturbingly, the incidence of new cases of heart failure is increasing due to the ageing of the population and the conversion of acute cardiac problems into chronic disorders. A novel technique that has been used for the treatment of heart failure is percutaneous ablation of the coronary sinus, where radiofrequency energy is delivered to the heart’s right atrium (RA) near the coronary sinus ostia. This technique has been proposed as a treatment for heart failure. It is however unclear how effective this technique delivers the right balance between efficacy and safety.

Studies conducted by Dr Linda Booth demonstrated that percutaneous ablation is effective in reducing the incidence of new cases of heart failure, but the exact mechanism by which this technique does so is not clear. The incidence of new cases of heart failure is increasing due to the ageing of the population and the conversion of acute cardiac problems into chronic disorders. A novel technique that has been used for the treatment of heart failure is percutaneous ablation of the coronary sinus, where radiofrequency energy is delivered to the heart’s right atrium (RA) near the coronary sinus ostia. This technique has been proposed as a treatment for heart failure. It is however unclear how effective this technique delivers the right balance between efficacy and safety.
after denervation. These findings demonstrate that radiofrequency catheter-based renal denervation is effective, but raise questions regarding the mechanism by which renal denervation causes a prolonged fall in blood pressure in hypertensive patients.

**Septic shock**

Sepsis is the major cause of death in intensive care units with a high mortality rate of 30–75 per cent. Sepsis causes more deaths than prostate cancer, breast cancer and AIDS combined and the annual number of cases of sepsis is increasing. Despite the high costs in terms of morbidity, mortality and health budgets, few advances have been made in understanding of the pathophysiological mechanisms of sepsis, and consequently new therapeutic strategies have not been developed.

One of the hallmarks of sepsis is a large fall in blood pressure that can lead to multi-organ failure and death. A primary treatment is to give vasopressor drugs to increase blood pressure, but in sepsis the responsiveness to the drugs is reduced, leading to severe hypotension. One theory to explain this disseminisation is that the large increase in sympathetic nerve activity, that helps maintain blood pressure in sepsis, also has a detrimental action to reduce responsiveness of blood vessels. Dr Yugesh Lankadav and Dr Junto Koka have therefore investigated the effect of treatment with a drug, clonidine, that acts in the brain to inhibit sympathetic nerve activity. Although clonidine might be expected to cause a greater degree of hypotension, it in fact reduced the decrease in blood pressure during sepsis. An explanation for this is our finding that in sepsis treatment with clonidine fully restored the responsiveness of blood vessels to drugs that increase blood pressure. Clonidine might therefore be a useful treatment for septic patients who are resistant to vasopressor drugs and it is now important to confirm these experimental findings in a clinical trial in septic patients.

**CLINICAL BRAIN FUNCTION IN HEALTH AND DISEASE GROUP**

**Lead:** Richard Macdonell

Our lab studies how diseases such as epilepsy and multiple sclerosis change the excitability of neurones. A second focus is on the physiology of neurorepair and neural repair.

**Research highlights for 2014**

We are currently conducting a placebo controlled study investigating whether the drug (4-aminoptyridine) can be used to improve upper limb and hand function in patients with multiple sclerosis. The drug has previously been shown to improve walking speed and quality of life in patients suffering from MS. We use clinical measures of hand function which may respond to using the drug, such as strength and dexterity and tactile discrimination.

We are also conducting neurophysiological measures of conduction in central nervous system pathways using the techniques of transcranial magnetic stimulation and somatosensory evoked potentials. The drug is thought to produce benefits by blocking potassium channels in demyelinated axons thus permitting conduction to be restored in areas damaged by MS. We are on track to have results of this study available in early 2016.

**NEUROVASCULAR BIOLOGY LAB**

**Lead:** Song Yao

**Research highlights for 2014**

Our group has made a very exciting finding in a primate part of the brain called the nucleus of the solitary tract (NTS). This region of the brain stem is essential for regulating blood pressure. For many decades it was assumed that the adult brain does not acquire more brain cells (or neurones) in adulthood. This was shown to be an incorrect assumption in the 1960’s when an American group at MT showed that the birth of new brain cells, termed ‘adult neurogenesis’ occurs in only two parts of the adult brain—one responsible for memory and the other responsible for smell.

We have recently demonstrated that adult neurogenesis also occurs in the NTS and, importantly, that this process plays a critical role in the regulation of blood pressure. Using a synthetic analogue of the building blocks of DNA our group found that adult neurogenesis in the solitary tract is increased in both genetically and experimentally induced hypertension models. The main challenge now is to understand how increased neurogenesis within the NTS contributes to hypertension. We believe this research will help us better understand the neurogenic origins of high blood pressure and reveal a new target for treating hypertensive patients.

**NEUROVASCULAR BIOLOGY LAB**

**Major international conferences**

- **2014**
  - Presented this work at the Pan-American Congress of Physiological Societies, Brazil.
  - Awarded with a BRID Research Fellowship.

**Collaborations**

- University of Sao Paulo, Sao Paulo Brazil.
- Rosal Institute, University of Edinburgh, Scotland.
- University of Bristol, United Kingdom.

**Clinical brain function in health and disease group**

**Editors:**

- Respiratory Physiology
- Integrative Physiology
- Neurology
- *European Journal of Neurology*

**Respiratory neurobiology lab**

**International conferences & editorial positions**

- **2014**
  - Oxford meeting, Royal College of Physicians.
  - Session speaker, session chair.
  - Editor in chief, Respiratory Physiology & Neurobiology (Elsevier).

**NEUROCARDIOVASCULAR GROUP**

**Editors:**

- Australian Journal of Physiology (Regulatory, Comparative and Integrative Physiology)
- Temperature

**Faculty:**

- University of Queensland.
- Monash University.
- Regen Idaex (Australia).

**Major national and international conferences 2014**

- World Congress of Cardiology, Melbourne.
- Pan-American Congress of Physiology, Iguassu Falls, Brazil.
I am passionate about improving the lives of people with Parkinson’s disease. It’s my life’s work. The thirst for scientific knowledge is important to me but knowing that the field can be directly applied to people, is immensely rewarding. My work gives me a real sense of achievement.

Finding a cure is no small task and it will take a coordinated effort. I would like to see all of the Parkinson’s groups, scientists and clinicians unite and to convince politicians to make this a national health priority. Together, we will win this battle.

Associate Professor David Finkelman: Head, Parkinson’s disease laboratory
COMMERCIALISATION
- Mr Stephen Spargo AM (Chair)
- Professor Geoffrey Donnan AO
- Dr Henry De Alipurua
- Mr Wayne McMaster
- Dr Ross MacDonald
- Dr Ergad Gold
- Professor Steven Petrou

FINANCE AND INVESTMENT
- Mr Craig Drummond (Chair)
- Mrs Jennifer Laboume
- Mr Mark Jones
- Professor Andrea Hull AO
- Professor Geoffrey Donnan AO
- Professor Graeme Jackson
- Mr Andrew Stripp
- Mr Peter Plecher

AUDIT
- Mr Mark Jones (Chair)
- Mrs Jennifer Laboume
- Mr Mark Jones
- Professor Andrea Hull AO
- Professor Geoffrey Donnan AO
- Professor Graeme Jackson
- Mr Andrew Stripp
- Mr Peter Plecher

NOMINATION
- Mr Harold Mitchell AC (Chair)
- Mr Andrew Abercrombie
- Professor James Angus AO
- Professor Geoffrey Donnan AO
- Mr Rob Gerrand
- Professor Andrea Hull AO
- Professor Anne Kelso AO

EXTERNAL SCIENTIFIC ADVISORY
- Professor Sam Berkovic AC
- Professor Alastair Buchan
- Professor Seth Grant
- Professor Seong-Seng Tan

BOARD COMMITTEES & FOUNDATION COUNCIL
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- Professor Alastair Buchan
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- Professor Geoffrey Donnan AO
- Dr Henry De Alipurua
- Mr Wayne McMaster
- Dr Ross MacDonald
- Dr Ergad Gold
- Professor Steven Petrou

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- Mr Mark Jones
- Professor Andrea Hull AO
- Professor Geoffrey Donnan AO
- Professor Graeme Jackson
- Mr Andrew Stripp
- Mr Peter Plecher

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- Mr Mark Jones
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- Professor Geoffrey Donnan AO
- Professor Graeme Jackson
- Mr Andrew Stripp
- Mr Peter Plecher

NOMINATION
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- Mr Andrew Abercrombie
- Professor James Angus AO
- Professor Geoffrey Donnan AO
- Mr Rob Gerrand
- Professor Andrea Hull AO
- Professor Anne Kelso AO

EXTERNAL SCIENTIFIC ADVISORY
- Professor Sam Berkovic AC
- Professor Alastair Buchan
- Professor Seth Grant
- Professor Seong-Seng Tan

COMMITTEES & FINANCE AND INVESTMENT
- Professor Anne Kelso AO
- Professor James Angus AO
- Professor Geoffrey Donnan AO
- Professor Andrea Hull AO

THE FLOREY FACULTY
- David Abbott
- Paul Adlard
- Timothy Aumann
- Kevin Barrham
- Ross Bathgate
- Philip Beart
- Christopher Bladin
- Joanne Britto
- Ashley Bush
- Dominique Cadilhac
- Fernando Calamante
- Leeanne Carey
- Robert Cherry
- Leonid Churilov
- Alan Connelly
- Julie Bernhardt
- Wah Chin Boon
- Nathalie Braussaud
- Amy Brodtmann
- Henr de Alipurua
- Brian Dean
- Geoffrey Donnan
- John Drago
- Simon Drew
- Jodie Duncan
- Mathias Dutruchmann
- Ben Emery
- David Finkelstein
- Andreas Gogos
- Ben Gu
- Andrew Gundlach
- Anthony Hannan
- Rachel Hill
- Malcolm Home
- Akhter Hossain
- David Howells
- Jason Howitt
- Graeme Jackson
- Bevin Jarrott
- Trevor Kilpatrick
- Joe Hyun Kim
- Andrew Lawrence
- Robin McAleny
- Gawan McColl
- Paul McCrory
- Stuart McDougall
- Michael McKinley
- Colin Masters
- Clive May
- Tobias Merson
- Saul Mullen
- Jess Nithyanantharajah
- Lucy Palmer
- Clare Parish
- Steven Petrou
- Chris Reid
- Blaine Roberts
- Ingrid Schefter
- Daniel Scott
- Karin Sitte
- Suresh Sundram
- Seong-Sang Tan
- Lachlan Thompson
- Bradley Turner
- John Wade
- Jim Wiley

THE FLOREY FACULTY & SENIOR POSITIONS

SENIOR POSITIONS
- Florey Deputy Directors
  - Dr Henry De Alipurua
  - Professor Graeme Jackson
  - Professor Colin Masters

- Group Finance Director and Company Secretary
  - Mr Peter Plecher

- Flourney Executive
  - Associate Professor David Howells
  - Professor Geoffrey Donnan AO
  - Professor Graeme Jackson
  - Dr Henry De Alipurua
  - Professor Ingrid Schefter AO

- Professor Julie Bernhardt
- Professor Philip Beart
- Professor Seong-Sang Tan
- Professor Steve Petrou
- Mr Peter Plecher

- Professor Alan Connelly
- Professor Andrew Lawrence
- Professor Ashley Bush
- Professor Brian Dean
- Professor Colin Masters

- Professor Geoffrey Donnan AO
- Professor Graeme Jackson
- Dr Henry De Alipurua
- Professor Ingrid Schefter AO
We appreciate the generosity of our donors and would like to especially thank those who have given $100 or more during 2014.

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Marilyn Armstr...
OUR DONORS

We appreciate the generosity of our donors and would like to especially thank those who have given $100 or more during 2014

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Damien O’Shea
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Leo Spivak
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Domena Stavri
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The Myer Charitable Trust
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Matt Harry – Marathon for the community
SUPPORTING RESEARCH

We gratefully acknowledge the tireless efforts of people in the community who raise funds to support our research, and thank the donors who have supported them during 2014

One in Five
Alex & Karl Waddell – River’s Gift
Ayla’s Fund

Andrew and Claire Heenan – Cycling for Ben
City2Sea runners
Kingsley Just – Roll for Research

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Margaret Wilson
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Parkville Campus


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64. Miligan CL, Li MY, Petrou S. KCNT1 gain-of-function mutations linked to human epilepsy are modulated by quinidine. Molecular & Cellular Epilepsy (Accepted)

65. Wimmer VC, Li MY, Berkovic SF and Petrou S. Cortical microarchitectures change in genetic epilepsy. Neurology. Accepted


75. Miligan CL, Li MY, Petrou S. KCNT1 gain-of-function mutations linked to human epilepsy are modulated by quinidine. Molecular & Cellular Epilepsy (Accepted)

76. Wimmer VC, Li MY, Berkovic SF and Petrou S. Cortical microarchitectures change in genetic epilepsy. Neurology. Accepted


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"The human brain is fascinating, not only in the processes it supports when healthy, but also in the manner in which it "breaks down" in the face of insults, and the way it attempts to "right itself" when break down occurs. I want to understand how cognitive function is supported by brain networks, and how network disruption through epilepsy alters cognitive ability."

Dr Chris Tailby
FINANCIAL STATEMENTS

Consolidated Statement of Comprehensive Income
(For the year ended 31 December 2014)

<table>
<thead>
<tr>
<th>2014</th>
<th>$'000</th>
</tr>
</thead>
<tbody>
<tr>
<td>Revenues from ordinary activities</td>
<td>54,164</td>
</tr>
<tr>
<td>Salaries and employee benefits</td>
<td>(36,474)</td>
</tr>
<tr>
<td>Raw materials and consumables used</td>
<td>(3,793)</td>
</tr>
<tr>
<td>Conferences and collaborations</td>
<td>(5,562)</td>
</tr>
<tr>
<td>Building occupancy</td>
<td>(4,130)</td>
</tr>
<tr>
<td>Research support services</td>
<td>(2,779)</td>
</tr>
<tr>
<td>General administration</td>
<td>(2,844)</td>
</tr>
<tr>
<td>Distribution of grant funds</td>
<td>(3,799)</td>
</tr>
<tr>
<td><strong>Net operating deficit before depreciation, amortisation and impairment</strong></td>
<td>(1,217)</td>
</tr>
<tr>
<td>Depreciation and amortisation</td>
<td>(6,375)</td>
</tr>
<tr>
<td>Fair value adjustment of non-financial assets</td>
<td>2,133</td>
</tr>
<tr>
<td>Impairment of non-financial assets</td>
<td>(228)</td>
</tr>
<tr>
<td><strong>Net operating deficit after depreciation, amortisation and impairment</strong></td>
<td>(5,687)</td>
</tr>
<tr>
<td>Building project income</td>
<td>46</td>
</tr>
<tr>
<td>Expenses related to the building project</td>
<td>(859)</td>
</tr>
<tr>
<td><strong>Net deficit for the year</strong></td>
<td>(6,500)</td>
</tr>
</tbody>
</table>

Other comprehensive income:
- Net gain on revaluation of financial assets | 61 |

**Total comprehensive income for the year - deficit** | (6,439) |

**Total comprehensive income attributable to members of the entity - deficit** | (6,439) |

**SOURCES OF REVENUE (Year Ended 31 December 2014)**

<table>
<thead>
<tr>
<th>$’M</th>
<th>% OF TOTAL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Government bodies</td>
<td>34.7</td>
</tr>
<tr>
<td>Commercial income</td>
<td>6.9</td>
</tr>
<tr>
<td>Private donors</td>
<td>4.5</td>
</tr>
<tr>
<td>Peer review funding</td>
<td>4.4</td>
</tr>
<tr>
<td>Miscellaneous</td>
<td>2.1</td>
</tr>
<tr>
<td>Investment income</td>
<td>1.6</td>
</tr>
<tr>
<td><strong>TOTAL</strong></td>
<td>54.2</td>
</tr>
</tbody>
</table>

FINANCIAL STATEMENTS

Consolidated Statement of Comprehensive Income
(For the year ended 31 December 2014)

<table>
<thead>
<tr>
<th>2014</th>
<th>$’000</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>ASSETS</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Current Assets</strong></td>
<td></td>
</tr>
<tr>
<td>Cash and short-term deposits</td>
<td>27,312</td>
</tr>
<tr>
<td>Trade and other receivables</td>
<td>4,369</td>
</tr>
<tr>
<td>Available-for-sale financial assets</td>
<td>5,858</td>
</tr>
<tr>
<td>Prepayments</td>
<td>122</td>
</tr>
<tr>
<td>Inventory</td>
<td>73</td>
</tr>
<tr>
<td><strong>Total Current Assets</strong></td>
<td>37,734</td>
</tr>
<tr>
<td><strong>Non-Current Assets</strong></td>
<td></td>
</tr>
<tr>
<td>Property, plant and equipment</td>
<td>9,982</td>
</tr>
<tr>
<td>Investment property</td>
<td>5,546</td>
</tr>
<tr>
<td>Other assets</td>
<td>60,875</td>
</tr>
<tr>
<td><strong>Total Non-Current Assets</strong></td>
<td>76,403</td>
</tr>
<tr>
<td><strong>TOTAL ASSETS</strong></td>
<td>114,137</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>2014</th>
<th>$’000</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>LIABILITIES</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Current Liabilities</strong></td>
<td></td>
</tr>
<tr>
<td>Trade and other payables</td>
<td>4,445</td>
</tr>
<tr>
<td>Provisions</td>
<td>6,455</td>
</tr>
<tr>
<td>Income in advance</td>
<td>158</td>
</tr>
<tr>
<td><strong>Total Current Liabilities</strong></td>
<td>11,058</td>
</tr>
<tr>
<td><strong>Non-Current Liabilities</strong></td>
<td></td>
</tr>
<tr>
<td>Provisions</td>
<td>661</td>
</tr>
<tr>
<td><strong>Total Non-Current Liabilities</strong></td>
<td>661</td>
</tr>
<tr>
<td><strong>TOTAL LIABILITIES</strong></td>
<td>11,719</td>
</tr>
<tr>
<td><strong>NET ASSETS</strong></td>
<td>102,418</td>
</tr>
</tbody>
</table>

**Funds**
- Retained surplus | 40,739 |
- Unrealised investment reserve | 6,40 |
- Merger / reorganisation reserve | 61,019 |
| **TOTAL FUNDS** | 102,418 |

We acknowledge the Victorian Government’s strong support, particularly through funding from the Operational Infrastructure Support Grant. All funding received through the Department of State Development, Business and Innovation and other government agencies are expended on our research activities and services to support the science. We also thank the State and Federal governments, the Potter Foundation and the Myer Foundation for their huge support for the Melbourne Neuroscience Project including the building of our new facilities. We also gratefully acknowledge the support of the Victorian Department of Health through the provision of an ongoing mental health grant.
On November 20, 2014, the Florey family was shocked by the loss of Alan, a much-admired scientist and colleague. He was the friendliest and most enthusiastic of researchers – always ready to lend a hand or to share a joke. His care of his own staff was renowned. Alan’s research will stand the test of time, contributing to our knowledge of dementia and helping us find a way to understand this terrible disease. Alan was poised to make some major advances in the pursuit of a peripheral Aβ-related biomarker for Alzheimer’s disease. Working closely with Ben Gu and James Wiley, he was convinced that a solution to this quest was close at hand. It now remains to us, his colleagues, to continue this quest in his memory.

The Florey has established the Dr Alan Rembach Memorial Travel Scholarship. Each year, we will award a young, talented researcher with the opportunity to collaborate with colleagues overseas at a conference or in a laboratory. Alan’s enormous contribution to science will live on.
The Florey Institute of Neuroscience and Mental Health acknowledges the traditional owners of this land, the people of the Wurundjeri people and the Kulin Nations. We pay our respects to their elders, past and present. We would like to acknowledge that our three sites rest on this precious land.