Meet one of the Florey’s big thinkers.

A brain in a dish, perhaps?

USE IT OR LOSE IT  Can brain enrichment slow mental decline?

SCI-FI OR FOR REAL?  Meet one of the Florey’s big thinkers.
A brain in a dish, perhaps?
I hope you enjoy reading this new offering - a summary of the great research we’re doing and a chance to meet the people behind some of our most interesting discoveries.

The last 12 months have been packed with scientific activity. There have been significant advances in our knowledge of the brain - both at the laboratory bench and in the hospital setting. On the following pages, you’ll find features of hope and ambition as well as stories demonstrating the urgent need for cures of devastating diseases.

Those of us working at the Florey are constantly reminded of the task at hand. 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, will transform the human condition.

We are at a crucial time in neuroscience research and I believe, will transform the human condition.

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

The Florey is home to nearly 600 researchers from all over the world who collaborate in the world’s third most-cited neuroscience facility. It is heartening to witness causal scientific connections being made and robust discussions taking place in corridors and hubs.

We experience overwhelming support from the community. Diseases of the brain and mind touch the lives of so many people and we appreciate the passionate interest shown in our work. The scientists are inspired 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.

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. We are grateful for the Federal Government’s establishment of the fund and for the support from the Opposition, the Greens, the Palmer United Party as well as from independent cross-benchers. Hard to do better than that!

We simply must retain a vibrant medical research sector, creating high-tech jobs and, significantly, improve the health of people all over the world.

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 intervention. 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 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 care system and a capacity to contribute to the economy. We are on the brink of an exciting new era.

Thank you again to our dedicated scientists and to our generous supporters. Please enjoy reading this magazine and know you have helped make discoveries happen.

The knowledge gained over the next 20 years, I believe, will transform the human condition.
Can worms help us slow ageing?

With ageing being one of the main risk factors for most diseases, the humble worm is at the forefront of understanding why. Dr Nicole Jenkins and Dr Gawain McColl use the microscopic, transparent roundworm, C elegans, to investigate and manipulate the ageing process. The Florey has a thriving population of C elegans. Just like people, worms begin as a single cell, grow, learn, reproduce and age. An ageing worm has a lot in common with an ageing person; with increased fat deposition, age-related loss of muscle and loss of function in neurons. The beauty of the worm is its relative simplicity; while a human has billions of neurones, the worm has precisely 302, and their average lifespan is only 14 days. The similarity between genes and disease pathways in C elegans and humans offers a sensational opportunity to test new theories in simple creatures with similar workings to our own, using approaches not possible in people. And because one ‘worm week’ equates to about 40 human years, they make a great model of ageing.

The Florey is home to some of the most advanced imaging techniques in the country. Nicole Jenkins and Dr Gawain McColl use the microscopic, transparent roundworm, C elegans, to investigate and manipulate the ageing process. The Florey has a thriving population of C elegans. Just like people, worms begin as a single cell, grow, learn, reproduce and age. An ageing worm has a lot in common with an ageing person; with increased fat deposition, age-related loss of muscle and loss of function in neurons. The beauty of the worm is its relative simplicity; while a human has billions of neurones, the worm has precisely 302, and their average lifespan is only 14 days. The similarity between genes and disease pathways in C elegans and humans offers a sensational opportunity to test new theories in simple creatures with similar workings to our own, using approaches not possible in people. And because one ‘worm week’ equates to about 40 human years, they make a great model of ageing.

A new way of seeing

The Florey is home to some of the most advanced imaging specialists in the world. The techniques pioneered by our team - including structural, diffusion, and functional imaging – are continuing to expand our understanding of epilepsy and other disturbances of brain function. Neurologists, neuropsychologists, neuroscientists, physicists and engineers work together to understand the machinations of the brain. We’re determined to improve patient management and care, and believe that advanced imaging techniques will point the way to novel interventions. According to Dr Chris Taftby: “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 insult, and the way it attempts to ‘right itself’ when break down begins.”

One ‘worm week’ equates to about 40 human years. They make a great model of ageing.

Getting rid of bad memories

Dr Despina Ganella is studying how to reduce childhood and adolescent fear memories to lessen the burden of anxiety and its persistence into adulthood. Dr Ganella has also shown that childhood maltreatment leads to rapid growth of the pituitary gland during adolescence in females but not males. This highlights that females may be particularly vulnerable to early life stress. She now wants to translate preclinical findings from the lab bench to the clinic.

In 2014, Dr Tim Aumann analysed the human brains of people from Scotland who died in mid-summer (long days) or mid-winter (short days). He found four times more dopamine neurones in the midbrains of those who died in summer than winter. The work shows the adult human brain is far more adaptable than previously thought and our environment can alter the amount of dopamine. Given that dopamine is a ‘feel good’ chemical, this might explain why our mood is elevated during summer. More importantly, Dr Aumann’s research tells us that sunlight or physical activity like ballroom or tango dancing – something you don’t already know – might be helpful in treating a number of diseases linked with midbrain dopamine imbalances, such as Parkinson’s disease, schizophrenia, attention deficit and hyperactivity disorder and drug addiction.

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 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 down the road. 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.

Professors 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.

Dr 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 which 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 stutterer! It’s really heart-breaking to see these children suffering, and see their parent’s lives so affected by this 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 think 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 ‘everyone’s a lazy afternoon’s work’.

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

Good morning sunshine

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In the late nineties, Anthony Hannan, then a young postdoctoral scientist on a Nuffield Medical Fellowship at Oxford University, decided to challenge the conventional wisdom about Huntington’s disease.

Huntington’s is a degenerative, incurable condition, which combines three disorders in one – motor disorder whereby movements become uncontrollable (e.g. chorea), psychiatric symptoms (e.g. depression) and cognitive deficits (culminating in dementia). Its symptoms typically appear around middle age, although at least 5 per cent of patients suffer childhood onset. It is ultimately fatal.

The textbook Anthony was reading at the time also noted that it was 100 per cent genetically determined: a life sentence.

Anthony and colleagues put that assumption to the test by changing the environment of mice that had a genetic mutation for Huntington’s, giving the rodents enhanced cognitive stimulation by providing ladders, tunnels and mazes for them to play in, and also more physical activity. The findings were striking: the “environmental enrichment” delayed the onset of the disease.

The discovery in 2000, published in the journal Nature, was the first demonstration ever in any genetic model of a brain disorder that environmental factors could delay the onset or slow the progress of a disease.

Anthony, based at the Florey since 2002, has since advanced the idea that the brain can, indeed, change itself. He now heads the Florey’s Neural Plasticity laboratory, overseeing a number of research projects aimed at understanding how genes and environment contribute to specific brain disorders, among them Huntington’s disease (with a focus on dementia and depression), autism, schizophrenia and anxiety disorders.

“The brain is the most plastic organ in the body, the only organ that can continue to develop throughout our lives,” he says. “One key aspect of this ‘neuroplasticity’ is adult neurogenesis – the birth of new neurons in the mature brain.”

The notion of ‘neuroplasticity’ was popularised by Canadian psychiatrist Norman Doidge, who wrote a best-selling book about it in 2007. The idea is so popular, in fact, that when Anthony recently wrote a news article about the brain and environmental factors, it went viral.

Cafe owner Tony who is living with the Huntington’s gene chats to Professor Anthony Hannan about a healthy diet and, along with other lifestyle choices, the possibility of delaying the onset of Huntington’s disease.

Professor Anthony Hannan is pushing brain plasticity to delay the inevitable.

Anthony’s research started a conversation in the international Huntington’s community about what we could do, for the first time bringing a sense of control and optimism. It was game-changing.
The good news is that many of the lifestyle choices that are good for the body are also good for the brain.

So does Anthony practise what he preaches? “It’s hard when you are ‘time poor’ but I try to maintain a healthy diet, walk a lot and enjoy cycling and swimming; and neuroscience is certainly a mentally stimulating career!” he says. “My public health colleagues now tell me that ‘sitting is the new smoking!’”

A Melbourne man, Tony, who owns a café specialising in healthy take-away is living proof of Anthony’s findings.

Tony was tested for the Huntington’s disease gene mutation in 1998, and found to have inherited the disease. He has followed Anthony’s research closely over the years. “Because there isn’t any sort of treatment or cure, being diagnosed with Huntington’s can give you a feeling of disempowerment and isolation,” Tony says. “Anthony’s research started a conversation in the international Huntington’s community about what we could do, for the first time bringing a sense of control and optimism. It was game-changing.”

Tony does yoga most days, meditates, eats healthily, hikes and says his business gives him plenty of mental stimulation. “As soon as I got married and had kids I constructed a lifestyle I thought was going to give me the best shot at life.”

Tony, who’s 36, is symptom-free. His five-year-old twin sons, conceived by IVF, don’t have the gene.

Here’s a distillation of some of the latest thinking.

**FOUR KEY WAYS TO IMPROVE YOUR BRAIN HEALTH**

**1. Stay physically active**

This seems obvious, but not everyone realises physical activity is good for the body AND it boosts brain health.

The brain and body are in constant, dynamic communication. Muscles release beneficial molecules that reach the brain, and exercise stimulates the heart and other body systems, benefiting the brain. It may stimulate the generation of new brain cells and connections.

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

**2. 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 dementia.

Cognitive stimulation may build a “brain reserve”, protecting and compensating for brain ageing. So what mentally stimulating activities could you do?

**3. 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.

**4. 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.

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

It generates all of our thoughts, feelings and movements. Indeed, it’s fundamental to all of our conscious experience.

Brain diseases show how devastating it is when the brain degenerates, dragging the mind and its many wonderful capacities down. Clearly, it’s time we all focused more on this most important organ, to improve brain health throughout our lives.

**Take-home message**

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 brain 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 Flinders will deliver new treatments for devastating disorders such as Alzheimer’s disease and other forms of dementia.
This beautiful image, produced by the Florey’s Dr Verena Wimmer, shows part of the cortex. In this epilepsy study, subtle changes in the neural anatomy of the somatosensory cortex can be seen. The red staining identifies all neurones; blue and green stainings illustrate different types of inhibitory neurones. For more images like this, visit the 2014 Annual Report for the Florey Institute of Neuroscience and Mental Health at florey.edu.au

About The Florey

Scientific publications published over the 10 years, 2004-2014: 3429
Publications from the Florey in 2014: 488
Cumulative citations, 2004-2014: 59909
Average citation per publication, 2004-2014: 17.5

Citations

Outreach

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

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.

Research highlights

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 looking at the levels of that protein in patient blood samples to accurately predict changes in patients’ mental abilities.

Childhood epilepsy: The gene hunters
Professor Ingrid Scheffer 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 – 20 – of the 40 or so genes involved in causing epilepsy.

Stroke by the numbers: Save a minute, save a day
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 15 minutes saved on the average 70 minute wait for treatment could equate to an extra month of healthy life.

Our team

482
All staff

49
Administrative and scientific support staff

157
Postgraduate students

433
Researchers

28
Countries represented by our staff and students

Year 12 students: 900

Students from 24 schools learned about the life of a neuroscientist.

Adults: 2000

Visited to attend lectures about various diseases of the brain and our quest to improve lives through improved treatments and cures.

Students: 2500

From 24 schools learned about the life of a neuroscientist.
Connecting the dots

Dr Henry De Aizpurua is a deputy director at the Florey and the man responsible for its business development. During his 15 years at the Institute, he has witnessed an explosion in knowledge about neuroscience. He’s seen the Florey evolve to bring together the bulk of neuroscience expertise in Melbourne and become by far the largest independent neuroscience institute in the world.

He’s watched it grow in global relevance to become among the top three or four leading neurosciences institutes in the world. And, he says, there’s more to come – much more.

Henry 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.

“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.

“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 bulk of neuroscience expertise in Melbourne known as a ‘connectome’.

“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.

“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’ve relying on big clunky 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.

“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 lifestyle 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 already has a strong link with the ABC’s Active Memory is going to be pivotal in giving the public the information it 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.”

The Florey is, aspires to be, and will be, a global leader in delivering some of these life-changing opportunities.
The relentless quest to find answers.

by investigating post-mortem brain tissue from the Victorian Brain Bank Network at the Florey.

"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 medicines. It also markedly reduces the rate of suicide among this group.

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.

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 drug works 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.

"What's exciting is that there are drugs being developed as a result of our work that target that particular muscarinic receptor - they're probably going to be tested in humans in the next two or three years," 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 brain that identify people with schizophrenia who are at risk in childhood.

"We're certainly hot on the lead of something we think is potentially important," says Suresh.

"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."

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 these 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." 


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A associate Professors Suresh Sundram and Elizabeth Starr are conducting new and exciting research into schizophrenia that they hope will lead to blood tests to identify those with the condition who are at risk of suicide, potentially slashing the rate of suicide in this group.

As a young doctoral student, Elizabeth Starr had the unusual opportunity to talk with people who suffered the disorders she was studying.

Elizabeth, then at the University of Saskatchewan in Canada, heard first-hand accounts of the huge impact schizophrenia, bipolar disorder and depression had on the lives of the people she met through the course.

It was an eye-opener for the young neuropsychopharmacologist.

"I think that as a lab scientist you do get locked into your ivory tower, focussing 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 suffers the disorders she was studying.

"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.

We're certainly HOT ON the lead of something we think is potentially important.

Alexander Eastwood 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 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 research project on the schizophrenia 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 tested at the high-pitched sounds produced when mice '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 jigs all 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.

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.

"The Florey is an incredible launching pad - it’s stimulating, social and cosmopolitan."

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."
Major philanthropic support will fast-track research into motor neurone disease.

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 relentless 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 form of gene therapy to substantially increase the lifespan of MND mice.

The research builds on previous work Brad has done at Oxford University, looking at a gene involved in a childhood form of MND called Spinal Muscular Atrophy (SMA).

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 measurably 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.”

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.

He says that once the team has demonstrated that the tool brings about the same effect in the mice – a two-month increase in survival – they will adapt it to a clinical trial in humans.

“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.”

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.”

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“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. “When I first read about MND, I thought ‘it’s tragic and terminal’. Then I thought ‘I need to help solve this’. Tell people that I have a lifelong commitment to work on this disease.”

“The Florey’s a great place to work. It has prestige. It’s unique. I don’t know of many places that are working on so many neurological disorders under the one roof. That means great collaboration.”

“At the start of my PhD, people would ask ‘is there going to be a cure’ and I’d say I wasn’t sure. Now I tell people that it’s not a matter of ‘if’ but ‘when’. An effective treatment or cure is on the horizon.”

Brad Turner has a strong ally. Ian Davis, a medico living with MND, is driving a high-profile 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 Pearl 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
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.

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 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!”

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.”

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!”

STORY CONTINUES >>
In 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.

“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.”

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.

Daniel, who was 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.

“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,” he 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.”

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

Ultimately, we want to use the network changes we see in the brain to predict if someone will go on to develop dementia.
A changing world

The Federal Government’s National Health and Medical Research Council (NH&MRC) 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 NH&MRC 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 raise funds 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 develop effective treatments for illnesses that affect the brain.

We are heartened by the growth in our income from donations. In 2014 we raised $3.88 million from private donors and philanthropists, community fundraisers, trusts and foundations, and bequests. We feel tremendously privileged to receive support from the many individuals who respond to our appeal letters during the year. These gifts, small and large, come from across Australia and are crucial to our achievements. We thank all our donors for their loyal support.

As part of this program we are fortunate to attract funds from philanthropic trusts and foundations that enable research projects which are focused 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 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 thankful to the organisations with their expertise.

Endowment Investments

The Florey Annual | 2014

INCOME

SOURCES OF INCOME 2014

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ENDOWMENT INVESTMENTS

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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.

The Florey Institute of Neuroscience and Mental Health is one of the largest brain research centres in the world and the biggest in Australia. Our scientists share a common goal — to improve people’s lives through brain research and, ultimately, to influence global wellbeing and health economics.

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. We are addressing these conditions to avoid suffering and to contain health-related expenditure.

The Florey is a world-leader in imaging technology, genetics, stroke rehabilitation and epidemiological studies. Mental health research is a growing focus with psychotic illnesses and neurodegenerative diseases demanding attention.

We study:
- Addiction
- Alzheimer’s disease
- Autism
- Cardiovascular disease
- Mental illness
- Epilepsy
- Huntington’s disease
- Motor neurone disease
- Multiple sclerosis
- Parkinson’s disease
- Stroke
- Sudden infant death syndrome
- Traumatic brain and spinal cord injury

To keep up to date with Florey events, news and research, visit florey.edu.au or email: info@florey.edu.au

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