THE UNIVERSITY OF MELBOURNE

Melbourne Neuroscience Institute

2017 Annual Report

Editor: Amy Bugeja
Designer: External Relations 23201

For further information visit: www.neuroscience.unimelb.edu.au

Contents

CHAPTER 1

Executive Summaries

Message from the Director

It is with great pleasure that we table the 2017 annual report for the Melbourne Neuroscience Institute (MNI). The MNI has now been extant for 8 years and during that time it has unwaveringly served to promote the Neurosciences and related disciplines at the University of Melbourne. This report serves to demonstrate both the current strength of Neuroscience research on campus and the role that MNI has played in fostering many of these activities.

The spectrum of Neuroscience research conducted at this University is impressive and what is presented in this report is an important but, by necessity, a small proportion of the exciting work that is being conducted. What is very apparent is that much of the work relies on strong collaborative interactions and often those collaborative interactions span several faculties. I am particularly pleased to see this, reflecting that the promotion of interdisciplinarity that has been one of the key goals of MNI, an outcome that we have been able to facilitate via our interdisciplinary seed funding and fellowship programs.

The research highlights are as broad as they are impressive. They range from fundamental research in model organisms such as xenopus to the results of large scale clinical trials. They include pushing the boundaries of man-machine interface in the realm of biomedical engineering to the role of music therapy to alleviate disease burden in Alzheimer's disease. Importantly, the highlights also indicate that we are attentive to the landscape in which we work and to the ethical implications of the discoveries that we make.

During 2017, we have also been planning for roll out of a neuroscience PhD program in 2018 to assist in training and optimising the opportunities available to the next generation of neuroscientists that we are nurturing. This will build on the didactic coursework and advanced workshops that are already available to our students. New offerings will include a Student Association that will help to ensure the content of the program is relevant to graduate researchers, as well as opportunities for dedicated mentorship and an internship experience.

Our public seminars during 2017 have been spectacular, with a fitting finale being the No Bell Prize, our traditional send off for the year. In this event a hand-picked group of our best and brightest scientists either excel or embarrass themselves when attempting to explain their research in plain English to their colleagues and to the lay community. Other highlights included a sell-out event interrogating unexpected links between the gut and the brain and a fascinating 'through the looking-glass' perspective on how virtual reality can advance neurological and cognitive rehabilitation.

Our international interface continues to strengthen. This is most apparent through our strong links with the Salpetriere in Paris and with the Hotchkiss Brain Institute in Calgary. The interaction with the Hotchkiss has been particularly strong, with this being the third year of our post-doctoral and student exchange program. We also engineered a very successful workshop with the Hotchkiss held in Calgary in May 2017 which focused on fostering collaborative interactions in epilepsy research. Some 14 researchers from Melbourne attended that event. In addition, we are also on the cusp of establishing a strong interaction with the University of Bonn, focusing initially upon the Neuroscience of decision making.

Most importantly, a sincere thanks to the members of our Advisory Board, in particular the Chair, Mark Hargreaves, and to our host Dean, Shitij Kapur from the Faculty of Medicine, Dentistry and Health Sciences. I would also like to thank senior colleagues who participated in the biannual Neurosciences Coordination Forum, all of whom have given key strategic advice to enrich the activities of the Institute, for the benefit of our scientists and the community at large. Finally, I would like to express my deep gratitude to the executive of MNI, Andrew Metha, Vikki Marshall, Amy Bugeja and Carmel McFarlane who throughout 2017 have worked tirelessly for the University and for the welfare of the Neurosciences, in general.

Prof Trevor Kilpatrick
Director, Melbourne Neuroscience Institute

Message from the Dean

The Melbourne Neuroscience Institute (MNI) and neuroscience-related research at the University of Melbourne has had another exceptional year in 2017.

The MNI provides a significant opportunity for the University and the Faculty of Medicine Dentistry and Health Sciences to consolidate and focus its activities in the Neurosciences, a research discipline that we collectively identify as a priority.

Since its inception, the MNI has continued to act as a catalyst to break down silos and strengthen collaborative links between neuroscientists and those engaged in related disciplines within the academy, and with external partners.

The MNI has had considerable impact by fostering key initiatives such as the Centre for Neural Engineering, Stem Cells Australia, The Melbourne Brain Centre Imaging Unit, the Music Mind and Wellbeing Initiative and the Yulgilbar Young Clinicians Dementia Network.

Most recently, the Institute has guided the development of a Neuroscience PhD program for our graduate researchers which should act as a value-add to their experience at the University and assist in future vocation selection.

Collectively, MNI activities have resulted in robust collaborations that have united neuroscientists with psychiatrists, psychologists, engineers, mathematicians, physical scientists and also those engaged with the social sciences. Importantly, by promoting several important key interdisciplinary thematic research initiatives, Melbourne Neuroscience Institute has also provided high profile branding for University neuroscience.

As in previous years, the MNI has continued to fund innovative research by providing significant financial support to fellowships for postdoctoral researchers, interdisciplinary seed-funding and student stipends to some of our best and brightest.

Finally, I would like to extend my thanks to Professor Trevor Kilpatrick for his superb strategic vision and leadership as Director of the Melbourne Neuroscience Institute.

Prof Shitij Kapur
Dean, Faculty of Medicine, Dentistry and Health Sciences

CHAPTER 2

Research
Research Initiatives

Music, Mind and Wellbeing

Director: Prof Sarah Wilson
Deputy Director: Prof Gary McPherson

The Music, Mind and Wellbeing (MMW) group represents a unique set of collaborations spanning music, science, health, education, and industry. The past year has been another busy and successful one for the MMW initiative, with our team involved in a broad range of research endeavours, community, and public engagement events. Over this past year we have also been working hard to create a new and improved MMW website, which has given MMW's public profile a much needed 'refresh'. The website went live in November 2017 and it will continue to grow and develop throughout 2018 with the primary aim of enhancing our engagement with members of the research sphere and broader community. MMW also continues to expand and promote its research profile within the academic community, with 2017 seeing the launch of the first MMW Enhancing Research Networks Symposium, in addition to the ongoing annual MMW Postgraduate Symposium.

The research and interests of the MMW initiative combine three core research strands encompassing (i) music neuroscience, (ii) music education, and (iii) health and wellbeing. Through work conducted within and across these streams, MMW continues to investigate the intersection of music, the mind and its positive influence on our wellbeing. Our work promotes an understanding of the best ways to engage with music in a variety of settings, including schools, tertiary training programs, hospitals, aged and palliative care facilities, and the community. This has important implications for building inclusive communities that embrace diverse and creative participation. Our many community engagement activities provide a platform for us to communicate our research findings and educate around the power of music on the brain and psychological functioning, both in response to training in healthy individuals and as a tool for rehabilitation in individuals with brain injury and disease.

Professor Sarah Wilson

Music Neuroscience Program

Research in the music neuroscience program covers a variety of topics, including (i) examining cognitive and personality factors underpinning our ability to engage with music, (iii) using music with people with brain disorders, to help improve their health outcomes and further our understanding of music networks in the brain, and (iii) methods to enhance the effectiveness of music therapy, such as eye tracking to measure visual attention during therapy.

An exciting venture from the music neuroscience program is being led by the Director of MMW, Professor Sarah Wilson, and the Deputy Director, Professor Gary McPherson, with the support of national and international collaborators and Postdoctoral Fellow, Dr Yi Ting Tan. This program has received funding through the Australian Research Council (ARC) to continue pioneering research investigating the genetic basis of music abilities. Individual differences in musical ability have sparked intense debate around the relative importance of nature and nurture in shaping music abilities. Our study will use singing to explore this issue. Pilot data has already been collected using an innovative online singing program with over 100 twins, recruited with the support of the Australian Twin Registry, to examine the heritability of singing ability. Our results show promising effects that will are currently being fully investigated in a larger twin sample with the support of the ARC funding.

Postdoctoral Fellow, Dr Yi Ting Tan

Educational Research Program

Under the leadership of Deputy Director, Professor Gary McPherson, and Research Fellow, Dr Margaret Osborne, our educational research program has focused on identifying and strengthening enablers of optimal music performance in secondary and tertiary education settings, as well as psychological wellbeing in the broader population of amateur and professional musicians. Initial findings have been published from an international longitudinal research study into practice quality and skill acquisition in tertiary musicians. An innovative new teacher-directed online performance skills training program for secondary school students has commenced, helping to prepare young musicians to deal with the unique challenges and pressures of musical study. These studies provide practical recommendations for music learners and teachers to support optimal engagement, performance and wellbeing in music.

Health and Wellbeing Research Program

MMW's health and wellbeing research program continues to conduct innovative research into the therapeutic use of music, for people with conditions such as acquired brain injury, spinal cord injury, cardiac disease, motor neuron disease, Parkinson's disease, dementia, and post-traumatic stress disorder. This year saw MMW Research Fellow and Music Therapist, Professor Felicity Baker, awarded a World Federation Music Therapy award for significant contribution to the development of the profession through her work exploring the therapeutic uses of songwriting. Professor Baker continued to achieve success throughout 2017, as she, and her team, which included MMW members Dr Jeanette Tamplin and Dr Imogen Clark, were awarded a substantial NHMRC grant for their world-first study into the use of music therapy for people with dementia.

MMW Research Fellow, Professor Felicity

MMW Research Fellow, Dr Jeanette Tamplin, testing the virtual therapy environment

MMW Research Fellow and Music Therapist, Dr Jeanette Tamplin, continued to receive significant public recognition for her research into a telehealth application for music therapy. Her work aims to develop an online virtual reality platform designed to deliver telehealth group singing interventions for people with quadriplegia to improve respiratory function, voice, mood, and social connectedness. The project involves the design and testing of a virtual environment (such as singing around a campfire) that will enrich both the group's experience and the participant's motivation to sing. New advancements in virtual reality technology are being incorporated into the environment to enhance the depth of the group's participation experience. As a result of her work on the Music Therapy and Virtual Reality, Dr Jeanette Tamplin, was a 2017 National Disability Award Finalist for Innovation.

Outreach and Education

The MMW community engagement program aims to promote new public attitudes that foster grass roots participation in music. In 2017, this involved a series of public events ranging from academic and public lectures to showcasing our work on ABC's Catalyst TV program, aired in October 2017. The latter featured the research of Professor Wilson and her collaborators on the genetic basis of singing and music ability as part of a special episode devoted to twins in medical and scientific research. As part of this episode, MMW Postdoctoral Researcher Dr Yi Ting Tan, in partnership with the Australian Twin Registry, demonstrated our data collection techniques using an innovative online singing program with the twins, as part of the ARC funded project exploring the genetic basis of musical ability.

Public Lecture Series: 'Music on the Mind'

'Music on the Mind' is a popular public lecture series co-hosted each year by MMW and the Melbourne Recital Centre since 2010. In 2017, this included two lectures from the MMW initiative, addressing the topics of 'Music and Trauma Recovery' and 'the Genetic Basis of Singing: Twins and Musical Ability'. The latter included a live performance of identical twins with absolute pitch singing together in harmony, which was a real highlight. This series has led to greater public engagement in music research, not only through sell-out attendances but also through interviews and articles in print, radio and online about our presentations and research.

MMW Enhancing Research Networks Symposium

MMW is committed to engaging with community organisations to foster an ongoing collaborative approach to music research and community-based interventions within Australia. To this end, MMW launched their first Enhancing Research Networks Symposium in late 2017, to bring together a number of community organisations and offer them the opportunity to present on their recent developments in research and community engagement. The aim of the symposium was to provide a forum for open discussion about potential collaborative endeavours with MMW at a community level for 2018.

MMW Postgraduate Symposium

MMW seeks to promote the careers of early researchers to foster the capacity for music research in Australia. In late 2017, MMW held its annual Postgraduate Symposium at The University of Melbourne, following the success of the inaugural Postgraduate Symposium in 2016. This event showcased some of the latest research being conducted by our postgraduates, with topics ranging from the neuroprotective benefits of music training for cognitive difficulties in people with epilepsy to exploring how rhythm synchronicity in drumming can foster prosocial behaviour between people.

Partnerships and goals for 2018

The MMW research program is underscored by highly-effective partnerships and interest from a wide range of research and service providers, including research collaborations with the Florey Institute of Neuroscience and Mental Health, the Networked Society Institute, The Centre for Neuroscience of Speech, Parkinson's Victoria, Austin Health, Melbourne Health, Monash Health, Calvary Healthcare, and the National Disability Insurance Agency. MMW also disseminates research and engages the public in collaboration with the Australian Music Centre, The Music Trust, The Centre for Cultural Partnerships, the Australian Music Therapy Association, The City of Melbourne, Places Victoria, and the Melbourne Recital Centre, and provides ongoing advice and consultancies for the Victorian State Government (VCAA) and the Federal Government.

In 2018, MMW will continue to maintain its strong public engagement profile and innovative research programs with plans already underway for collaboration on international conferences and continuing the successful symposia and community engagement events held this year. In 2018, there will be a strong focus on fostering collaborative partnerships with various community organisations, with the aim of developing a post-doctoral research scholarship that will directly benefit community participation in music.

Melbourne Brain Centre Imaging Unit

Director: Prof Roger Ordidge
Research Fellows: Dr Brad Moffat (senior);
Dr Amanda Ng; Dr Sonal Josan; Dr Jon Cleary

The Melbourne Brain Centre Imaging Unit supports a broad spectrum of research into the structure and pathology of humans. The Unit hosts two flagship scanners: a Siemens PET/CT scanner and a 7T Siemens MR Research scanner, both for human studies. This world-class facility was funded by the University of Melbourne, the Florey Institute for Neuroscience and Mental Health, the National Imaging Facility (NIF) and the Victorian Biomedical Imaging Capability (VBIC).

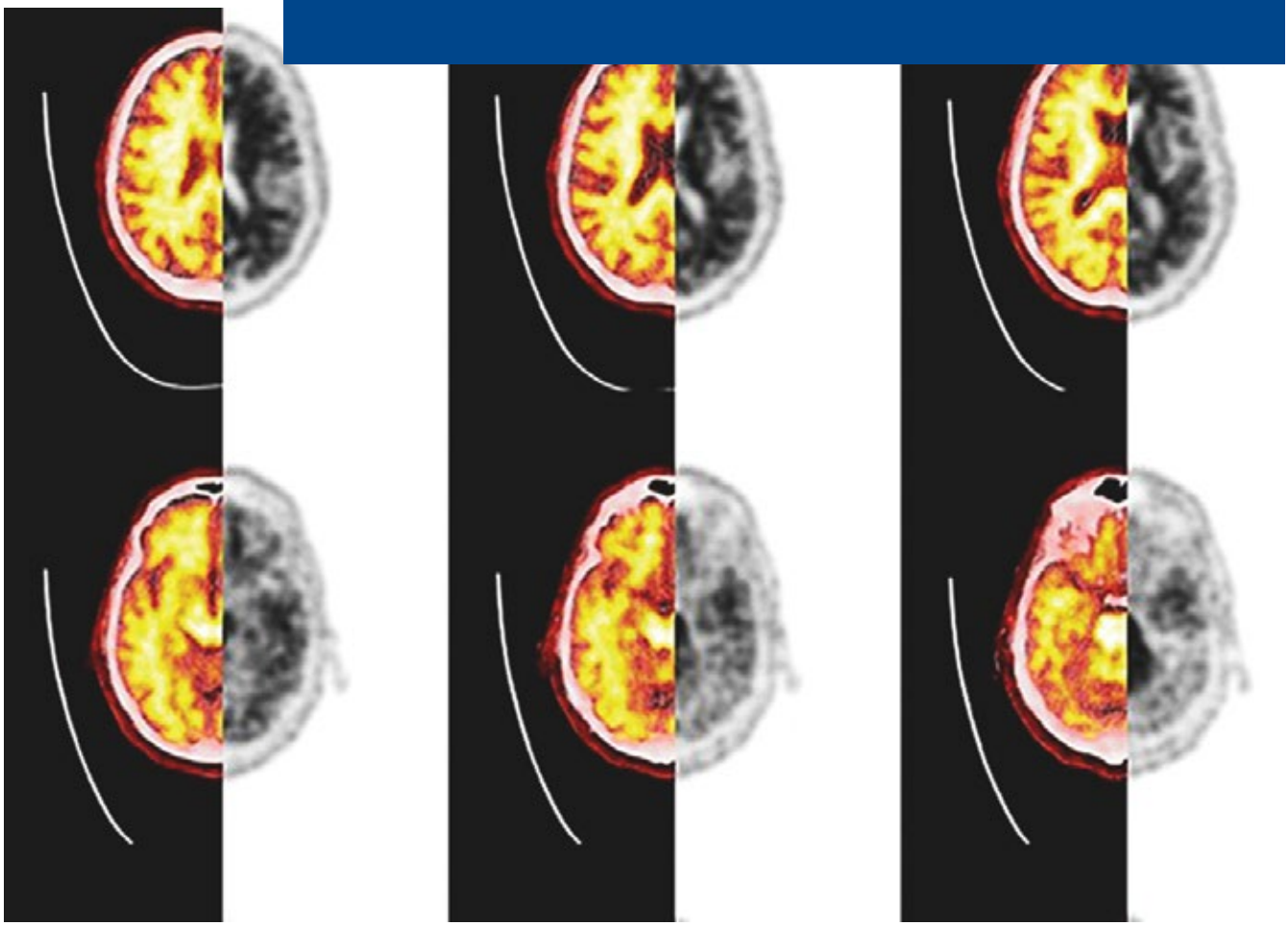
Research

PET/CT scanner

The PET/CT scanner is being used by researchers from the University of Melbourne, the Florey, and by many external research institutions and companies. A principal project is the measurement of beta-amyloid (Aβ) plaques relating to the development of Alzheimer's Dementia, but projects also include trials of new radiopharmaceuticals and CT on animal and human anatomical samples.

PET tracer studies show changes up to 30 years before symptoms of Alzheimer's appear. PET/CT scans are used to measure the amount of Amyloid plaque accumulating in the brain over these mid-life decades prior to the onset of symptomatic Alzheimer's Disease. According to Colin L Masters MD, Laureate Professor of Dementia Research:

> **"These scans are now used to evaluate, target and manage a range of putative therapies designed to prevent this terrible disease."**

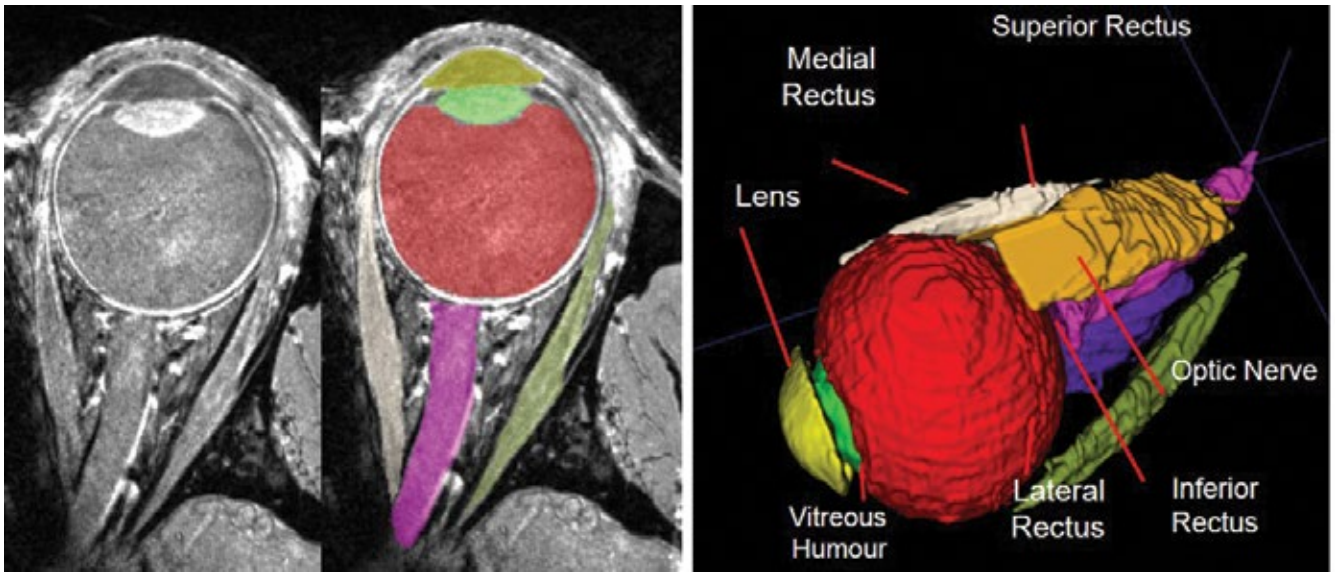


Flutemetamol PET tracer images are shown in color on the left next to CT scans of the contralateral brain regions on the right in the multi-section image of the human brain. Courtesy of Prof Rowe and Rob Williams

The 7T MRI scanner

The 7T MRI scanner is being used to develop new MRI scan protocols that utilise its high magnetic field (7 Tesla) to obtain new contrast and image sensitivity to human brain disease. Studies in Multiple Sclerosis and Alzheimer's Disease are underway. Delivery of an eye coil in 2017 which enables dedicated ocular imaging at high resolution has been a welcome new development (Figure 2).

Interrogation of the eye provides a 'window into the brain' for the study of many brain disorders using MRI in conjunction with standard optical techniques. We have also recently added a cervical spine MRI coil for imaging the upper spinal cord to further facilitate a number of studies, for example participants with multiple sclerosis.



Images obtained using new eye coil and anatomically segmented in coloured regions. Courtesy of Dr J Cleary and Rebecca Glarin.

Partnerships and goals for 2018

- Florey Institute for Neuroscience and Mental Health
- The National Imaging Facility (NIF)
- The Victorian Biomedical Imaging Capability (VBIC)
- Siemens Medical Systems
- Cyclotek Ltd
- Monash University
- The Royal Melbourne Hospital

Our continuing goals for 2018 include:

- Expansion and refinement of research studies for both the PET/CT and 7T MRI scanner.
- Research and development of new techniques for high field MRI scanning.
- Testing of new radiotracers for PET/CT scanning, particularly to further studies of the detection and treatment of Alzheimer's Disease.
- Improvement of work practices, computing and facility lay-out to provide a more efficient and convenient platform for research studies.

Stem Cells Australia

Program Leader: Professor Melissa Little Deputy Program Leader: Professor Christine Wells. Head of Education, Ethics, Law & Community Awareness Unit: Associate Professor Megan Munsie

Stem Cells Australia (SCA) is the Australian Research Council's Special Research Initiative in Stem Cell Science, bringing together leading researchers from across Australia to explore the potential role of stem cells in a range of currently intractable diseases.

This unique collaboration links leading experts from across Australia to develop novel approaches to address stem cell regulation and differentiation. In addition to supporting excellence in stem cell research, SCA also leads public debate and discussion about important ethical, legal and societal issues associated with stem cell science, and provides core service to support the stem cell research community.

This year, we welcomed a new leadership portfolio to the initiative: Professor Melissa Little and Professor Christine Wells. Professor Melissa Little, Program Leader, is based at the Department of Paediatrics, University of Melbourne and the Murdoch Children's Research Institute, and brings a wealth of experience to the role.

Professor Little has a strong vision for the future of Australian science in this important area of medical research. Joining Professor Little in the leadership team is Professor Christine Wells, Director of the University of Melbourne's Centre for Stem Cell Systems, who took on the role of Deputy Program Leader.

The initiative was successful during 2017 in securing an additional year of funding under the Australian Research Council Special Research Initiative scheme. This support will allow collaborative stem cell research across more than a dozen Australian universities and medical institutes to extend the fundamental understanding of stem cell science, ultimately lead to new ways to diagnose, understand and treat disease.

Research Highlights

Four main areas of stem cell biology were the focus of SCA's research activities in 2017 – control of pluripotency and reprograming, regeneration and repair in the brain, regeneration and repair in the heart and the development of blood – with members contributing to over 140 publications in prestigious journals such as Blood, Cell Stem Cell, Nature Biotechnology, Nature Communications, Nature Genetics and Nature Immunology.

Within the Neural Regeneration and Repair theme, led by Professors Perry Bartlett and Trevor Kilpatrick, several important discoveries were made. Working with Professor Perry Bartlett was Dr Dhanisha Jhaveri from the University of Queensland, who discovered a new population of adult brain stem cells in the amygdala, the region of the brain involved in fear learning and processing emotions. These finding have important implications for age- and mood-related disorders. Professor Perry Bartlett's team have also shown that the brain's immune cells respond to exercise by producing new neural cells.

The Kilpatrick laboratory at the University of Melbourne and the Florey Institute continues to explore ways to harness the activity of inflammatory cells known as microglia - normally resident within the brain - for therapeutic benefit. Neonatal microglia have been isolated and injected into the adult central nervous system to determine whether they can transform the microenvironment to one that is conducive to endogenous repair. Ultimately human induced pluripotent stem cells will be used to derive microglia-like cells for therapeutic testing. Members contributed to key review in Nature Reviews Neurology outlining how regenerative therapies could be applied to multiple sclerosis.

The laboratories of Associate Professor Clare Parish and Dr Lachlan Thompson at the Florey continued to develop and refine their capacity to generate specific subsets of neurons from stem cells in vitro and to transplant these cells to understand their function and potential, for example, to treat Parkinson's disease. Neural cell lines have also been generated that carry suicide genes to enable unequivocal establishment of the efficacy of the transplanted cells in experimental models and to establish a 'fail safe' approach by which transplanted cells could be killed if their behaviour become dysregulated in clinical trials.

Computational biology is also a strength of Stem Cells Australia. Researchers from Australia, including Professors Christine Wells and Alistair Forrest, and from Japan have completed landmark studies in non-coding RNA. These studies, published in Nature, reveal how non-coding RNA regulates the flow of genetic information in different tissues; disruption of this flow may lead to many different disease types, including cancer. The team also mapped, at an unprecedented scale, the level of thousands of non-coding RNA in hundreds of human cell types. This information was developed into a free online map that allows anyone to explore the patterns of microRNAs across tissues of the body.

Professor Melissa Little

Professor Christine Wells

Twenty-one of Australia's best scientists have been elected to the Australian Academy of Science for their outstanding contributions to science. Amongst the 2017 Fellows are Professor Melissa Little, Stem Cells Australia's Program Leader and Theme Director of Cell Biology at the Murdoch Children's Research Institute, and Professor David Gardner, reproductive biologist at the University of Melbourne and a Chief Investigator in our consortium.

The calibre of Stem Cells Australia's young scientists was also recognised: Dr Ben Cao from CSIRO received the prestigious Gilead award for his project in inducing drug-resistant leukemic cells to become sensitised to chemotherapy.

Outreach and Education

Throughout 2017 Stem Cells Australia has partnered with key national and international research organisations, patient advocacy groups, teacher associations, academics, industry and professional bodies to deliver a suite of educational activities. We have also continued to raise awareness about the policy implications of stem cell research, especially related to the sale of unproven stem cell 'treatments' in Australia and abroad. We welcomed the announcement that the Australian Government will introduce regulatory changes in 2018 to address the sale of unproven stem cell treatments, increasing safeguards to protect patients from harm and bringing Australia into alignment with international standards. The changes will be made to ensure the Therapeutic Goods Administration (TGA) will have greater regulatory oversight of the manufacturing and clinical use of autologous cells and tissues of this area.

Stem Cells Australia continued to work closely with high school teachers and students in an effort to take our research out of the lab and into the classroom. Joint events with specialty life sciences education initiatives such as Gene Technology Access Centre (GTAC) and the Melbourne Neuroscience Institute were successful in engaging students and teachers with stem cell science.

Continual engagement with the community is imperative to the Stem Cells Australia initiative through public forums and media outreach. Associate Professor Megan Munsie was the keynote speaker at MOVE Koadlow Public Lecture: stem cells and muscle, bone and joint health, and was also invited to participate in a number of podcasts and interviews.

Partnerships

Collaboration is core to SCA operations. Our initiative involves researchers from the University of Melbourne, the University of Queensland, the University of New South Wales, the Victor Chang Cardiac Research Institute in Sydney, the Walter and Eliza Hall Institute of Medical Research (WEHI), FINMH, Monash University, CSIRO Material Science Division and Murdoch Children's Research Institute, with additional partners joining in 2018.

Goals for 2018

As we head towards our seventh year of funding we build on key research outcomes and incorporate new partners into the initiative. Stem Cells Australia is now poised to harness the immense potential of stem cells for new diagnostic, therapeutic and biotechnological applications. In the next twelve months SCA will be seeking to:

- Transition to our three new research themes: Regenerative Medicine, Disease Modelling and Designer Cells
- Further strengthen the collaborative focus within our current research portfolio
- Expand our national and international collaborative networks across bioengineering, nanotechnology, stem cell biology, advanced molecular analysis, clinical research and industry
- Continue to call for regulatory reform to curb the sale of unproven stem cell treatments in Australia
- Continue to provide bespoke educational opportunities for high school students, teachers and the public.

Within the Parkville Precinct we will support neuroscience researchers at the University of Melbourne and the Florey through:

- Access to the latest high-end flow cytometric machinery and services in located Flow Cytometry Facility,
- Establishing stem cell platforms to investigate the genetics of epilepsy, the pathogenesis of Alzheimer's disease, and brain repair, and convening seminar and postgraduate student programs.

Centre for Neural Engineering

Director: Prof Stan Skafidas
Deputy Director: Prof Steven Petrou

The Centre for Neural Engineering (CfNE) is an interdisciplinary centre, established to undertake research in neuroscience and neural diseases. The CfNE draws together leading neuroscientists, neurologists, psychiatrists, cell biologists, geneticists, electrophysicists, chemists, physicists and engineers from the University of Melbourne and partner institutions.

Research Highlights

A Label-Free, Quantitative Fecal Hemoglobin Detection Platform for Colorectal Cancer Screening

In collaboration with Professor Patrick Kwan, in the Department of Medicine, Professor Stan Skafidas and his team have demonstrated a proof of concept for an early diagnostic test for colorectal cancer screening. The early detection of colorectal cancer is vital for disease management and patient survival. Fecal hemoglobin detection is a widely-adopted method for screening and early diagnosis. Fecal Immunochemical Test (FIT) is favoured over the older generation chemical based Fecal Occult Blood Test (FOBT) as it does not require dietary or drug restrictions, and is specific to human blood from the lower digestive tract. To date, no quantitative FIT platforms are available for use in the point-of-care setting. The team reported in the journal Biosensors proof of principle data of a novel low cost quantitative fecal immunochemical-based biosensor platform that may be further developed into a point-of-care test in low-resource settings and that is comparable to that of conventional laboratory based quantitative FIT diagnostic systems.

Inflammation and Microglia

Working together with Professor Stan Skafidas and Dr Babak Nasr based at the CfNE, Ms Emma Byers, an honours student within the IBP laboratory has utilised state of the art helium ion microscopy (HIM) to generate new and exciting data related to understanding how the brains immune cells, microglia, respond to inflammation. Microglia are increasingly being implicated in the underlying causes of Autism Spectrum Disorder (ASD) and other complex psychiatric disorders such as schizophrenia due to important roles in regulating inflammation within the brain and because of their more recently identified roles in being able to prune connections (synapses). Moreover, microglial and synaptic abnormalities have been seen in both ASD and schizophrenia. Using HIM, this project involved activating microglia with the inflammatory molecules lipopolysaccharide (LPS) and interferon-gamma (IFN-) and for the first time relating ultrastructural changes in the morphology of these cells to the release of pro-inflammatory cytokines. We have demonstrated that upon activation with both LPS and IFN- and the release of the pro-inflammatory molecules, IL-6 and TNf-alpha, that there is collapse of processes and flattening of the cell surface of microglia. Conversely, treatment with the anti-inflammatory cytokines IL-4 or IL-10 leads to reduced pro-inflammatory molecules and the generation of processes of microglia that resemble non-treated controls. This work has important implications for understanding microglial functions, with implications across many neurological disorders where microglia are known to be perturbed.

Making Astrocytes and Microglia from Stem Cells

In collaboration with Associate Professor Mirella Dottori, we have started developing protocols to produce astrocytes and microglia from stem cells derived from individuals with ASD. Ms Liliana Laskaris, a PhD student within the IBP laboratory has demonstrated that stem cells can be used to generate cells that express microglial markers. This work is ongoing and provides important tools to allow us to grow astrocytes and microglia in the dish from living individuals with ASD to try and recapitulate the characterisation of both abnormal and reactive cells that exist within the brain of these people for translational outcomes.

Inflammation, Astrocytes and mGluR5

In collaboration with Dr Karen Gregory and Professor Arthur Christopolous at MIPs, Ms Ting Lee, a PhD student within the IBP laboratory has demonstrated that mGluR5 may play a role in regulating the activity of astrocytes, a key brain cell that is responsible for providing structural and functional support within the brain. This project involved the activation of astrocytes with an inflammatory molecule, polyinosinic-polycytidylic acid (poly I:C) and the measurement of the number of mGluR5 receptors they express. We have demonstrated that in activated astrocytes there was a decrease in the number of mGluR5 receptors, corresponding to the release of pro-inflammatory molecules. This result is interesting providing a link between the observations that inflammatory changes are present within the brains of individuals with ASD and our previous work that there is decreased expression of mGluR5 in these people. Ongoing work for this project involves using drugs to alter mGluR5 signalling so that we can assess whether it is possible to reduce levels of pro-inflammatory molecules in activated astrocytes.

No preliminary evidence of differences in astrocyte density within the white matter of the dorsolateral prefrontal cortex in autism

While evidence for white matter and astrocytic abnormalities exist in autism, a detailed investigation of astrocytes has not as yet been conducted. Such an investigation is further warranted by recent observation that neuroinflammation is implicated in the pathogenesis of autism, with astrocytes being key players in this process. We have now assessed astrocyte density and morphology within the white matter of the dorsolateral prefrontal cortex (DLPFC) in individuals with autism.

Sections of DLPFC white matter from individuals with autism (n = 8, age = 4-51 years) and age-matched controls (n = 7, age = 4-46 years) were immunostained for glial fibrillary acidic protein (GFAP). The density of astrocytes and other glia were estimated via the optical fractionator, astrocyte somal size estimated via the nucleator, and astrocyte process length via the spaceballs probe.

We found no evidence for alteration in astrocyte density within DLPFC white matter of individuals with autism versus controls, together with no differences in astrocyte somal size and process length.

Our results suggest that astrocytic abnormalities within the white matter in the DLPFC in autism may be less pronounced than previously thought. However, astrocytic dysregulation may still exist in autism, even in the absence of gross morphological changes. Future investigations would benefit from assessing functional markers of astrocytes in light of the underlying pathophysiology of autism.

A Silk Fibroin Bio-Transient Solution Processable Memristor

Jason Yong has been working on bio-resorbable, environmentally friendly, transient integrated circuits which represent a new class of electronics pave the way towards new possibilities in the fields of environmental monitoring, biomedical diagnostics, sensors and the emerging field of electroceuticals. This new class of devices is capable of robust and reliable operation even when embedded within living tissue, and without causing deleterious inflammatory reactions. Importantly, they can dissolve after use, circumventing the need for their retrieval and disposal from the environment or in biological applications their removal, thereby reducing risk associated with added surgical procedures. Today's electronic devices are typically fabricated using highly toxic materials and processes which limits their applications in environmental sensing applications and mandates complex encapsulation methods in biological and medical applications. Our recent development is a fully resorbable, high density bio-compatible and environmentally friendly solution processable memristor (a form of memory device) using silk fibroin protein, which should have great utility in a broad range of applications.

Research
Research Highlights

Breakthrough: Medicinal cannabis and severe epilepsy

A major scientific breakthrough finds that a type of medicinal cannabis significantly reduces convulsive seizures in children with a severe form of epilepsy

By Imogen Crump, University of Melbourne

A form of medicinal cannabis has for the first time been shown to reduce seizures in a severe form of epilepsy, with a few children now seizure free after taking it.

A study of children suffering from Dravet syndrome, a severe epilepsy that begins in infancy with drug-resistant seizures and a high mortality rate, found that 5 per cent of subjects reported that seizures stopped after being treated with cannabidiol, a non-psychoactive form of cannabis. Overall 43 per cent of children with the syndrome had a 50 per cent reduction in seizure frequency with cannabidiol.

An international team of researchers including University of Melbourne Chair of Paediatric Neurology and Austin Health Director of Paediatrics, Professor Ingrid Scheffer, studied cannabidiol for the treatment of seizures. The results are published in The New England Journal of Medicine.

Known as CBD, cannabidiol is a natural compound found in cannabis seeds, stalks and flowers, that does not have the psychoactive properties of tetrahydrocannabinol, or THC.

“This is a major scientific breakthrough,” says Professor Scheffer. “It’s the first scientific evidence that cannabidiol works. There have been anecdotal reports in the past, and people with firm beliefs that it works in epilepsy, but this is the first time it’s been proven.”

The trials saw 120 children and young adults across the US and Europe receive cannabidiol or a placebo, in addition to standard anti-epileptic treatment. The research was conducted for the Cannabidiol in Dravet Syndrome Study Group, and was a randomised, double-blind and placebo-controlled trial.

Researchers measured seizure frequency over a 14-week treatment period while the trial was underway. They found that the average frequency of convulsive seizures per month decreased from 12.4 to 5.9 among those children on cannabidiol, compared with a decrease from 14.9 to 14.1 among those on the placebo.

“I am delighted that we finally have high-level evidence that cannabidiol is effective for uncontrolled seizures in Dravet syndrome,” says Professor Scheffer.

Read full article: https://pursuit.unimelb.edu.au/articles/breakthrough-medicinal-cannabis-and-severe-epilepsy

"If you can render any child or adult seizure free, that's huge. It could contribute to stopping any further deterioration, or help development in a positive sense."

Can sunshine help your brain?

New research suggests adequate vitamin D in midlife may help women maintain at least some of their brain power as they age

By Cheryl Critchley, University of Melbourne

A sunny day can make you feel happy, but it may also help retain some of your cognitive powers. New research suggests that vitamin D, often obtained through sun exposure, might be good for our brains, particularly those of women.

The observational study, published in Maturitas, investigated the association between midlife vitamin D levels and cognition in Australian women over 10 years. It used data involving 252 participants aged 55-67 from the Women's Healthy Ageing Project.

The study found that sufficient midlife vitamin D levels, which works out to be more than 25 nanomoles per litre (25nmol/L), were associated with improved aspects of executive function in ageing. It also identified a potential midlife window where ideal levels of vitamin D could protect against some types of cognitive decline.

Lead author Dr Alicia Goodwill, an Honorary Fellow at the University of Melbourne's Department of Medicine (Royal Melbourne Hospital), says executive function relates to a number of processes and cognitive control functions.

"These include attention, cognitive inhibition, cognitive flexibility and working memory," she says. "In this study, the main processes of executive function assessed were cognitive flexibility and attention."

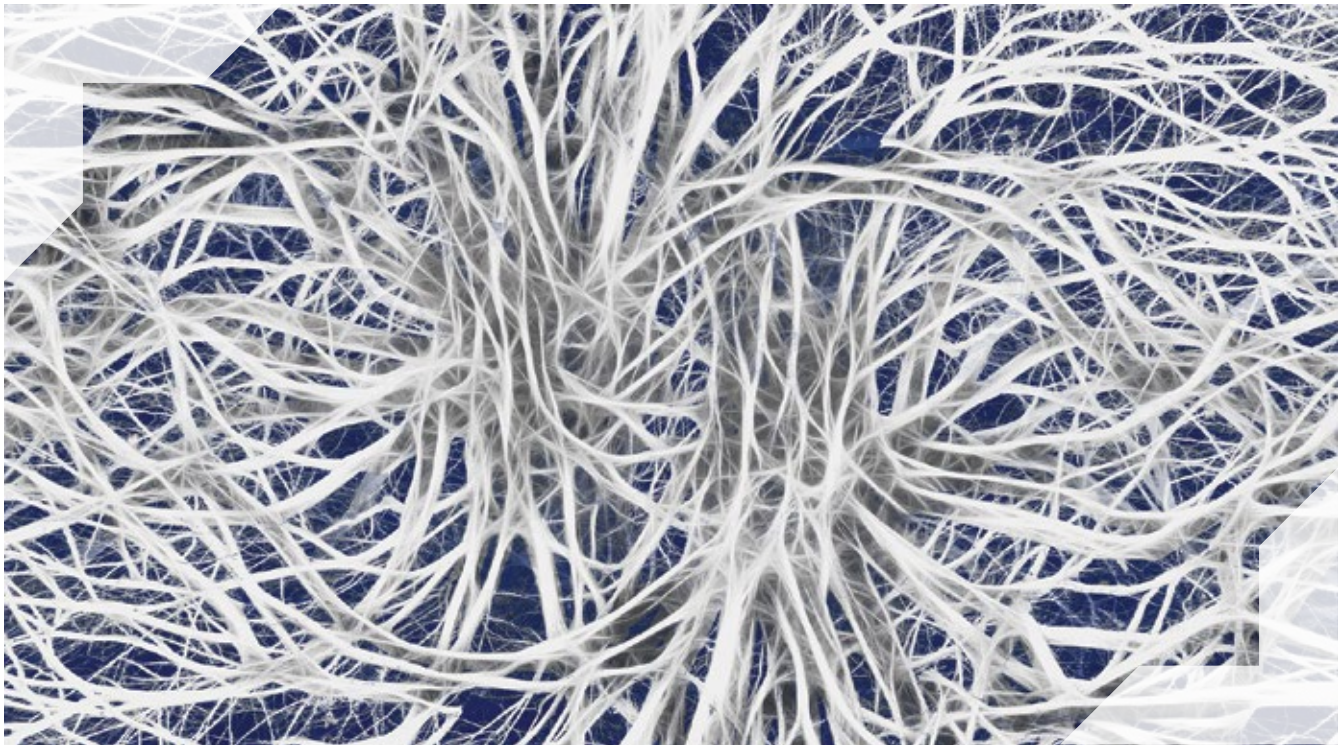
The researchers found that although there was some evidence to suggest a more pronounced effect of vitamin D status on cognitive processes in women, until now no study had followed this association from midlife to late-life.

Women (age range 55-67 years) with vitamin D levels above 25nmol/L maintained better executive functioning in late-life, in particular improved cognitive flexibility, attention and psychomotor speed," it found.

Memory did not appear to be affected by vitamin D levels in this study, but Dr Goodwill says that declines in memory performance often occur later than other cognitive domains, and may not be clinically detectable until women reach their seventies.

She says the findings are another potential piece in a research puzzle that has identified dementia risk factors such as type 2 diabetes, hypertension, obesity, smoking, depression, physical inactivity, and low cognitive stimulation or low education.

Read full article:
https://pursuit.unimelb.edu.au/articles/can-sunshine-help-your-brain?



Breakthrough in motor neurone disease research gives hope

Copper could hold the key to a radical new treatment to help those affected by this indiscriminate and fatal disease

By Florienne Loder, University of Melbourne

When a person is diagnosed with Motor Neurone Disease (MND), it's a race against time. Symptoms are severe – muscle weakness, cramps, slurred speech, weak grip, fatigue, pain, insomnia, behaviour changes and a constant dry mouth. Many sufferers do not survive more than five years because the progressive destruction of their brain's neurons that control muscles means lung failure is inevitable. There is no cure.

The lack of an effective treatment haunts sufferers, but now, after 10 years of work by researchers at the University of Melbourne, Bio21 Molecular Science and Biotechnology Institute and the Florey Institute of Neuroscience and Mental Health, a human trial for a drug that could fight this devastating disease has begun.

This high-stakes research to create a treatment for such an unforgiving disease is thanks to a collaboration between three scientists, Associate Professors Kevin Barnham, Anthony White and Paul Donnelly, who have been the driving force behind this discovery.

Cu(-ATSM), the drug to treat MND, entered phase I clinical trials at Macquarie University in November. But before it could reach human trials, there was years of hard work, Associate Professor Barnham says.

"The initial focus of our work was on Alzheimer's disease where it was thought that copper drove the formation of amyloid plaques. We reasoned if you could just remove this copper you could eliminate plaques, and you'd have the solution," says Associate Professor Barnham. And so research focused on reducing plaques.

"Then we thought, perhaps it's the other way around? Maybe cells are expelling the copper and so we've actually got a situation of copper deficiency. So, what happens if you deliver the copper back?"

What was needed was a way of delivering copper back into the brain cells. Serendipitously, this is when Associate Professor Barnham was introduced to Associate Professor Donnelly, who was already working on such molecules.

"I had made 35 different copper compounds, which I gave to Kevin and Tony to test," Associate Professor Donnelly says.

For Alzheimer's disease, the compound was Cu(-GTSM). As it is stable in biological systems, and cell permeable, it can cross the blood-brain barrier and then release copper.

"This gave us the perfect way to test the effect of copper, because we had a perfect control in a related compound, Cu(-ATSM) that, under normal conditions, does not deliver copper," Associate Professor Barnham says. Equipped with the two compounds Cu(-GTSM) and Cu(-ATSM), the team began conducting their experiments.

Both patients and researchers are hopeful. However, the issue of funding remains a sticking point for essential future research.

"We are just scratching the surface of the mountain of compounds Paul has developed," Associate Professor White says. "If we have one drug in clinical trials from the first 20, how many more potential clinical drugs exist in Paul's library of hundreds?"

"The compounds are there, the knowledge to investigate is there, the techniques exist, we just need funds for researchers to do the work."

Read full article: https://pursuit.unimelb.edu.au/articles/breakthrough-in-motor-neurone-disease-research-gives-hope?

Predicting epileptic seizures, just like the weather

A new tool can predict the likelihood of epileptic seizures, paving the way for a forecasting app that could be used every day

By Philippa Karoly, University of Melbourne

Every morning you wake up and check the weather app on your smartphone, to see if it will rain. If the forecast probability is high enough, let's say 80 per cent, you decide to bring an umbrella to work.

Now, imagine waking up and not knowing if you will have a seizure that day. You might not be able to go to work at all. This is the uncertainty faced by people with epilepsy every day. An app providing a daily seizure forecast would be life changing – and that is exactly what our team of neuro-engineering researchers at the University of Melbourne is developing.

Led by Professor Mark Cook, our team has recently published a powerful new framework for seizure forecasting. Published in Brain Journal of Neurology, it is the longest forecasting study (where data is used to make reliable predictions about the future) undertaken in humans.

The framework paves the way for us to develop a daily seizure forecast app. We envisage users will be able to enter information about their seizure activity, medication and other lifestyle factors that can be combined with environmental data and brain recordings. This information will then be aggregated to tell the user how likely they are to have a seizure that day.

Depending on personal preference and the acuity of the forecasting model, seizure likelihood can be presented as five risk levels, corresponding to 20 per cent increments of increasing seizure likelihood. After long-term monitoring the forecasts can be personalised, in response to individual seizure patterns.

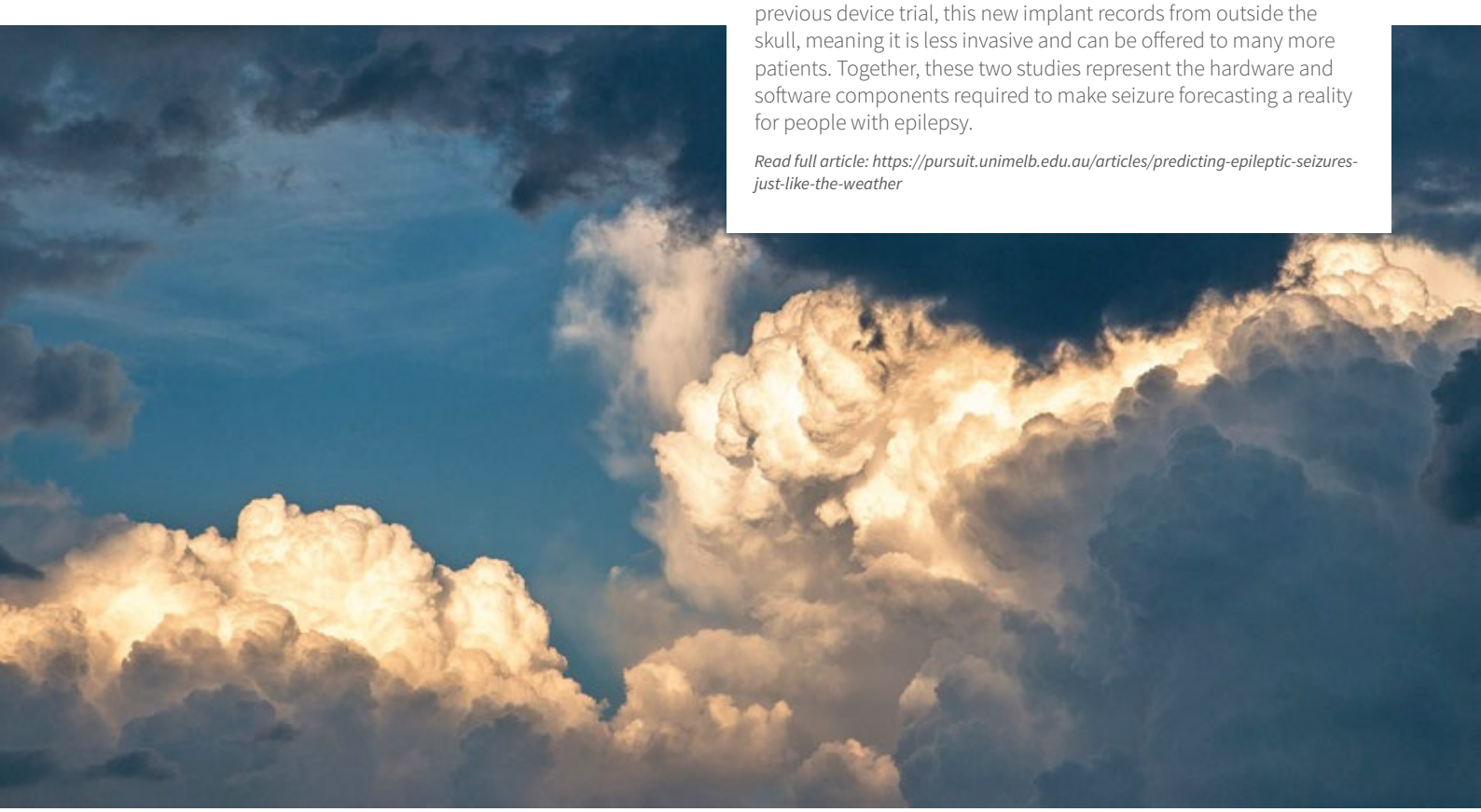
Providing patients with probabilities, rather than certainties, is a more realistic way to forecast seizures. People with epilepsy can then tailor their lifestyles to minimise their risk. For instance, only exercising when their seizure forecast drops below 20 per cent, or taking additional protective measures once the forecast climbs above 80 per cent.

Previous attempts to develop prediction systems for epilepsy patients have almost always failed due to low volumes of data. To combat this problem, long-term analysis was critical, and so we used the world's longest continuous database of brain recordings as our dataset. This data were recorded from the surface over the brain during a previous trial for an implantable seizure warning device, which ran three years and involved fifteen patients with drug resistant epilepsy.

The results from this study showed that seizure prediction was feasible; however, the performance was not successful for all patients. We have now used the same data to show seizure forecasting is viable for more people. The framework we applied provides better predictive performance than any other method previously trialled.

Our results come at an exciting time for epilepsy patients. Colleagues have recently developed an implantable device that can continuously monitor the electrical activity of the brain. Unlike our previous device trial, this new implant records from outside the skull, meaning it is less invasive and can be offered to many more patients. Together, these two studies represent the hardware and software components required to make seizure forecasting a reality for people with epilepsy.

Read full article: https://pursuit.unimelb.edu.au/articles/predicting-epileptic-seizures-just-like-the-weather



Unpicking the myth of Testosterone Rex

Our long-held views on what causes gender differences are wrong. A new book argues it's more complicated than we think.

By Garry Tippett, University of Melbourne

Imagine this thing called Testosterone Rex. According to the old tales, he – most definitely he – is a dangerous beast: powerful; aggressive; competitive; risk-taking; promiscuous and potent, able to sire a hundred babies every year, from as many partners.

Or consider, perhaps, Testosterone Rex as a force. Measured in mere nanograms, this potent hormonal essence surges in gestation to physically determine if we become male rather than female. But more than that, says the old wisdom, it is "that special substance" that gives men and women intrinsically different natures, making them two separate kinds of people.

Better yet, see it as a mindset, grounded in tradition. Testosterone Rex, says Cordelia Fine, is "that familiar, plausible, pervasive, and powerful story of sex and society. Weaving together interlinked claims about evolution, brains, hormones, and behaviour, it offers a neat and compelling account of our societies' persistent and seemingly intractable sex inequalities".

But, says Fine, Professor in History and Philosophy of Science at the University of Melbourne, advances in scientific understanding have made this T Rex extinct.

And even if it is not quite expired, Professor Fine, through her new book Testosterone Rex: Unmaking the Myths of Our Gendered Minds, has fired a burst of well-aimed silver bullets into its quivering carcass.

The book is a sharp corrective to the pop science of men from Mars and women from Venus. Professor Fine has been described as "the mistress of 'it's a bit more complicated than that'" and she assembles a mass of scientific evidence – across biology, anthropology, psychology and neuroscience – to disprove the myth that testosterone, or the lack of it, shapes men and women into virtually separate species.

We are spellbound by biological sex, she writes. "After all, sex categories – whether you have female or male genitals – are obviously fundamental for reproduction. Sex categories are also the primary way we divide the social world."

When a baby is born their sex is usually the first thing asked about them and it may be the last thing we remember of them – after a lifetime of their being directed down a "male" or "female" stream in school, play, work and social status.

"Perhaps it's not surprising, then, that we often think of biological sex as a fundamental force in development that creates not just two kinds of reproductive system, but two kinds of people."

Read full article: https://pursuit.unimelb.edu.au/articles/unpicking-the-myth-of-testosterone-rex

A trade in desperation: The rise of stem cell tourism

Book extract: As medicine and health care around the world undergo major changes, a new book "Stem Cell Tourism and the Political Economy of Hope" looks at the rise of people travelling in the hope of a cure

By Megan Munsie, Alan Petersen, Claire Tanner, Casimir MacGregor and Jane Brophy

In Australia, in recent years, there have been a number of news reports of patients and carers travelling overseas for stem cell treatments. Their journeys are part of a wider international trend, commonly referred to as stem cell tourism, whereby patients and their carers travel across geographical borders and jurisdictions to receive treatments that are experimental or clinically unproven, and hence, may not be available to them where they live.

The stories featured in the news are often framed within a now-familiar narrative—desperate patients full of hope investing in treatments that promise much, and scientists and doctors voicing frustrations about entrepreneurial 'charlatans' or 'cowboys' operating at the margins of medicine and exploiting 'regulatory loopholes' to sell 'snake oil'.

Why, authorities ask, do patients and carers embark on such treatments that are unlikely to provide benefit, are expensive, and potentially in inflict great harm?

By their accounts, patients and carers tended to embark on the search for information, about the condition itself and about treatment options, very soon after diagnosis, and often in the absence of definitive expert advice.

Ivan, a father-carer of a child with cerebral palsy, articulated a commonly expressed view; namely, that 'no one gave us any real direction so we sort of had to do all the research ourselves'.

Research can be long and tortuous, spanning in some cases a period of years, and take individuals and their families down numerous avenues, and sometimes 'blind alleys'. Their post-diagnostic experience is thus in many respects similar to that of other patients, such as those suffering genetic conditions, long reported in the literature.

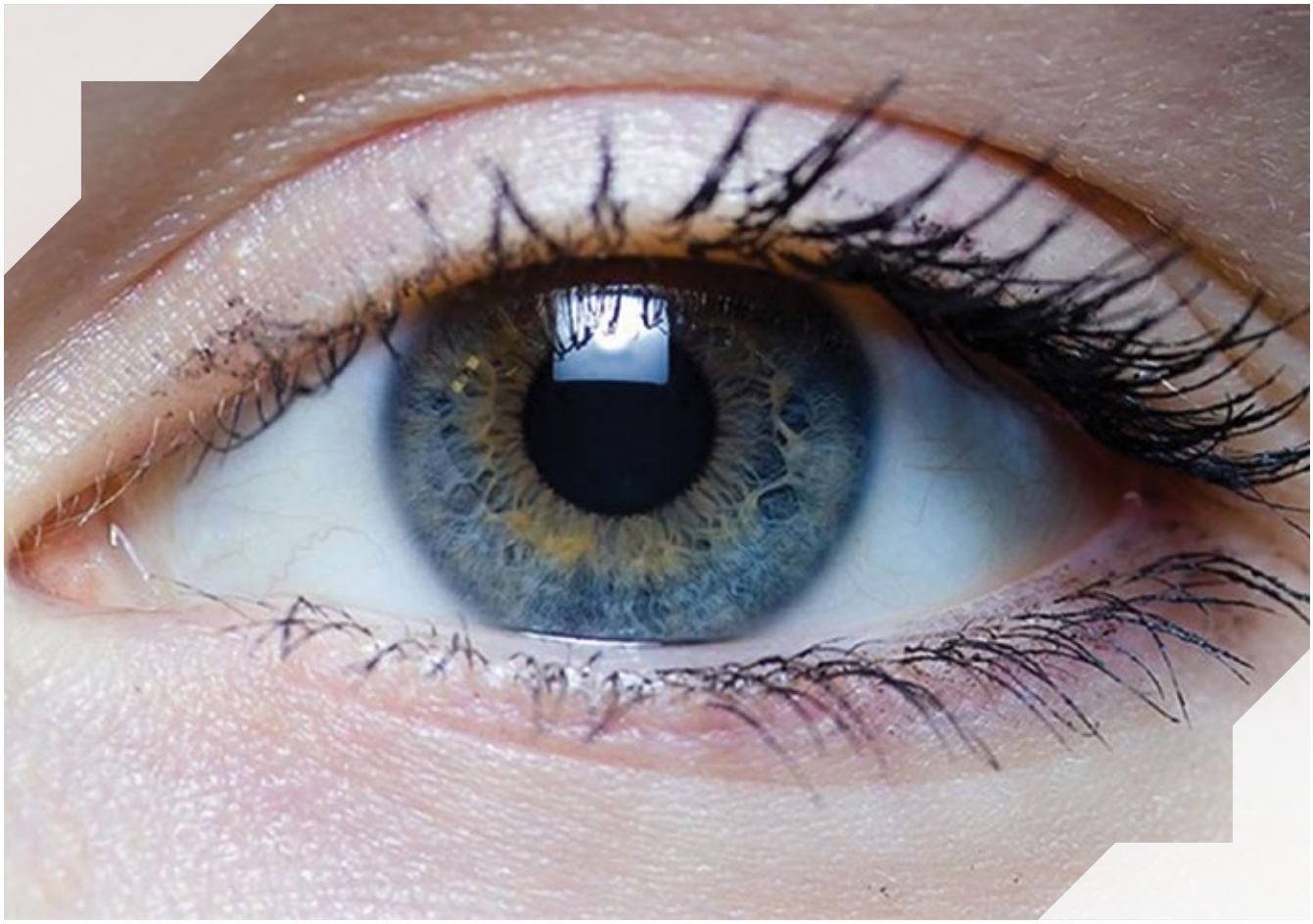
However, the rise of the internet and social media, along with the burgeoning number of online resources, has radically changed the architecture of 'choice'. During their investigations, patients and carers encounter an array of online resources, found primarily via search engines such as Google, and information provided by disease-specific patient communities, individual patients and their families, as well as information offered by providers on their websites.

The nature of the condition and the prognosis constrain options and the potential and urgency to pursue those that are available. Individuals who embark on a stem cell treatment are in most cases struggling with severe, life-limiting conditions (e.g. spinal cord injury, motor neurone disease, multiple sclerosis, cerebral palsy), some terminal and, for many, time is of the essence.

As one patient, Greg, with a progress degenerative neurological disease affecting movement, explained in relation to his decision to pursue stem cell treatment in China: 'If you're in a condition like mine or cancer ... you will try these sorts of things. If you haven't got a condition like that you tend to be more sceptical.'

As he reasoned, stem cell treatment 'seemed to have more going for it' than 'the whole range of things out there' and, as they were financially able to undertake treatment, 'Well, why not try it now while I can?'.

Read full article: https://pursuit.unimelb.edu.au/articles/a-trade-in-desperation-the-rise-of-stem-cell-tourism



New drug reduces rate of progression of incurable eye disease

An international study has found a way to slow the progression of dry age-related macular degeneration

By Nicola Webber, University of Melbourne

An international study including researchers from the Centre for Eye Research Australia (CERA) and the University of Melbourne has found a way to slow the progression of dry age-related macular degeneration (AMD) - one of the most common causes of vision loss in people over the age of 50.

The Phase 2 clinical trial (known as the FILLY trial) was sponsored by Apellis Pharmaceuticals and included 246 patients across 40 testing sites, seven of which were in Australia.

Principal Investigator Robyn Guymer from CERA and the University of Melbourne says she is delighted with the results. “In the past decade, we have made tremendous advances in treating one of the late complications of AMD which is called wet AMD, where blood vessels leak in the back of the eye and destroy vision rapidly,” Professor Guymer says.

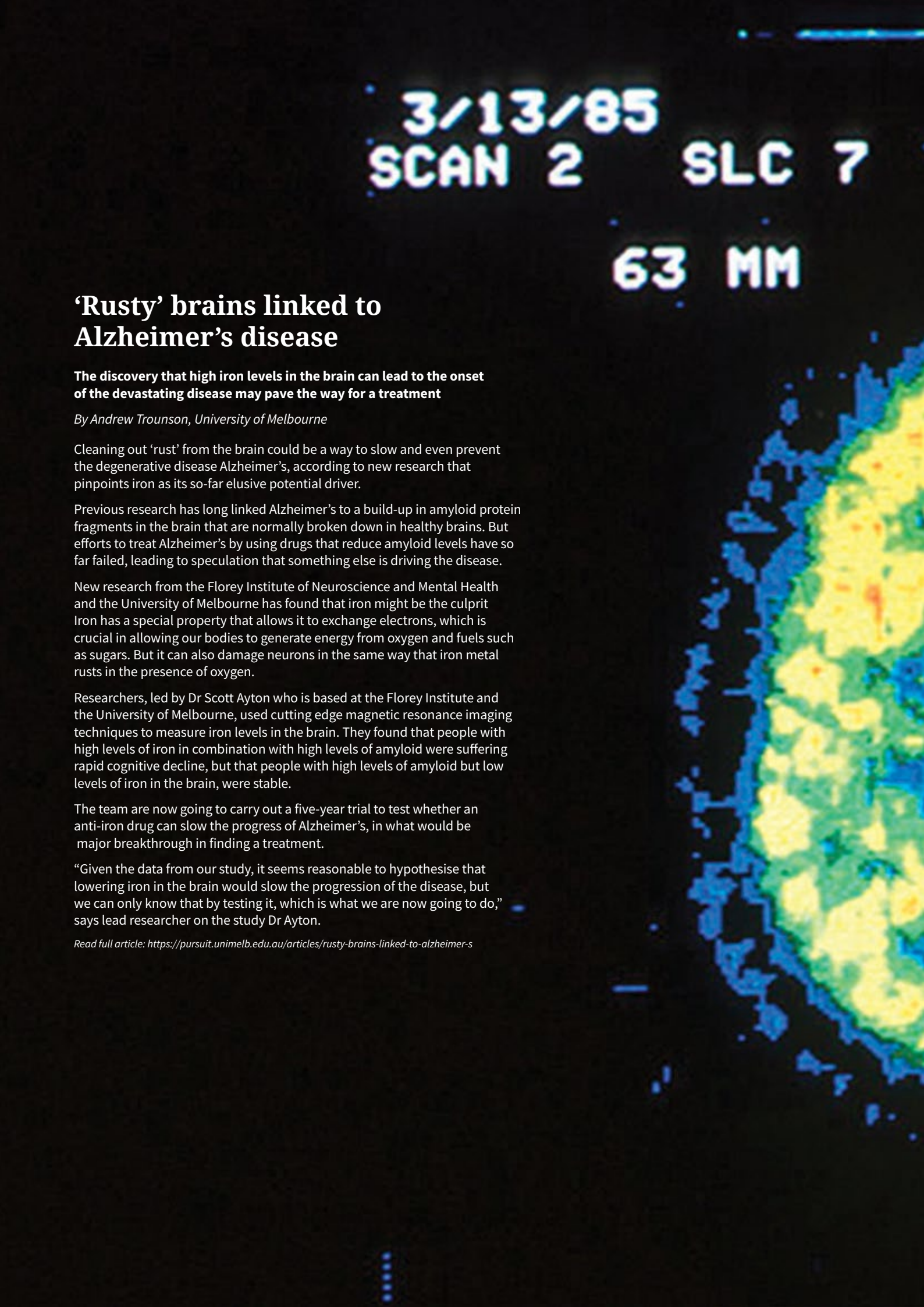
“Now we are directing our attention to treating the other irreversible late complication of AMD, called dry AMD or geographic atrophy (GA).”

Dry AMD or GA is a condition where the cells in the retina die slowly over many years, eventually leading to irreversible loss of vision. “It is like having moth eaten holes in your vision and they slowly all join up in the middle part of the vision, destroying the ability to read, drive and recognizing faces,” Professor Guymer says.

Apellis Pharmaceuticals developed a new compound called APL-2 for treating these patients with GA. Patients were given injections either monthly or every other month for 12 months, resulting in a reduction in GA lesion growth of 29 per cent and 20 per cent respectively, compared to control patients.

Additionally, in a post hoc analysis, a greater effect was observed during the second six months of the study: a reduction in GA lesion growth rate of 47 per cent with monthly administration, and a reduction of 33 per cent with every other month administration.

Based on these positive results, Apellis plans to proceed with Phase 3 studies as soon as possible.



‘Rusty’ brains linked to Alzheimer’s disease

The discovery that high iron levels in the brain can lead to the onset of the devastating disease may pave the way for a treatment

By Andrew Trounson, University of Melbourne

Cleaning out ‘rust’ from the brain could be a way to slow and even prevent the degenerative disease Alzheimer’s, according to new research that pinpoints iron as its so-far elusive potential driver.

Previous research has long linked Alzheimer’s to a build-up in amyloid protein fragments in the brain that are normally broken down in healthy brains. But efforts to treat Alzheimer’s by using drugs that reduce amyloid levels have so far failed, leading to speculation that something else is driving the disease.

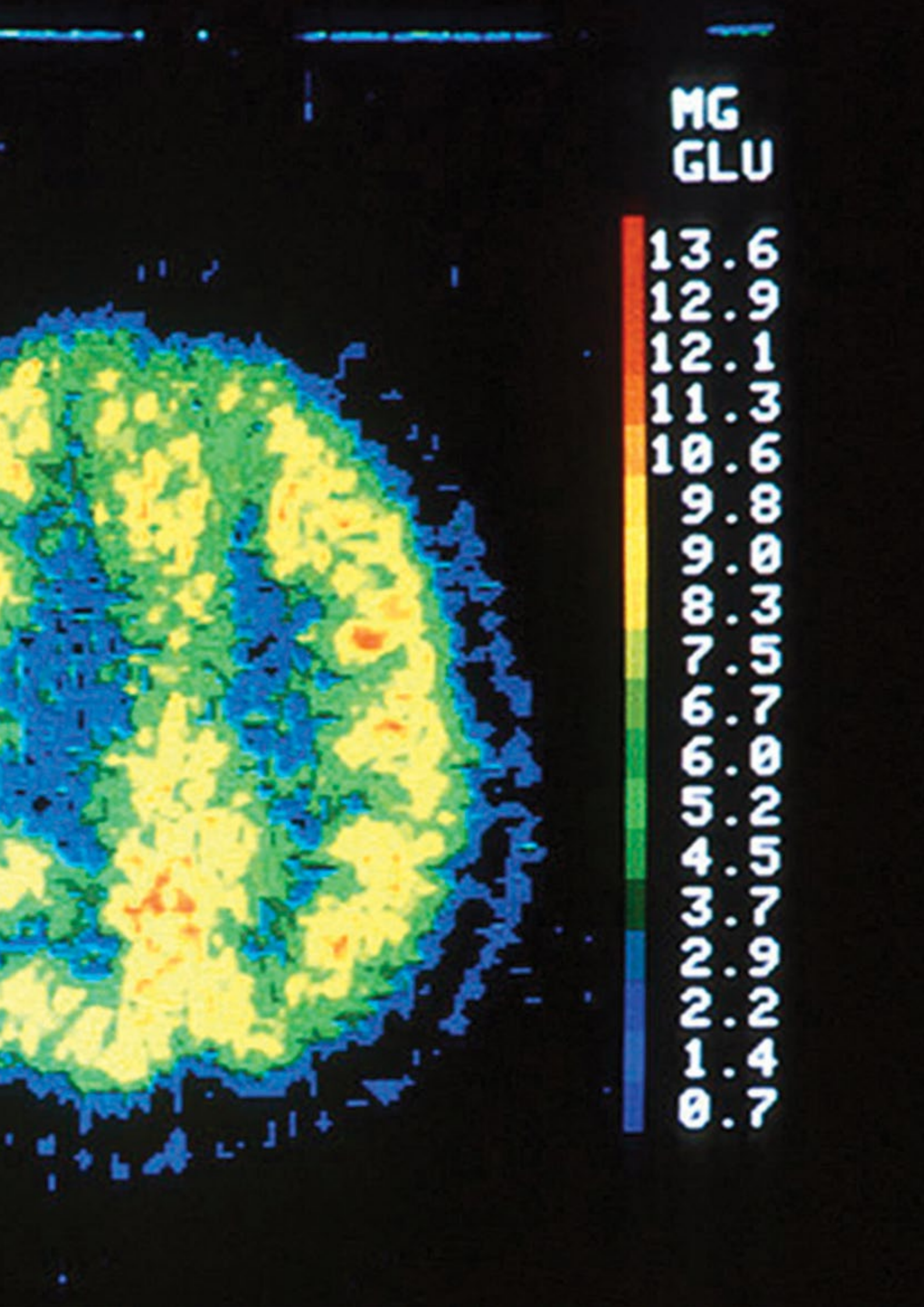
New research from the Florey Institute of Neuroscience and Mental Health and the University of Melbourne has found that iron might be the culprit Iron has a special property that allows it to exchange electrons, which is crucial in allowing our bodies to generate energy from oxygen and fuels such as sugars. But it can also damage neurons in the same way that iron metal rusts in the presence of oxygen.

Researchers, led by Dr Scott Ayton who is based at the Florey Institute and the University of Melbourne, used cutting edge magnetic resonance imaging techniques to measure iron levels in the brain. They found that people with high levels of iron in combination with high levels of amyloid were suffering rapid cognitive decline, but that people with high levels of amyloid but low levels of iron in the brain, were stable.

The team are now going to carry out a five-year trial to test whether an anti-iron drug can slow the progress of Alzheimer’s, in what would be major breakthrough in finding a treatment.

“Given the data from our study, it seems reasonable to hypothesise that lowering iron in the brain would slow the progression of the disease, but we can only know that by testing it, which is what we are now going to do,” says lead researcher on the study Dr Ayton.

Read full article: https://pursuit.unimelb.edu.au/articles/rusty-brains-linked-to-alzheimer-s


MG
GLU
13.6
12.9
12.1
11.3
10.6
9.8
9.0
8.3
7.5
6.7
6.0
5.2
4.5
3.7
2.9
2.2
1.4
0.7

Clearing the fog of dementia with song

Music's ability to trigger our deepest memories and emotions could help improve quality of life for people with dementia

By Kate Stanton, University of Melbourne

Anyone who's known a loved one with dementia can testify to its cruelty – the frustration, anger and sadness that comes from watching someone you love slip away.

Dementia, the umbrella term for conditions with a severe decline in mental function, can be an incredibly painful experience, marked by confusion, distress and a profound sense of loss. It's also increasingly common. Dementia is now the second leading cause of death in Australia.

There is no cure, but researchers, including Professor Felicity Baker, co-director of the University of Melbourne's National Music Therapy Research Unit, are looking for new ways to help people cope.

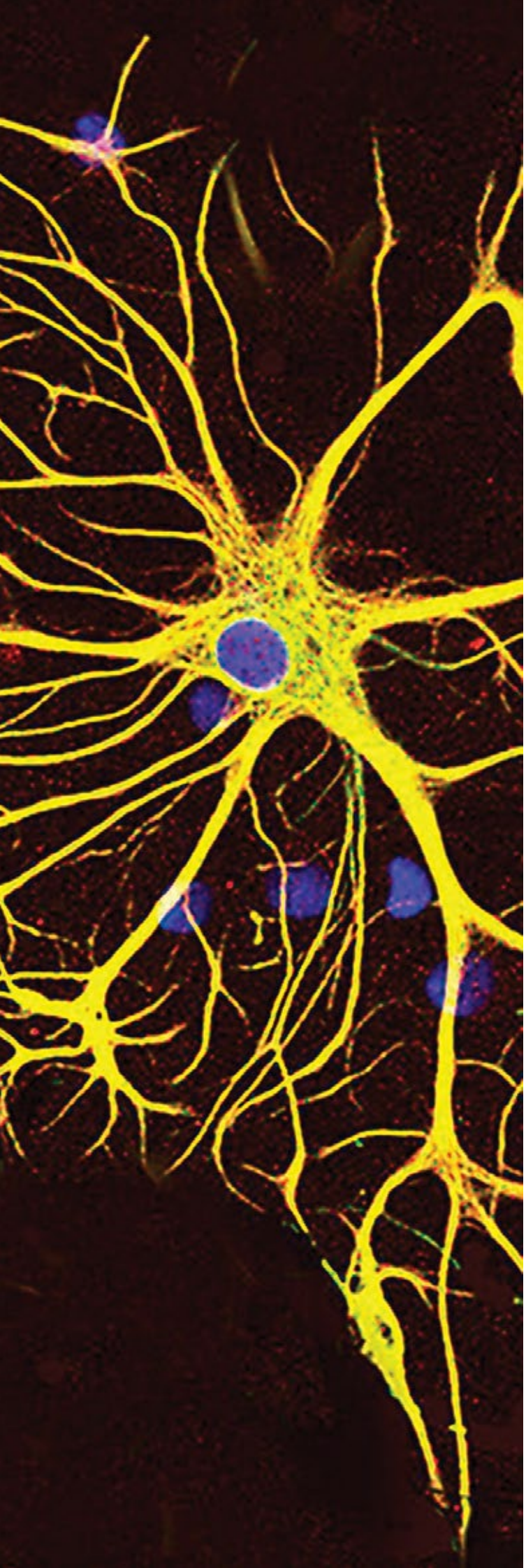
Professor Baker studies how music, especially singing and songwriting, can be used to treat people with a range of conditions – from young people with traumatic brain injuries to adults with substance abuse issues. She says music therapy can be a way for people living with dementia – and their carers – to deal with its symptoms.

"We know that managing dementia with medication actually can make people more confused," she says. "We need to be creative in finding ways that people with dementia can manage the challenges they face, and to address distressing symptoms such as agitation and depression."

Professor Baker recently developed a songwriting program for people living with dementia and their carers at Caladenia, a care centre based in Melbourne's eastern suburbs. Participants worked together in small groups to write and compose songs with a music therapist.

"With music, they're really engaged in a way that they're not in other activities," says Professor Baker. "They're offering their ideas and perspectives. They're happy to argue with each other about what they think the lyrics should be and whether the lyric fits the melody."

Read full article: https://pursuit.unimelb.edu.au/articles/clearing-the-fog-of-dementia-with-song?



Jekyll and Hyde cells: their role in brain injury and disease revealed

New research has shown how normally helpful brain cells can turn rogue and kill off other brain cells following injury or disease.

By Cheryl Critchley, University of Melbourne

Astrocytes have long been implicated in the pathology of a range of human neurodegenerative diseases or injuries including Alzheimer's, Huntington's Parkinson's disease, brain trauma and spinal cord injury.

But how they are produced and what their roles in disease may be, has been as yet unknown. The paper, *Neurotoxic reactive astrocytes are induced by activated microglia*, provides an understanding of the mechanism involved and for the first time provides hope that a lot of these diseases may in fact be treatable.

The study, published recently in Nature and led by researchers at The University of Melbourne and Stanford University, provides deeper understanding of the functions of injured or diseased astrocytes found in the Central Nervous System (CNS) following acute injury and chronic neurodegenerative disease.

In a healthy brain, astrocytes are vital for the normal functioning of the brain - providing nutrients to support neuron viability, releasing factors that aid formation of connections between nerve cells known as synapses, as well as many other important functions.

One puzzle has been that in some circumstances the astrocytes appear to have a toxic effect on neurons, whereas in others they support neuronal viability and connectivity.

Researcher Dr Shane Liddelow from the University of Melbourne's Department of Pharmacology and Therapeutics, and the Department of Neurobiology at Stanford University, said astrocytes are often characterised as 'helper' cells but they can also contribute to damage caused by brain injury and disease by turning toxic and kill other types of brain cells.

"These apparently opposing effects have been a puzzle for some time. By characterising two types of astrocytes this paper provides some answers to the puzzle," he said.

"Following nerve damage, astrocytes form scar tissue that can help in the regeneration of severed fibres. But we have also discovered that under certain conditions, they can turn and become negatively reactive, causing cell death," Dr Liddelow said

For many decades, the trauma and neurodegeneration research focus has been on neurons. Researchers are excited by the discovery of these neurotoxic reactive astrocytes, because for the first time, these findings imply that acute injuries of the retina, brain and spinal cord and chronic neurodegenerative diseases, may all be much more treatable and even reversible than first thought.

By providing new insights into the process of neurodegeneration, researchers can look at new pathways for dealing with neurological diseases and injuries, by targeting these toxic astrocytes, in addition to neurones in neuropsychiatric diseases or oligodendrocytes as for instance in multiple sclerosis.

Ultimately, there is still hope that one day it may be possible to switch back astrocytes from the "toxic" to the "helper" state, a long-term target for Dr Liddelow and colleagues.

Brain stent to let five paralysed people control exoskeleton

Mind control without the side effects. That's the aim of a device that could help people control robotic limbs using thought alone – without the need for brain surgery. The device will be trialled in people with paralysis next year.

By Alice Klein, New Scientist

Several groups are developing brain-machine interfaces that allow people who are paralysed to operate a bionic exoskeleton just by thinking about it. These devices decode electrical brain signals and translate them into movement of robotic limbs.

Usually, brain signals are detected via electrodes attached to the scalp or implanted directly in the brain. Placing them on the scalp avoids surgery, but the signals are muffled by the skull. Direct implantation allows precise recordings but the electrodes can stop working because the brain treats them as foreign bodies and wraps them in scar tissue.

Now, a research team led by Thomas Oxley at the University of Melbourne has developed a way of implanting electrodes in the brain without opening up the skull.

Their electrodes are attached to a metallic mesh tube that is guided through a small incision in the jugular vein in the neck and up into a blood vessel in the brain. There, the electrode can measure signals from nearby brain cells on the other side of the vessel wall.

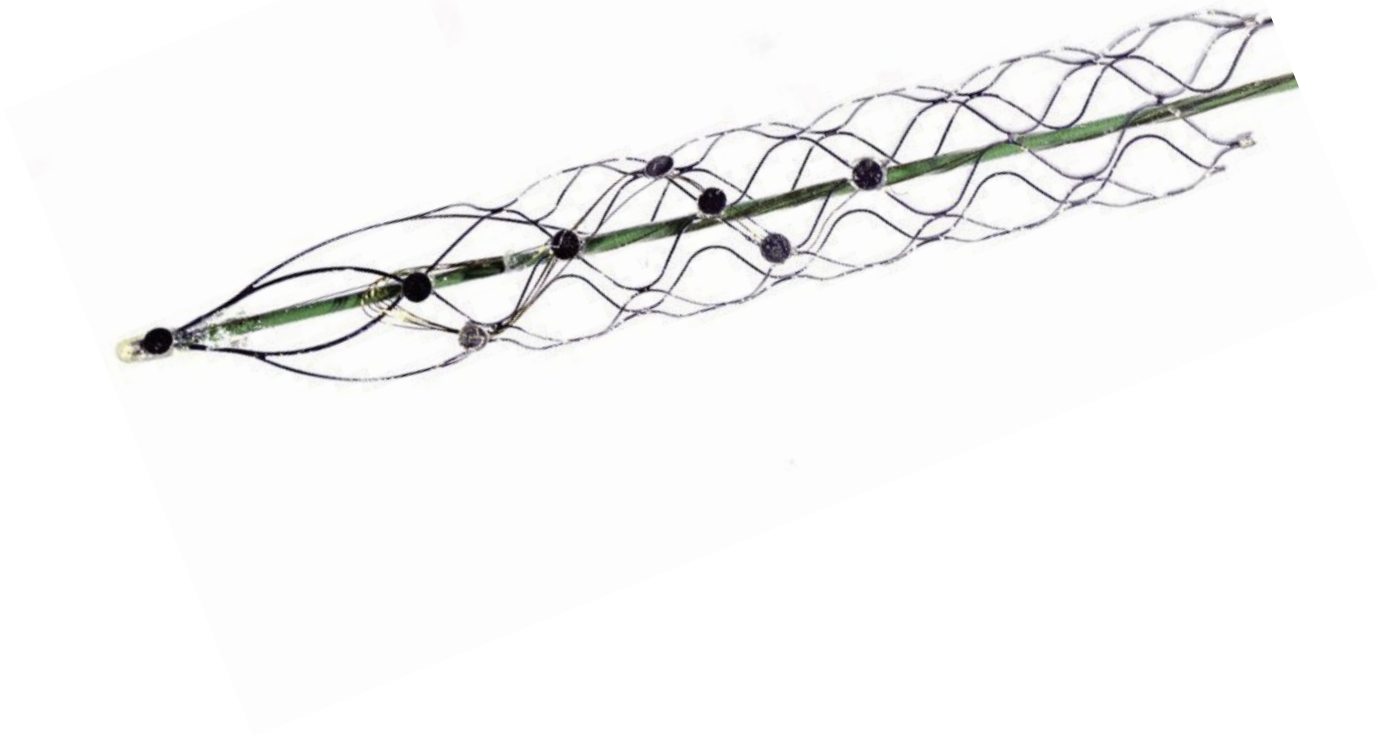
The technique is borrowed from cardiologists, who slide similar tubes called stents into arteries to keep them open.

The electrode-studded stent – or "stentrode" – was tested in the brains of live sheep in 2016 (Nature Biotechnology). Like a cardiac stent, it sat in the blood vessel without causing any adverse effects. Because the metallic mesh does not directly touch brain tissue, no inflammation or scarring occurred over the six-month trial. "The brain doesn't even know it's there," says David Grayden at the University of Melbourne, who oversaw the engineering of the device.

The matchstick-sized stentrode was able to clearly detect electrical brain signals. "The recordings are not quite as detailed as those from directly implanted electrodes, but they're close," says Grayden.

The team is now planning a clinical trial at the Royal Melbourne Hospital that will start next year. Up to five patients with no use of their arms or legs due to spinal cord injury, stroke, motor neurone disease or muscular dystrophy will be involved.

Read full article: https://www.newscientist.com/article/mg23431261-600-brain-control-via-blood-vessel-stent



Repairing brain injury by learning from a fish

In the quest to repair brain cells after injury or disease, scientists are learning from the zebrafish, which can heal its own tissue

By Nerissa Hannink, University of Melbourne

In the waterways around the Himalayas lives a small, stripy fish. As it goes about its daily life searching for food and avoiding predators, the zebrafish can perform an amazing feat to keep itself alive. If injured, even in the eye or brain, it can repair itself using cells that reside within the injured tissues to fully restore function.

In contrast to humans, zebrafish are masters at regenerating their nerve cells. But scientists at the University of Melbourne are studying how they activate certain cells to heal eye injuries with the aim of replicating the process in humans.

"Unlike damage to our skin, which we can repair well, unfortunately an injury to the human eye, brain or spinal cord results in little nerve cell regeneration and a permanent loss of neural functions," Dr Patricia Jusuf says.

Dr Jusuf and her team, as well as many others around the world, use the zebrafish as a model animal because they belong to the same vertebrate family as humans, and therefore share the crucial genes that enable nerve cell creation. Also, their entire genome has been sequenced, making the zebrafish an ideal place to find answers to genetic questions about human health.

Her team focuses on understanding how regeneration occurs in the eye's nerve cells, which are affected in neurodegenerative visual diseases, and are similar to nerve cells in the brain and spinal cord.

Read full article: https://pursuit.unimelb.edu.au/articles/repairing-brain-injury-by-learning-from-a-fish

Shining a light on stem cell therapy to treat gut motility

A new study from the Departments of Anatomy & Neuroscience and Physiology at the University of Melbourne has shown that transplantation of stem cells into the bowel wall has the potential to treat some intestinal motility disorders.

Within the wall of the bowel, there is an extensive nervous system. These neurons, called the enteric nervous system, play an essential role in controlling gut motility. Diseases of the enteric nervous system result in motility disorders that are some of the most challenging conditions for clinicians to manage as there are currently no effective treatments.

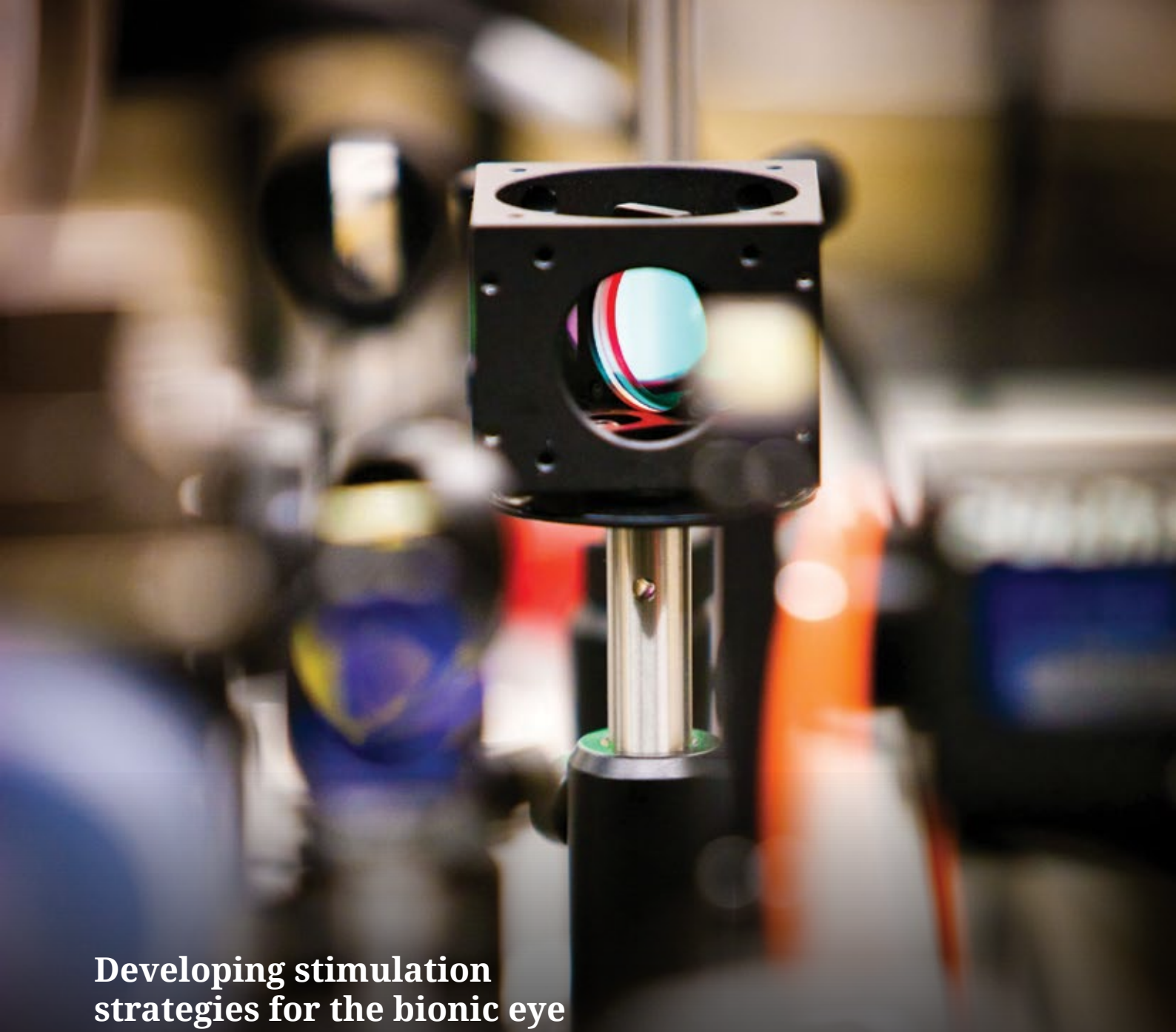
Dr Lincon Stamp, the first author of the new study, used a mouse model to examine whether stem cell transplantation might be used to treat intestinal motility disorders caused by diseases affecting the enteric nervous system.

Lincon transplanted neural stem cells, which had been isolated from the bowel of young mice and which expressed a light sensitive ion channel, into the colon of recipient mice. One month later, Rachel Gwynne, an electrophysiologist, recorded responses in the colonic muscle of the recipient mice in response to light stimulation, which selectively activates the transplanted cells. Rachel found that light stimulation induced responses in the colonic muscle of recipient mice.

"Our study showed that transplanted stem cells generate multiple different types of enteric neurons that integrate, release the correct neurotransmitters and regulate the function of the muscle of the bowel wall," said Dr Stamp.

Several years ago, a study from the UK showed that neural stem cells can be isolated from the human bowel using routine endoscopic techniques. Dr Stamp said that cells isolated from healthy bowel regions of patients might therefore be used to treat motility disorders.

The new study from Professor Heather Young's laboratory in collaboration with Professors Joel Bornstein and Andrew Allen and colleagues at the Florey Institute for Neuroscience and Mental Health will be published in Gastroenterology, the leading journal in the field of gastrointestinal research and disease, and was funded by an NHMRC grant.



Developing stimulation strategies for the bionic eye

Bionic Vision Australia is developing the Bionic Eye to target two degenerative retinal diseases: Retinitis Pigmentosa (RP) and Age-related Macular Degeneration (AMD).

By Sarah Whittle and Julian Simmons, University of Melbourne and Nick Allen University of Oregon. Published by The Conversation.

Both diseases result in loss of photoreceptors, the light-sensitive cells in the eye. Electrical stimulation of the remaining cells in the retina, usually retinal ganglion cells, can provide a sense of vision, where the perceived "light" is called "phosphenes".

Stimulation strategies for bionic eyes typically encode image brightness by stimulating different electrodes with different amounts of electric current. The resulting phosphenes are ideally round in shape, though the shapes can vary from electrode-to-electrode and from patient-to-patient. It may be possible to control phosphene shapes by careful choice of electrodes to stimulate at any given time. In particular, elliptical phosphenes may be possible, giving the ability to directly present edge information to patients. This information about the edges of objects is known to be important to perceive the outline of objects.

Based on this, Isabell Kiral-Kornek undertook research in one of the psychophysics booths in the Centre for Neural Engineering on a novel stimulation strategy for the bionic eye that extracted edge information from images and encoded them using oriented elliptical phosphenes. She tested whether encoding edge orientation using elliptical phosphenes could lead to better alphabetic letter recognition than standard brightness-based phosphene encoding.

Isabell conducted a study with simulated phosphene vision with 12 normal-sighted volunteers. The picture shows an example of a volunteer reading some text off an iPad with virtual reality goggles; the computer screen shows what the volunteer is seeing at the instant the photo was taken.

The two different stimulation strategies were compared as Isabell varied several parameters including letter sizes and distances between phosphenes. She found that the average letter recognition accuracy was significantly better with the proposed elliptical phosphene strategy (65%) that standard brightness encoding (47%).

This research holds promise for assisting bionic eye users in the future to improve their vision performance.

Growing up in disadvantaged areas may affect teens' brains, but good parenting can help

New research has found growing up in a disadvantaged neighbourhood may have negative effects on children's brain development. But for males, at least, positive parenting negated these negative effects, providing some good lessons for parents.

Living in a disadvantaged neighbourhood (where there are more people who have low income jobs or are unemployed, are less educated, and have less access to resources) can cause stress, and has been linked with psychological and social problems in children and adolescents.

This may come about because of limited access to resources such as quality education and medical care, or because adults in these neighbourhoods have fewer ties to the community and are less likely to monitor children.

But how could neighbourhood disadvantage lead to problems? During childhood and adolescence, the brain is growing and changing rapidly, making it "plastic" or malleable, and susceptible to being changed by experience. So one way neighbourhood disadvantage might lead to negative outcomes in children and adolescents is by changing the way the brain develops.

We studied adolescents aged 12 to 19 from a broad range of neighbourhoods in Melbourne. We investigated whether neighbourhood disadvantage and family socioeconomic status were associated with brain development and functioning (including school completion).

We found growing up in a disadvantaged neighbourhood had detrimental effects on adolescent brain development, but that measures of family-based socioeconomic status (such as parental income, occupation or education) were not related to brain development.

Our results suggest growing up in more disadvantaged neighbourhoods may lead to slower cortical brain development. The cortex is the outer layer of brain, and plays a role in nearly all brain processes related to attention, perception, memory, thought, problem solving, language, motor functions and social abilities.

The altered development may be due to increased stress associated with living in a disadvantaged neighbourhood. The effects of stress on the structure of the brain are well known. Stress hormones might lead to changes in brain development by damaging brain cells, or disrupting the normal processes by which brain cells (and their connections with each other) mature over time.

It's important to note, though, that while we found altered brain development was associated with disadvantaged neighbourhoods, we can't prove one caused the other.

Read full article: https://theconversation.com/growing-up-in-disadvantaged-areas-may-affect-teens-brains-but-good-parenting-can-help-78392

CHAPTER 3

Engagement

Public Outreach

Melbourne Neuroscience Institute Public Seminar Program

In 2017, the MNI proudly oversaw an excellent array of free public seminars that featured noteworthy and engaging local and international speakers. The general-public were keenly engaged in the substantial range of topics presented, which saw popular seminars on virtual reality, neuro-hype and the link between the gut and the brain promptly selling out.

The MNI enjoyed partnering with many fantastic collaborators, including but not limited to, the Melbourne Networked Society Institute, the Melbourne Social Equity Institute, The Gene Technology Access Centre (GTAC), Stem Cells Australia, Faculty of Science, Music, Mind and Wellbeing, the Therapeutic Technologies Research Initiative, and the Disability Research Initiative. We wish to extend a warm thanks to all our collaborators.

Virtual reality in neuro-rehabilitation: what does the future look like? (5 April 2017)

No longer within the realms of science fiction, virtual reality technologies are advancing neurological and cognitive rehabilitation.

Whether it be used in conjunction with transcranial stimulation to improve cognitive ability in people with Parkinson's disease, or used on its own to deliver telehealth group singing interventions for people with quadriplegia to improve respiratory function, voice, mood, and social connectedness, augmented and virtual reality programs have opened a new world of research.

In this seminar, we explored how augmented and virtual reality is being used as a therapeutic tool to improve cognitive function.

Growing organs in a dish: from science fiction to reality? (3 May 2017)

Innovation is essential to better understand how the body develops, what happens in disease and to ultimately produce new treatments for patients. Recent discoveries such as the ability to use stem cells to grow mini-organs in the laboratory, provide a new way to assist researchers to learn more about the human body and advance medical research. But how far has the science progressed? What is involved and who can such research help now or in the future?

While headlines about growing mini-organs in a dish often imply these advances are a way to produce replacement organs and bypass the waiting list for organ donation, the reality is somewhat different.

This forum showcased Melbourne researchers who are at the forefront of this emerging area of science. They discussed how they use stem cells to understand how organs such as the kidney, brain and gut develop as well as how mini-organs can be used to develop better treatments for cancer. Researchers also discussed the ethical, social impact and public perception of this research.

The extraordinary link between the gut and the brain (3 August 2017)

Our gut and brain are linked by an expansive network of neurons, chemicals and hormones that provide feedback about our mood, whether we are hungry, or if we've ingested a disease-causing microbe.

The relatively new appreciation of how gut health can affect our brains is leading to a shift within medicine, and specifically a shift towards maintaining and improving healthy gut bacteria. The "brain in your gut" provides us an emerging and remarkable glimpse into the enteric nervous system and its role in regulating brain development and behaviour.

In this seminar, we looked at how diet and nutrition can affect the treatment and prevention of mental disorders, the link between the gut bacteria and various disabilities, and digestive tract disorders.

Science Week 2017: This is your brain on virtual reality (17 August 2017)

Virtual Reality has already been used successfully to treat youth and adult mental health conditions such as phobia and it may also be beneficial for young people suffering a broader set of conditions such as psychosis and depression. In an aged care setting, Virtual Reality is being considered as a form of enrichment care.

Researchers discussed ways in which virtual reality is being explored as a therapy for youth and adults with mental health conditions and disorders.

Neuro-hype: do all the answers to mental health lie within the brain? (26 October 2017)

Neuropsychology has seized the public's imagination, and although there are incredible developments in this field which increase our collective understanding of who we are as humans, is it the only answer to understanding and improving mental health?

We are bombarded with headlines like 'What Serotonin Has To Do With Depression And How To Make More' and 'Are You Socially Anxious? It Might Be Your Genes' Fault'. Increasingly we are finding an excess of 'neuro-hype' in the media may lead people to believe that the brain in isolation is responsible for our mental health. What are the implications of this? Does this affect the stigma surrounding mental illness?

Critiques of prevailing approaches also come from the "neurodiversity" movement, arguing for the acceptance and support (rather than correction) of the diversity of human minds as a normal part of human experience.

In this public seminar and panel, we explored the dangers of this oversimplified understanding of neuropsychology, and asked why we cannot understand the mind and mental health by studying the brain in isolation.

This event was recorded by the Big Ideas program for the ABC.

The No-Bell Prize (28 November 2017)

Just how difficult is it for brain and mind researchers to speak without jargon when describing their research?

The annual "No-Bell Prize" pits researchers against each other to take three minutes to explain their research in an entertaining and jargon-free way to a panel of expert science communicators and audience.

Any overly-technical term earns a warning bell from the panel, and then requires further explanation.

Once again we were expertly hosted by MC Dr Shane Huntington, Host and Producer of the 3RRR Science radio program Einstein A Go Go.

Our engaging judges included:

- Robyn Williams, Science journalist and broadcaster
- Sarah Brooker, Director, Science in Public
- Dr Jared Cooney Horvath, Educational Neuroscientist at the University of Melbourne

Contestants:

- Professor Christine Wells, Director of the Centre for Stem Cell Systems
- Professor Cassandra Szoeke, Consultant Neurologist, The Royal Melbourne Hospital and Director, Healthy Ageing Program, Department of Medicine
- Associate Professor Olivia Carter, Perception and Pharmacology Laboratory Director
- Professor Peter Bossaerts, Experimental Finance and Decision Neuroscience
- Professor Felicity Baker, Co-director, National Music Therapy Research Unit

With fierce competition from researchers discussing topics such as stem cells, aging and dementia, and consciousness itself, the scores results in an unfortunate tie between four of the contestants. Due to this, the No-Bell Prize for the most 'entertaining' presentation was instead awarded to Professor Peter Bossaerts, Experimental Finance and Decision Neuroscience.

The Melbourne Neuroscience Institute provided support and sponsorship to:

Students of Brain Research (27 July 2017)

The 2017 Students of Brain Research committee organised the registration of SOBR as an incorporated association in March of 2017. The official registered name is now Students of Brain Research Incorporated.

On Thursday 27 July, 2017 SOBR hosted its annual Professional Development Dinner at The Windsor Hotel, Melbourne. There were 106 local brain research students, and 29 distinguished VIP scientists, industry representatives, and science communicators from across 14 local universities and research institutes attending. The theme of the night was "Bridging the gap between research and industry" and focussed on how students and ECRs might use their research in an industry setting.

SOBR structured the night slightly differently from previous years, in an effort to have input from a range of different industry researchers. The keynote speaker was Prof Emeritus Richard Silberstein, the CEO of Neuro-Insight. They then had a panel of experts discuss their experience of research in industry, including:

- Dr Nicole Den Elzen
- Executive GM, Research Management & Strategy, Baker IDI Heart and Diabetes Institute
- Dr Lesley Braun
- Director, Blackmores Institute
- Prof Daniel Hoyer
- Chair and Head, Department of Pharmacology and Therapeutics; Deputy Head of School of Biomedical Sciences, University of Melbourne

Dr Andi Horvath was kind enough to once again host the evening with her usual flare.

Therapeutic Technologies, Stem Cells and Drug Discovery (18 September 2017)

A meeting that brought together interdisciplinary researchers to discuss important progress in the areas of organoids and organ-on-a-chip technologies.

Yulgilbar Alzheimer's Research Program "Best and Brightest" Talks (18 October 2017)

Alzheimer's disease is a major – and growing – problem affecting our ageing society. It also is one of Australia's research strengths.

The Yulgilbar Alzheimer's charity's Best and Brightest Talks highlighted much of the innovative research taking place in this field in Australia. Talks showcased experiments with 'mini-brains' in the dish and the structural changes they can display that mimic Alzheimer's disease, how retinal imaging may screen for Alzheimer's decades before symptoms appear, and how ultrasound might help to prevent the build-up of plaques in the brain.

Music, Mind and Wellbeing Postgraduate Research Symposium (22 November 2017)

This symposium comprised presentations by current PhD candidates who are conducting music research at the University of Melbourne as part of the Music, Mind and Wellbeing Initiative. The afternoon served as a forum for graduate researchers across music neuroscience, music education, music psychology, and music therapy to share their research findings and to facilitate broader networking and collaboration between disciplines conducting music research within the University of Melbourne.

Ethics in Science (7 December 2017)

With the rapid advancement of science, ethical dilemmas arise frequently. These dilemmas range from the use of embryonic stem cells or animals in research, deciding how much power to give robots and artificial intelligence, how far to go with clinical trials in humans or using modern technology to decide whether one should turn off the life support of someone in coma.

Though science is not infallible, it is essential that scientific research is pursued with integrity and transparency and to the highest possible standards. Scientists owe this dedication and honesty to their pursuit of truth and to the tax-payer who both funds and is the beneficiary of the research.

At this forum, five internationally renowned scientists working in different fields addressed some of these ethical issues and answered questions from the floor.

Podcasts

5 Things About: Five things about teenage brains

It's well accepted that teenagers are… strange. But why?

What is it about the teenage brain that makes them so different to adults? Can neuroscience explain why they won't clean their rooms?

Find out what's really going on up there from educational neuroscientist Jared Cooney Horvath.

Listen here: https://soundcloud.com/5-things-about/teenage-brains

5 Things About: Five things about stroke rehab environments

We know that stroke rehabilitation requires motivation and an absence of stress. But how can we create spaces that are both motivating and calming? How can we make sure that there are enough stimuli to encourage neuroplasticity and recovery of lost function? In this episode, Jan Chamberlain, Program Manager at the Centre of Research Excellence in Stroke Rehab and Brain Recovery chats to PhD Ruby Lipson-Smith about the intersections of architecture, psychology and neuroscience and discovers that the majority of spaces for stroke rehabilitation are not currently fit for purpose.

Listen here: https://soundcloud.com/5-things-about/stroke-rehab-environments

Eavesdrop on Experts: The psychology and science of poo

Why is poo a taboo? How do our lavatory practices affect our health? What is a toilet graveyard? How can mapping our defecation spots help improve sanitation? Which cultures are the most likely to use excrement-related swear words? Come with us as we weave between psychology and science to unpick and unpack the wonders, weirdness and wackiness of one of our most primal activities. Welcome to (slightly more than) five things about poo.

With guests Prof Nick Haslam from The University of Melbourne and PhDc Naomi Francis from the Nossal Institute, Melbourne, Australia.

Listen here: https://soundcloud.com/eavesdrop-on-experts/bonus-5-things-about-poo

Melbourne Brain Symposium and Mendelsohn Award (12 October 2017)

The Melbourne Brain Symposium 2017 took place on Thursday 12 October and featured an esteemed program of local and international speakers.

The Melbourne Neuroscience Institute, University of Melbourne and the Florey share a proud history of hosting the annual Melbourne Brain Symposium.

In the sixth anniversary of our occupancy of the Kenneth Myer Building, we paid tribute to the remarkable breadth of neuroscience focused research happening here and internationally. We owe a great deal of gratitude to our speakers, which comprised:

Martha Clare Morris, Rush University Medical Centre
Nutrition and Prevention of Dementia: The MIND Diet

Kay Double, University of Sydney
Shared protein pathologies in neurodegenerative disease: new clues to disease mechanisms

Simon Dennis, University of Newcastle
Understanding the neural representation of recollective experience using experience sampling technologies

Erica Fletcher, University of Melbourne
Mechanisms and new treatments for age related macular degeneration

Peter Stys, University of Calgary
The axo-myelinic synapse: locus for physiology, target of disease

The Mendelsohn Student Lecture was once again held in 2017. In honour of Frederick Mendelsohn, AO FAA, Emeritus Professor the University of Melbourne and past Director of the Howard Florey Institute and R Douglas Wright Professor of Experimental Physiology and Medicine from 1997 to 2009, the award seeks to recognise and honour outstanding students in the Neurosciences. The successful applicant has the right to deliver a lecture to communicate the outcomes of their graduate research to the Neuroscience community, alongside presentations from eminent scientists.

Congratulations to our finalists:

Ashley Marsh (first)
The identification and characterisation of human disorders of axon guidance.

Leigh Walker (runner up)
Expanding beyond the current dogma of addiction neurology.

Piero Perucca (runner up)
The genetic of focal epilepsy: epidemiological, diagnostic and therapeutic aspects.

SOBR Student Symposium (11 October 2017)

The Student Symposium was held (with thanks to the generous sponsorship of the Melbourne Neuroscience Institute and the Florey Institute) at the Kenneth Myer Building on Wednesday 11 October. There were 179 attendees and 72 student presenters, from 9 institutions and organisations across Victoria, and one interstate. This event provides students with the opportunity to network, share their research, and to receive feedback from expert reviewers and judges. The free symposium consisted of four student oral sessions, two poster sessions, as well as two plenary lectures from Prof Arthur Lowery (Monash University and Centre for Integrative Brain Function) and Prof Jayashri Kularni (Monash Alfred Psychiatry Research Centre).

All presentations were of an incredibly high calibre. A warm congratulations to the 2017 Oral and Poster presentation winners, who were each awarded research stipends:

Oral winners

1. Rose Crossin
2. Crystal Li
3. Joao Covita

Poster winners

1. Cem Buyukata
2. Sally Grace
3. Shayden Bryce

Excellence:

Stuart Oldham
Cassandra Wannan
Amy Shepherd
Ben Castine
Greg Kennedy

Education

Advanced Research Workshops in Neuroscience

Four advanced Workshops in neuroscience targeted to RHD students were conducted in 2017, as follows:

1. Bioinformatics resources for neuroscientists, led by Dr Vicky Perreau (July- 2017); 7 RHD student attendees
2. Ion channel function, led by Prof Ian Forster and Prof Steve Petrou, July 2017; attended by 5 RHD students and 4 staff members.
3. Magnetic Resonance Imaging (MRI) led by Dr Jon Cleary and Prof Roger Ordidge, Sept. 11-Oct. 18, 2017; attended by 6 RHD students and 4 post-doctoral scientists.
4. Neural Computational Modelling led by Dr Levin Kuhlman, Dec. 2017; attended by one RHD student and 3 post-doctoral scientists.

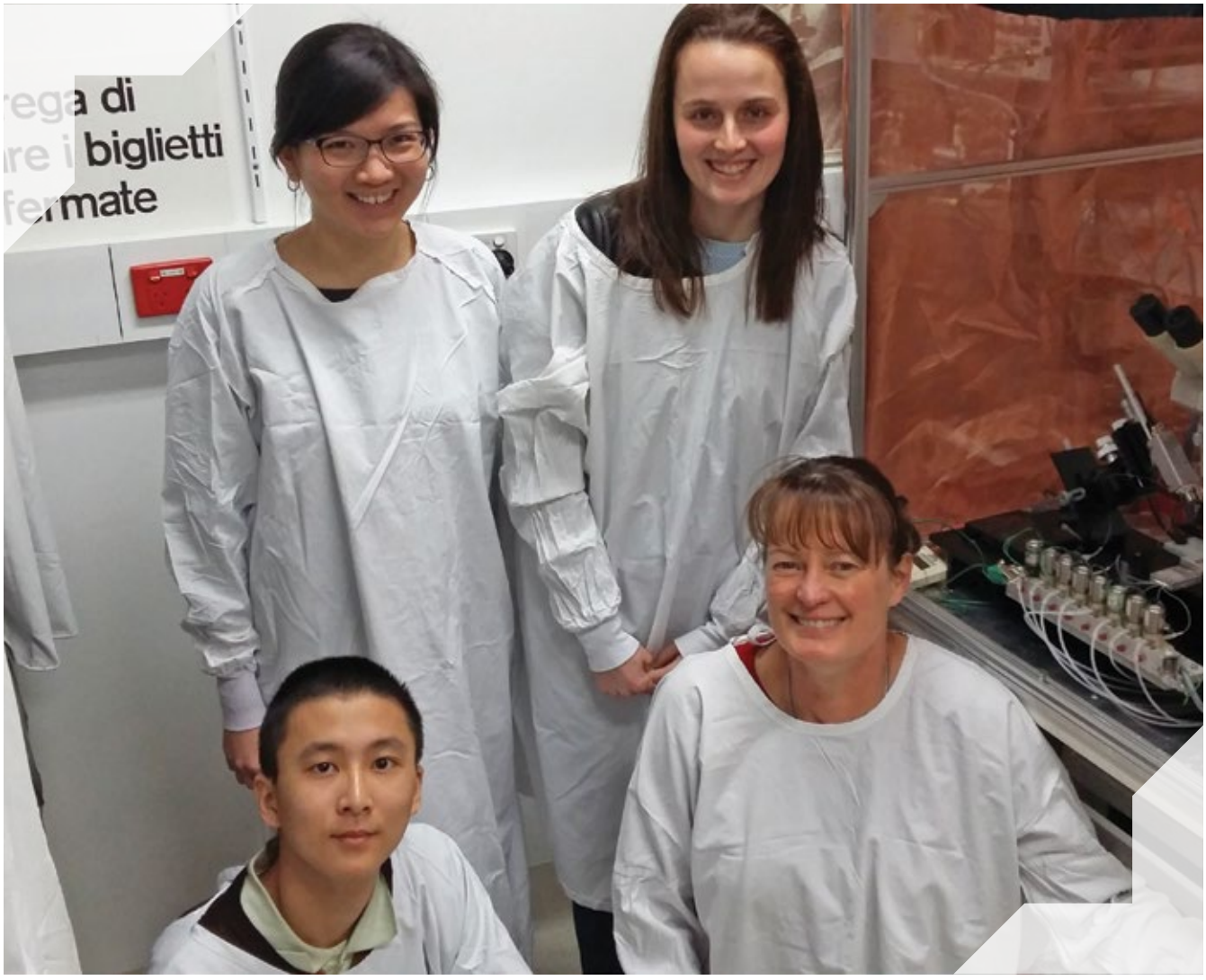
The workshops were again a huge success with much positive feedback from students. Interest in attending the workshop was expressed from organisations external to the University, including from high school students. Of the MRI Workshop, participants wrote:

"I thoroughly enjoyed the course and it exceeded my expectations. Thanks to Jon and all for their efforts."

"The presenters pitched the lectures at a very good level, particularly Jon. They were able to answer all of our questions and present clear examples of how particular concepts work".

100% of participants said they would recommend this workshop to colleagues.

Certificates of completion were provided to all attendees of the Bioinformatics and Ion channel function workshops, and on request for other workshops. From 2018, advanced workshops in Neuroscience will be offered as one of several optional elements of the new Melbourne Neuroscience PhD Program (MNPP), but supported and co-ordinated by the MNI.



Melbourne Neuroscience PhD Program

Julie Martin was appointed MNPP project officer in March 2017. The brief for this establishment year was to develop a Neuroscience PhD program that included the current coursework and advanced workshops and investigated and established additional offerings that would enhance the Neuroscience PhD students' experience beyond a single core thesis. All PhD programs were directed to assist in satisfying the following objectives as determined by the University of Melbourne:

1. Achieve timely completion rates of 75% by 2020;
2. Enhance the research training experience for students;
3. Improve destination outcomes within and outside the Academy;
4. Recruit higher calibre students; and
5. Better align research training offerings with University of Melbourne research strengths.

From the beginning, planning for the MNPP emphasised engagement and input from the targeted student cohort. On 5 September 2017, a small group of Neuroscience PhD students attended a session to hear about the new Melbourne Neuroscience PhD Program (MNPP) and to discuss the feasibility of developing a MNPP Student Association. Prof Trevor Kilpatrick (Director, MNI) began by describing the principles behind the inception of the MNPP. A/Prof Andrew Metha (Deputy Director, MNI) and Julie Martin (MNPP Project Officer) elaborated on the components that contribute to the MNPP (coursework, workshops, seminars, scholarships and awards, exchange, internships and career training). Dr Keely Bumsted-O'Brien from the WEHI spoke from experience on the steps to develop a successful skills/mentor program using a survey and workshopping the findings. The afternoon concluded with an informative discussion about how Neuroscience PhD students would be best represented and self-supporting given the diverse representation within the cohort.

This event was followed up with a survey sent to PhD neuroscience students asking about the skills they already have (but don't necessarily know they have) and skills they would like to have to optimise their future employment opportunities.

A workshop was held on Tuesday 17 October 2017 led by facilitators Dr Keely Bumsted-O'Brien (WEHI) and Dr Caroline Owen (Peter Mac), who have been successful in running skills workshops for postgraduate students. Using the responses from the pre-workshop survey, the workshop program was based on investigating what students want from their PhD experience and how they can go about fulfilling those wants. The workshop explored the possibility and implications of developing a mentorship program between PhD students and Early Career Researchers. The workshop also addressed how representation of MNPP students, from such a diverse range of academic backgrounds, might be achieved. Sixteen neuroscience PhD students attended the workshop.

The discussion, enthusiastic ideas and support from the attendees were commendable. From this workshop a MNPP Student Survey and Workshop Report was produced. The findings in the report will serve to inform development of the MNPP in 2018.

There were multiple opportunities to consult with current Neuroscience PhD students about the creation of a MNPP Student Association. Whilst some noted that there were already many existing Neuroscience based groups, it was acknowledged that it is important to develop an association that has representation from all existing groups and faculties of the University of Melbourne that have Neuroscience PhD students.

Also acknowledged was the ideal that Neuroscience PhD students should have a voice in guiding the academic and professional offerings available to graduate researchers enrolled in the Melbourne Neuroscience PhD program. This would involve representation on the MNPP Steering Committee.

Students who contributed to the MNPP student survey and workshop keenly supported the practice of mentoring and mentorship. Attendees at the workshop indicated that this is an area the Student's Association could manage after receiving training and assistance in setting up such a program.

Of interest to Neuroscience PhD students is the opportunity to undertake an internship related to their research topic. In 2017 we consulted with APR.Intern (formally AMSI Intern), a national program facilitating collaboration between universities and industry. PhD candidates, with the support of their academic supervisors, can undertake a 4-5-month research internship to address a R&D challenge outlined by the organisation.

In 2017, coursework continued to be managed by Dr Kathy Lefevere. The MNPP is open to proposals for new topics for courses and workshops that may come from engagement with MNPP students, supervisors and stakeholders. Discussions have commenced with a range of PhD program representatives about mutual attendance and auditing of subjects that could be relevant to Neuroscience PhD students from a broad range of disciplines.

In 2018, the new cohort of PhD students will be informed about the MNPP through their relevant schools and departments and their PhD supervisors. The MNPP student association will begin to engage with and involve students who have registered to participate in the MNPP. Internship offerings will be provided which utilise collaborative interactions with academics and industry. The MNPP is in a good position for growth and development through interactions between the MNI team, the Florey and MNPP students.

Major outcomes achieved by this group by the end of 2017 included a University of Melbourne web presence, marketing collateral, a social media profile, the education of PhD Program officers about the resources available to programs and their PhD students, internal marketing opportunities and clarification that the engagement of PhD students in programs will be voluntary.

In 2018, further outreach will be focussed on school & departments and Neuroscience PhD students' supervisors.

A MNPP Community LMS/Blackboard site now exists and will act as a repository for information and a means for communication about the various offerings of the MNPP to PhD students who have registered to participate in the MNPP.

Yulgilbar Alzheimer's Clinicians Research Network (YACRN)

Considerable progress has been made in the second year of this program. Although there is considerable overlap in the studies being conducted, each of the five clinician-researchers involved in the program has a focus project covering an important aspect of Alzheimer's disease and other dementias. Experimental designs have been fine-tuned, human ethics submissions have been approved, and whole genome sequencing and data analysis has commenced.

Focus studies include (i) Young Onset Dementia (YOD) - defined as dementia in persons <65 years of age); (ii) dementia resilience – why do some people who carry high-risk alleles for dementia not develop the disease, and can we use this knowledge to develop approaches to slow down disease progression; (iii) does optical imaging for amyloid deposition in the retina correlate with amyloid deposition in the brain; (iv) where does Lewy Body dementia fit in to the picture; and (v) what is the impact of stroke on the development of dementia ?

The calendar year of 2017 has also been a successful funding year for the programme, with a $300,000 grant awarded by the Ian Potter Foundation (health and disability sector) in March, along with $300,000 in matched funds from Mr Baillieu and Mrs Sarah Myer, for a total of $600,000. These funds will be used for much needed MRI and PET brain scans of study subjects and unaffected controls. These studies will be useful in addressing our understanding of this debilitating disease and hopefully, enable prediction of disease onset at a stage where some intervention can be used to improve the quality of life for dementia sufferers, their loved ones and carers.

We acknowledge the generous funding of the Yulgilbar Foundation, the Myer Family company, Portland House Inc., and the CF Leung Memorial Trust, translating to combined funding of $2.1M, additional to the $600,000 above.

Secondary Schools Work Experience

The MNI is proud to run one of the most comprehensive and diverse science-based work experience programs for secondary school students in Australia.

Students have the opportunity to gain valuable work experience in a diverse range of neuroscience related research groups. The MNI is committed to providing a secondary schools work experience program designed to:

- contribute to the development of the skills of young people;
- ease the transition of students into the workplace; and
- demonstrate the wide variety of interesting careers available within neuroscience research.

Students have the opportunity of working with a different researcher each day, covering disciplines as broad as engineering, neurology, clinical science, medicine, music and ethics. Students can visit several laboratories and clinical settings which could include bionics, neural engineering, disorder-based laboratories (e.g. Parkinson's disease, Alzheimer's disease, multiple sclerosis, epilepsy) and imaging facilities. Students take part in varied activities, including dissections, experiments, and other hands-on activities. They also learn about the scientific process, how funding is obtained and, above all, how science works in the 'real-world'.

The MNI work experience program received excellent feedback in 2017, with one student commenting 'This program was amazing and I'm disappointed it is over. I've never learnt so much in only five days!'.

Elizabeth Blackburn School of Sciences Extended Investigation Program

In 2017, over 30 volunteer research mentors from The University of Melbourne supported Year 11 students from the Elizabeth Blackburn School of Sciences with their Extended Investigation projects.

Mentors and matched students met regularly to discuss the various phases of the research process including developing a research question, designing a method, analysing data and writing up a 4,000-word written report.

Highlights of the year included the October poster-symposium, at which students, mentors, teachers and family members met to view and discuss the cohort's research posters.

Australian Brain Bee Challenge Victorian State Final

Melbourne hosts the 2017 Australian-New Zealand Brain Bee Challenge Victorian State Final.

On Wednesday 19 July, one hundred and seventy-five Victorian Year-10 students and thirty-two teachers from as far as Donald (281km) and Bright (321km) gathered last month at the University's Ian Potter Auditorium (Kenneth Myer building) to participate in the 2017 Australian-New Zealand Brain Bee Challenge State Final.

This annual event, hosted by the Melbourne Neuroscience Institute (MNI), University of Melbourne and the Florey Institute of Neuroscience and Mental Health (FINMH), and further sponsored by Monash University and RMIT University, was once again a huge success with the buzz of excitement palpably evident in the eyes of all attendees.

Professor Geoff Donnan of the FINMH welcomed the gathering to the Victorian "home of the brain" and introduced Emeritus Professor Frederick Mendelsohn who provided the Plenary address telling the students of his own personal path and "life in brain science".

Quizmaster Dr Tom Keeble launched the main business of the Brain Bee Challenge, and excitement built over who would emerge the State's Individual and Team finalists. Prizes this year included a giant model of the human brain, trophies, cash and a range of wonderful classic and contemporary neuroscience books sponsored by Readings.

The tension was broken momentarily as keynote speaker A/Prof Mirella Dottori enthralled attendees by describing her latest research into brain organoids: "mini-brains in a dish". Then it was back to business… results after tense competition in the Team Challenge were: 1st - The Mac.Robertson Girls' High School; 2nd - Mentone Girls' Secondary College; and 3rd - Methodist Ladies' College. Congratulations to all!

A highpoint of the day for both teachers and students were the pre-lunch tours of the Harry Brookes Anatomy Museum, the DAX Centre gallery and various neuroscience laboratories. Once again, the volunteering tour leaders deserve special commendation for inspiring the students with their infectious enthusiasm for science and research. After lunch the tables were turned as the teachers challenged their neuroscience knowledge by competing in a friendly game of Neuro Trivial Pursuit - much to their students' delight!

Before the Final Challenge began, Dr Jess Nithianantharajah, Head of the Synapse Biology & Cognition laboratory, Florey Institute of Neuroscience and University of Melbourne gave an inspirational address, describing her career pathway culminating in her laboratory's work aimed at "Connecting the dots in the brain". Our 2016 State Champion, Miss Alysha Wanigaratne of John Monash Science School also described her year as Champion, and her experiences attending the Australian Neuroscience Society annual conference last December.

After a closely contested round amongst eight finalists, Miss Elaine Cheung of The Mac.Robertson Girls' High School emerged the Individual State Champion for 2017. Congratulations to the runners up from Methodist Ladies' College and The Mac.Robertson Girls' High School, and indeed to each of the final contestants (and their teachers)! All those involved in this excellent event should feel deservedly proud of their efforts to promote interest in brain science, which clearly remains at a high level in the State of Victoria

Scientists in Schools

Scientists and Mathematicians in Schools (SMiS) is a program managed by CSIRO on behalf of the nation. It provides skilled volunteers the opportunity to have a positive impact and to make a difference to science, technology, engineering and maths (STEM) education in primary and secondary Australian schools.

Creating and supporting flexible partnerships between STEM professionals and teachers, provides access to real-world, contemporary experiences that promote understanding of the importance of STEM and inspiring students.

The MNI is a proud ambassador of this program..

CHAPTER 4

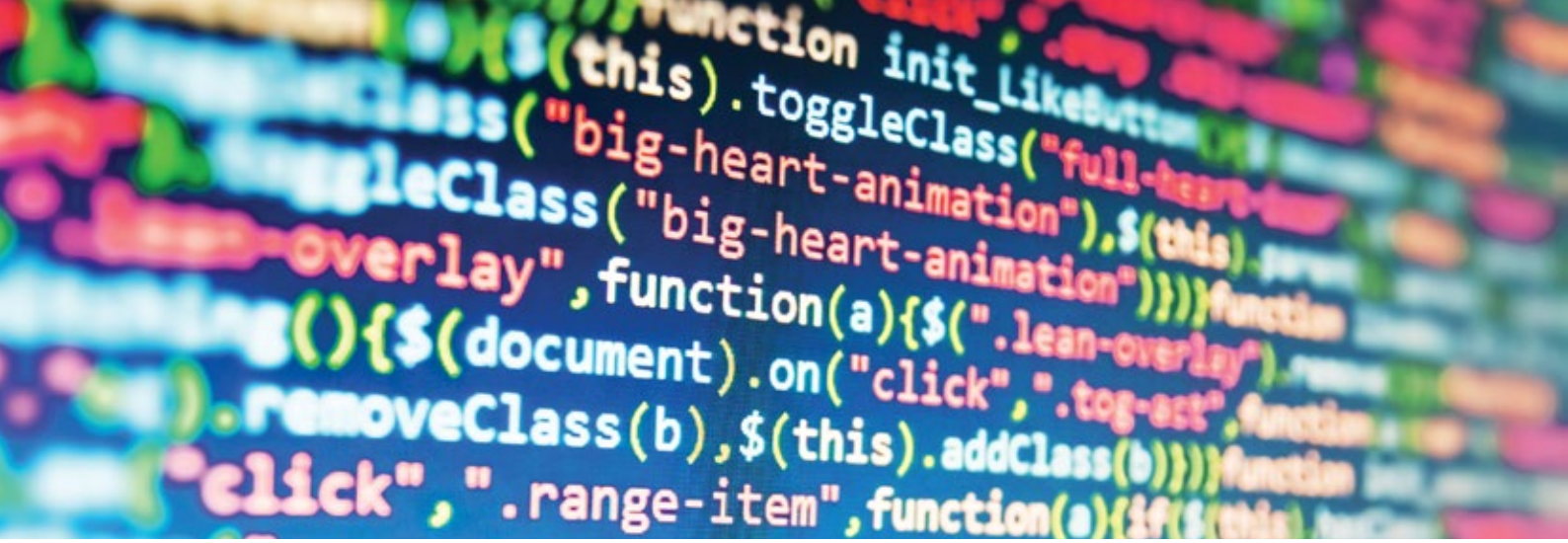
Partnerships

Melbourne Brain Centre and the Florey Institute of Neuroscience and Mental Health

We continue to work well with our partner organization, the Florey. The MNI and the Florey continue to have complementary roles, with MNI delivering a breadth of opportunity to neuroscientists given our strong focus on interdisciplinarity involving active engagement with the physical sciences, engineering, psychology and the social sciences.

We partner with the Florey on several key initiatives. These initiatives include:

- course work and advanced workshops for our graduate researchers
- the annual Melbourne Brain Symposium
- partnerships with the Universite Pierre et Marie Curie and with the University of Calgary
- shared Chairmanship of the Directors Coordination Forum to provide a seamless oversight of operational matters pertaining to the three campuses of the Melbourne Brain Centre
- shared Chairmanship of the Neurosciences Coordination Forum to scope high level strategic initiatives in the Neurosciences and in related disciplines on campus



IBM

The MNI is pleased to have played an important role in catalysing interactions between IBM and key neuroscientists and clinicians, which has culminated in the establishment of an ARC Training Centre in Cognitive Computing for Medical Technologies, awarded in 2017. As is often the case, the funded initiative germinated from a series of dialogues and scoping meetings that in this instance followed an MNI sponsored workshop entitled, 'Applying Advanced Technology to Advance Precision Neuroscience', held in October 2015. The workshop was championed by the MNI Director, as well as Michael Egan (Business Development Director, Faculty of Science) and Noel Faux (IBM) and resulted in important discussions focused on cognitive computing and its application to neurological diseases.

The Training Centre in Cognitive Computing for Medical Technologies has received $4.1 million in funding from the Australian Research Council. The initiative is headed by Professor Tim Baldwin from the Department of Computing and Information Services. The Centre will train PhD and Postdoctoral researchers in novel ways to apply machine learning to data intensive medical problems including epilepsy seizure prediction, optimising man-machine interfaces for prosthetics, prognosis prediction for those with Alzheimer's and the development of intelligent search tools for clinicians.

Siemens

The MNI continues to promote ongoing productive interactions with Siemens. This has been most obviously enunciated via the Melbourne Brain Centre Imaging Unit where the University via the Chair of Imaging Science, Professor Roger Ordidge, and Siemens continue to collaborate to advance the utility and performance of ultra-high field (7 Tesla) Magnetic Resonance Imaging. In addition, the University and Siemens, together with Neurosciences Victoria, Monash University and key health care providers continue to foster interactions in this area, in particular scoping the role that imaging can play in advancing the care of patients with traumatic brain injury.

Hotchkiss Brain Institute

This has been another successful year in the partnership between the Melbourne Neuroscience Institute and the Rebecca Hotchkiss Brain Institute (RHBI) at the University of Calgary. The two main activities were: participation by three Fellows in the HBI International Scholar Exchange Program, and a shared symposium focusing on epilepsy, attended by delegates from Melbourne.

International Scholar Exchange Program

In 2017, three exchanges occurred with the scholars having been selected via competitive application.

(i) Dr Christopher D. d'Esterre (M.D.) *visited Melbourne for 4 weeks in Feb. 2017. He worked with a host lab headed by Professor Vincent Thijs, M.D. PhD based at the Melbourne Brain Centre, Austin Hospital.*

PROJECT TITLE:

"Voxel Based Lesion Symptom Mapping in Acute Ischemic Stroke: Eloquence-weighted MR Imaging".

This project aimed to investigate the utility of optimised MRI scans in acute stroke patients to map the stroke lesion (rather than mapping the infarct/dead brain tissue following the stroke), ultimately to inform decisions about whether to risk removal of a clot in the acute stroke phase. Correlations between lesion mapping and patient outcome were used to guide these decisions.

Dr *d'Esterre* wrote: "The exchange allowed me to interact with other principle investigators in Melbourne. Specifically, Dr Nawaf Yassi of the Royal Melbourne Hospital is now a collaborator and we discussed the possibility of initiating a fellowship with him in the near future. I also attended several stroke rounds at both the Austin and Royal Melbourne hospitals, acquiring a sense for how stroke treatment is done in another part of the world. I was also fortunate enough to attend the Florey Vascular Cognitive Impairment Symposium which gave me insight into what projects I could engage through future collaborative interactions."

(ii) Mr David Wright (PhD candidate, University of Melbourne) visited the HBI for 4 weeks during March 2017 where he was hosted by HBI's Dr Richelle Mychasiuk.

PROJECT TITLE:

"Glymphatic function, telomere length and neurodegeneration: an interdisciplinary investigation of mTBI"

(iii) Dr Hongfu Sun from the HBI visited the MBC (Parkville) for 7 weeks from May-June 2017, hosted by Dr Scott Kolbe.

PROJECT TITLE:

"Validation of Quantitative Susceptibility Mapping (QSM) for brain iron measurement using Laser Ablation Inductively Coupled Plasma Mass Spectrometry (LA-ICP-MS) in MS post-mortem brains"

Multiple sclerosis (MS) is a debilitating condition typically beginning in young adulthood. A wide range of therapies are available or in development that may slow the disease. Monitoring treatment effectiveness includes the use of MRI. However, the conventional "lesion-centric" measurements have limited prognostic value for following the course of disease, as they correlate poorly with disability levels. New MRI techniques that correlate more strongly with disability are needed.

Quantitative Susceptibility Mapping (QSM) is an advanced MRI contrast sensitive to magnetic susceptibility sources, such as brain iron or other metals. Accumulation of brain iron in deep grey matter regions in MS has been reported to correlate with the disease in several pathological studies, and therefore has been proposed as a biomarker of MS disability. I have invented new approach to performing this QSM technique and tested the method on MS subjects using high field MRI studies.

Dr Hongfu Sun wrote of his international scholar exchange experience:

"The facility at the MBC Imaging Unit in Melbourne was of great benefit to me, and is a resource that was not available at the HBI. The 7 Tesla MRI is a state-of-art scanner that is only available at a few sites worldwide. I was very fortunate to get this opportunity to undertake my work on this ultrahigh field MRI scanner. Other benefits include deep interactions with the scientists at the MBCIU, enabling an effective exchange of ideas and the development of academic networks. As well as the dedicated exchange at the University of Melbourne, I also visited two MRI labs in Australia, both located at the University of Queensland (Brisbane) where there is also a 7 Tesla MRI scanner. It was most beneficial to give talks at these centres and to get useful feedback from the audience. The secondment certainly broadened my knowledge and perspectives.

Biennial Joint Symposium on Epilepsy

Collaborative activities between the Hotchkiss Brain Institute (HBI) at the University of Calgary and both the University of Melbourne's Melbourne Neuroscience Institute (MNI) and the Florey Institute of Neuroscience and Mental Health began in 2011.

The University of Melbourne hosted a joint symposium in August 2015 on the topic of sport concussion. This event included discussion of the global state of sport concussion research, presentations on the concussion-related research programs from 15 of the 33 participating researchers, and roundtable discussions of approaches to advance collaborative projects.

A key outcome of the 2015 symposium was the recognition that the HBI, MNI and the Florey Institute have great opportunity for collaboration in a wide spectrum of projects, including but not limited to sports concussion. The Directors of both the MNI and HBI expressed interest in organizing a subsequent research symposium in 2017, to be hosted at the HBI, to explore possible collaborations in additional areas of overlapping research strengths, in epilepsy research.

The HBI Epilepsy NeuroTeam is led by Drs Nathalie Jetté and Cam Teskey, who agreed to host this symposium. Calgary participants included members from both the Hotchkiss Brain Institute and the Alberta Children's Hospital Research Institute. Epilepsy research spans from basic science to population health investigations to clinical trials, and is a focus area of the campus-wide Brain and Mental Health research strategy at the HBI.

A delegation of 13 epilepsy clinicians and researchers from the University of Melbourne and from the Florey Institute of Neuroscience and Mental Health participated in the 2-day symposium held from 1 – 2 May 2017. Delegates from the University of Melbourne received travel support from the Melbourne Neuroscience Institute.

The following clinicians, researchers and clinician-researchers from the two Melbourne-based organisations participated:

University of Melbourne:

- Professor Sam Berkovic (Dept. Medicine, Austin Health)
- Dr Katherine Howell, consultant neurologist (Royal Children's Hospital)
- Dr Dean Freestone (Dept. Medicine, St. Vincent's Hospital)
- Dr Andre Peteson (Dept. Medicine, St. Vincent's Hospital)
- Associate Professor Michael Hildebrand (Dept. Medicine, Austin Health)
- Dr Ken Myers (Research Fellow, Epilepsy Research Centre, Dept. Medicine, Austin Health)

University of Melbourne and FIMNH joint positions:

- Professor Steve Petrou (University of Melbourne Dept. of Medicine and the Florey)
- Dr Chris Reid (University of Melbourne Dept. of Medicine, St. Vincent's Hospital and the Florey)
- Dr Genevieve Rayner (Melbourne School of Psychological Sciences and the Florey)

Florey Institute of Neuroscience and Mental Health:

- Professor Graeme Jackson (Division Head, Melbourne Brain Centre-Austin Campus)
- Dr Melody Li (Post-doctoral Fellow, Epilepsy)
- Dr Thijs Dhollander (Post-doctoral Fellow, Imaging Division)
- Dr Amir Omidvarnia (Post-doctoral Fellow, Medical Data Scientist).

Of note, Dr Omidvarnia was also an International Exchange Scholar visiting the HBI in 2016.

CHAPTER 5

Funding Initiatives

Grants and External Funding

Highlights of grant and external funding active in 2017

Ian Potter Foundation Health and Disability Grant

A productive year was had in 2017 in regards to external funding. The MNI was awarded a $300,000 grant from the Ian Potter Foundation, plus matched funding from Mr Baillieu Myer AC and Mrs Sarah Myer, for a total of $600,000 for 3 years (May 2017 to May 2020) in support of the project *"Improving diagnosis, understanding, modelling and treatment for Alzheimer's disease (AD) and other forms of dementia"* (IPF Grant ID 20170379).

This grant shall be used to fund much needed MRI and PET brain scans of dementia study participants, as well as Whole Genome Sequencing (WGS) on DNA from selected dementia patients and controls across several longitudinal and one retrospective dementia study.

This project has 5 main goals, including a unique one that focuses on carers and families of those suffering with dementia, which is: "To garner feedback from the dementia patient carer/family perspective including information on coping mechanisms used during the assessment and progression of YOD. Cognitive and behavioural/neuropsychiatric changes will be tracked, informing carer programs and improving understanding of potentially dementia-type specific interventions, services and respite that carers and participants require".

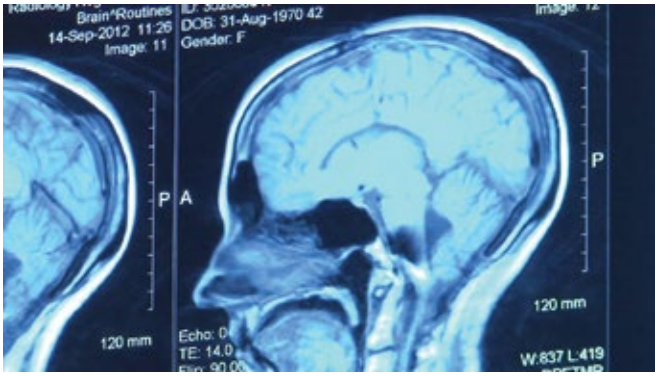
This grant will supplement the funds and goals of the wider program below.

Income in 2017 (Year 1): **$200,000**

The Yulgilbar Alzheimer's Clinicians Research Network Grant (July 2016 – July 2019).

This grant is in its second year and has been made possible by the combined generous funding of the Yulgilbar Foundation, the Myer Family company, Portland House Inc., and the CF Leung Memorial Trust, translating to total funding of $2.1M over 3 years, additional to the $600,000 above. The program has progressed extremely well in 2017 with cohorts recruited for various longitudinal studies and one retrospective study of dementia. This has triggered payment of the year 2 grant income.

Income in 2017: **$690,000**



Pilot Project Testing Targeted Nanoparticles

This grant of $10,000 was awarded to the MNI by the Yulgilbar Foundation, with a cash co-contribution of $10,000 from MNI, for a total of $20,000 (one year). The co- investigators named on the grant are: Prof Frank Caruso (ARC Australian Laureate Fellow), Department of Chemical and Biomolecular Engineering, the University of Melbourne; Dr Kristian Kempe (NHMRC-ARC Dementia Research Development Fellow, Monash Institute of Pharmaceutical Sciences, Monash University; Prof Ashley Bush (The Florey Institute of Neuroscience & Mental Health) and the University of Melbourne; Dr Olga Shimoni (NHMRC-ARC Dementia Research Development Fellow and Senior Lecturer), School of Mathematical and Physical Sciences, University of Technology Sydney.

The overarching goal of this project is to design tailor-made brain delivery vehicles, which are modified with targeting ligands that allow for the efficient encapsulation and triggered release of Alzheimer's Disease related drugs into the brain.

This seed funding from the Yulgilbar Foundation has initiated an interdisciplinary project between polymer chemists, materials scientists and neuroscientists. Based on the results collected in this project the investigators are planning to apply for external funding from either the NHMRC or the ARC in 2019 as further preliminary studies need to be performed beforehand. Longer term, this collaboration is expected to generate new potent drug delivery systems for the treatment of neurodegenerative diseases.

Income in 2017: **$10,000**

Total external amount received in 2017: **$900,000**

Interdisciplinary Seed Funding

Pharmacogenetic silencing of neuronal pathways

CI: Andrew M. Allen
Co-Investigators named on grant: Ross Bathgate

The mammalian nervous system is an organ of unparalleled organization and complexity. One of the key goals of modern neuroscience is to unravel this complexity in order to understand how the brain works and what goes wrong in disease. We are developing a novel tool that will enable us to control specific brain pathways to examine their connections and function.

Transcranial Direct Current Stimulation (tDCS) – Is it the perfect placebo?

CI: Olivia Carter
Co-Investigators named on grant: Jason Forte, Dean Freestone, Andrew Zalesky

Transcranial direct current stimulation (tDCS) is a form of neurostimulation that is simple to administer and can be implemented at home using commercially available devices. There is currently a great deal of scepticism in the scientific community about the utility of tDCS beyond an active placebo. This scepticism has arisen because the mechanism of action of tDCS are unknown and there is a wide disagreement in experimental results. One impediment to progress is the current inability to conduct proper, controlled experiments, because the subject can sense if the device is on, via a tingling sensation on the scalp. The goal of the current project is twofold. 1) We aim to develop a NEW sham using electrode configurations that can only stimulate cutaneous somatosensory pathways and will use psychophysical testing to demonstrate the new sham is perceptually equivalent to active tDCS. 2) We will use EEG to determine whether the new sham tDCS results in measureable brain responses that differ relative to no stimulation (placebo effects) and active tDCS (stimulation specific effects).

A comprehensive, multi-level zebrafish assay to provide mechanistic insight into genetic associates of human behaviour

CI: Patrick T. Goodbourn
Co-Investigators named on grant: Patricia R. Jusuf, Bang Bui, Mirana Ramialison

How do our genes affect the way we experience the world? Modern molecular genetics promises unprecedented insights into human psychology. Yet, identifying the neural mechanisms that mediate gene–behaviour relationships remains a fundamental challenge of modern neuroscience. One useful approach is to generate genetic knockouts in a model organism. However, to gain genuine mechanistic insight, a comprehensive assay to characterise genetic effects at cellular, network, functional and behavioural levels is required. The overarching goal of this new research program is to connect genes, brain and behaviour by using the zebrafish *(Danio rerio)* vertebrate model to identify neurobiological mechanisms that link genetic variation with individual differences in behavioural measures of perception and performance. To this end, the proposed project has two central aims.

Aim 1. Build a new standardised pipeline: We will develop and optimise a comprehensive, multi-faceted zebrafish protocol for probing genetic associates identified in human studies. The pipeline will provide comprehensive histological, electrophysiological and behavioural characterisation of the fish.

Aim 2. Demonstrate proof of concept: We will perform the first translation of a human genetic associate of perception to a genetic model system. In the first instance, we will examine a genetic variant linked to visual contrast sensitivity, the ability to detect variations in light intensity.

Development of peptide NT-3 structural mimetics as treatment for hidden hearing loss

CI: Richard (Tony) Hughes
Co-Investigators named on grant: Susan Northfield, Stephen O'Leary, Hayden Eastwood

Hearing loss is estimated to be the most common disability in the developed world. In Australia, 3.5 million people experience some degree of hearing loss, at an economic cost of $11.75 billion a year. The most insidious and earliest hearing impairment is a neural injury, where connection with the sensory "hair" cells of the cochlea is lost. This disturbs the clarity of sound, but cannot be detected on standard hearing tests, so it is sometimes called "hidden" hearing loss. It is permanent, causing trouble with communication.

We believe we have found a possible treatment for this neural injury, which has the potential to reduce both the impairment and the costs associated with hearing loss. The treatment involves applying a single, combined dose of two neurotrophins locally to the inner ear: brain-derived neurotrophic factor (BDNF) and neurotrophin-3 (NT-3).

This is a promising development; however, the administration of neurotrophins as potential therapeutics has some well-known complications (they are difficult to produce; break-down quickly; bind to multiple receptor types). In this project, we are developing peptides that mimic specific regions of neurotrophins, and are able to overcome the obstacles of the neurotrophins themselves. We have previously made a BDNF mimetic, and have now begun to design and synthesise a mimetic of NT-3.

Quantitative Neuropathological Correlates of Advanced Ultra High Field MRI of Brain Microstructure in Multiple Sclerosis

CI: Roger Ordidge
Co-Investigators named on grant: Jon Cleary, Scott Kolbe, Amanda Ng, Ashley Bush, Scott Ayton, Catriona McLean

Multiple sclerosis (MS) is the most common cause of chronic neurological disability in young adults in developed countries, affecting >2.5 million worldwide. Novel advanced MRI techniques have emerged which may improve this sensitivity by exploring physical brain microstructure. One is a technique called Quantitative Susceptibility Mapping that measures the fundamental magnetic properties of tissue and is strongly correlated to both demyelination and brain iron concentration (an exciting biomarker of neurodegeneration in a number of disease processes, also present in high concentrations in macrophages). Another is diffusion imaging, which probes the preferred travel of water protons, allowing detailed visualisation and quantitation of intact white matter axonal tracts. Despite the promise of these techniques, with large-scale clinical studies in progress worldwide, significant controversy remains as to their true biophysical basis and thus ultimate clinical utility.

This collaborative pilot study aims to perform detailed direct comparisons of quantitative MRI techniques to physical, quantitative assessments of iron, myelin and axonal density in MS and healthy control ex-vivo brains. We will obtain 3 MS and 3 control fixed whole brain hemispheres from the Victorian Brain Bank and image the tissue using high-resolution anatomical, QSM and diffusion MRI sequences on an ultra-high field, 7 Tesla scanner. The system permits high resolution (as low as ~100µm) and stronger susceptibility contrast, giving the best possible direct comparison with histology.

Ultra-deep sequencing of oligodendrocyte lineage genes to investigate the role of somatic mutation in multiple sclerosis

CI: Justin Rubio
Co-Investigators named on grant: Michael Barnett, Stephen Leslie, Andrew Fox

Multiple sclerosis (MS) is the most common demyelinating disease of the central nervous system, affecting over 20,000 people in Australia and 2-3 million globally. An area of significant unmet clinical need is progressive MS because it is associated with significant disability and is currently therapeutically intractable. Knowing what genes are involved in progressive MS, and disease progression more generally, would increase understanding of its underlying biology and facilitate the development of targeted treatments.

This project is exploring the possibility that genetic mutations, which are restricted to the cells that make myelin (oligodendrocytes, OL), could drive progressive MS and that the genes themselves could be future therapeutic targets. As a proof-of-concept, this project aims to conduct "massively parallel" DNA sequencing of 20 genes involved in OL development and function to determine whether they may harbour damaging mutations. Key to this experiment are techniques we have developed to isolate and study genomic DNA from OLs in pathologically characterized post-mortem neural tissue from people with MS.

Using Decoded Brain Signals to Control Prosthetic Limbs

CI: Dean Freestone
Co-Investigators named on grant: Mark Cook, David Grayden, Stefan Harrar, Sam John, David Auckland, Terry O'Brien, Yan Tat Wong, Tom Oxley

Targeting Tyro3 To Promote Remyelination In Multiple Sclerosis

CI: Trevor Kilpatrick
Co-Investigators named on grant: Michele Binder, Junhua Xiao, Jonathan Baell, Helene Sabroux

Multiple sclerosis (MS) is an inflammatory disease of the central nervous system (CNS), and is a common cause of neurological disability, affecting over 2 million people worldwide. The primary target of attack in MS is the oligodendrocyte, and the myelin these

cells produce. Demyelination, the loss of myelin that insheathes axons, impairs CNS function by disrupting electrical impulses and exposes axons to inflammatory attack. After a demyelinating event, some spontaneous, albeit incomplete, remyelination occurs but as the disease evolves into its progressive phase remyelination fails, leading to the degeneration of exposed axons.

Progression of disability in MS correlates with accumulated axonal degeneration, which in turn is influenced by the extent of demyelination and the loss of oligodendrocytes. Current MS therapies are anti-inflammatory and although efficient in limiting the relapses that characterise recent onset MS, they do not prevent subsequent disease progression, for which no treatments are available.

This project will seed a novel multi-disciplinary and transformative approach to the management of progressive MS. Important aspects of the work include:

1. Assembly of a truly interdisciplinary group of collaborators in order to identify binding partners of a myelin promoting receptor tyrosine kinase
2. Preliminary interrogation of whether the binding partners exert agonist/ pro-myelinative activity

Melbourne Neuroscience Institute Fellowships

The MNI Fellowships provide an opportunity for the University to promote interdisciplinary research projects in the Neurosciences and related disciplines. There are two Fellowships available each year and the 2017 round was highly competitive.

The successful applicants were Dr Susan Northfield, School of Biomedical Sciences and Dr Bao Nguyen, Department of Optometry and Vision Sciences.

Ultra-high field imaging of the human eye

Bao Nguyen

The proposed project aimed to capitalise on recent advances in magnetic resonance (MR) imaging and the arrival of a customised eye coil (only one of two in the world) at the Melbourne Brain Centre. The specific goal of the project was to non-invasively image the structure of the human eye using the latest technologies and provide a unique opportunity to study ocular pathologies such as glaucoma, a disease affecting the optic nerve. There is very recent interest in the susceptibility of the optic nerve to mechanical stress in glaucoma, particularly at its point of insertion at the back of the eye. The project combines ultra-high field MR imaging in 2D and 3D to view the entire eyeball and optic nerve, and high resolution optical coherence tomography (OCT) to view the layers of the retina and posterior portion of the eye, in individuals who may be more susceptible to mechanical overloading (e.g. people with elongated eye length due to high short sightedness). The findings of this study will provide further insight into risk factors associated with susceptibility to optic nerve damage.

Development of BDNF peptide mimetics as tools to study and potentially treat Multiple Sclerosis

Susan Northfield

My research involves developing peptides that mimic the function of a specific loop-region of a protein called Brain-Derived Neurotrophic Factor (BDNF). These peptides allow us to study how BDNF interacts with its native receptors and can potentially be further developed as therapeutic agents. The overarching aim of my research fellowship is to develop more membrane-permeable analogues of my lead peptide candidate, TDP6, which acts via the TrkB receptor and promotes the growth of myelin in the CNS (just like BDNF, the protein on which it was modelled). Enhancing membrane permeability is a crucial first step toward improving blood-brain barrier penetration of the peptides, which is vital for any CNS-related therapeutics or chemical biology tools required to study multiple sclerosis.

Strategic Australian Government Research Training Program Scholarship

The MNI was allocated three Australian Government Research Training Program (RTP) scholarships (formerly known as APA scholarships) to award in 2017. Scholarships are open to eligible, high-achieving RHD students undertaking interdisciplinary neuroscience-related research projects by competitive application. Award recipients receive a generous stipend for 3 years. The MNI provides a further $3,000 to the student, and $2,000 to the supervising laboratory, per annum.

2017 Awardees

Hayley Jach, Melbourne School of Psychological Sciences
Research project title: *"Towards a Neurobiologically Plausible Model of Personality"*

Laura Ellet, Pathology Department.
Research project title: *"The role of prion strain in disease progression and pathogenesis"*

Madeline Nicholson, Department of Anatomy & Neuroscience
Research project title: *"Investigating the roles of nerve cell signals in enhancing brain myelination"*

Since 2011, MNI has awarded 16 Australian Government Research Training Program Scholarships, 8 of which are under management in 2017.

CHAPTER 6

Governance

Advisory Board

The Advisory Board aims to ensure the MNI is aligned with important developments in the Neurosciences and to provide avenues for engagement with those who might wish to commission or undertake research through collaborative interaction in the Neurosciences and related disciplines of research at the University. Board members have strong credentials whether at the University of Melbourne, or the private, public and non-government sectors and act as advocates on behalf of the MNI.

The MNI would like to extend thanks Prof Mark Hargreaves who - as Chair - has provided tremendous oversight and guidance to the board and MNI.

MNI extends a warm thanks to departing member, Dr Andrew Milner for his exceptional service to the MNI Advisory Board. In mid-2017, MNI welcomed Dr Anthony Filippis from Neurosciences Victoria and Professor Stephen Davis from the Melbourne Brain Centre, Royal Melbourne Hospital.

Scientific Consultative Forum

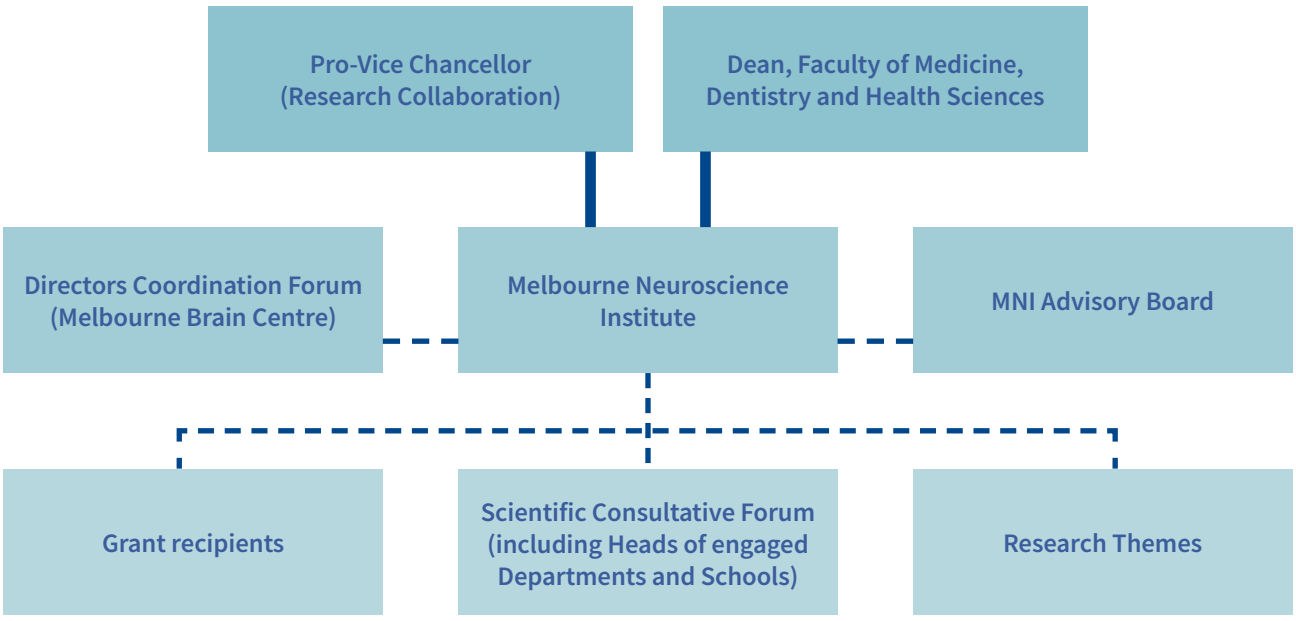
The Scientific Consultative Forum comprises the Heads or their delegates from Departments involved in neuroscience-related research. Members of the forum assist the MNI by providing a coordinated vision for the award of core research support funds provided by MNI and by providing key strategic advice, ancillary to that provided by the MNI Advisory Board.

2017 Advisory Board Membership

Name	Title
Professor Mark Hargreaves (Chair)	*Pro Vice-Chancellor (Research Collaboration & Partnerships), UoM*
Professor Trevor Kilpatrick	*Director, Melbourne Neuroscience Institute, UoM*
Professor Greg Qiao	*Assistant Dean (Research), Melbourne School of Engineering, UoM*
Professor Karen Day (Professor Laura Parry as sub)	*Dean, Faculty of Science, UoM*
Dr Andrew Milner	*Chief Executive Officer and Managing Director, Neurosciences Victoria*
Dr Anthony Filippis	*Chief Executive Officer and Managing Director, Neurosciences Victoria*
Professor Stephen Davis	*Professor of Translational Neuroscience at the University of Melbourne, Director of the Melbourne Brain Centre and Neurology at the Royal Melbourne Hospital*

Name	Title
Professor Perry Bartlett	*Inaugural Director, Queensland Brain Institute*
Associate Professor Andrew Metha	*Deputy Director, Melbourne Neuroscience Institute, UoM*
Professor Glenn Bowes	*Deputy Dean, Faculty of Medicine, Dentistry and Health Sciences, UoM*
Professor Bob Williamson	*Chief Scientific Officer, Yulgilbar Foundation; Ex-Secretary for Science Policy, Australian Academy of Science; Honorary Professorial Fellow, Faculty of Medicine, UoM*
Dr Keith McLean	*Director Manufacturing Flagship, CSIRO*
Dr Andrew Nash	*Senior Vice President, Research, CSL Limited*

Governance Structure



The Melbourne Neuroscience Institute team:
Andrew Metha, Vikki Marshall, Trevor Kilpatrick, Amy Bugeja, Carmel McFarlane

THE UNIVERSITY OF
MELBOURNE

Melbourne
Neuroscience Institute

Level 5, Kenneth Myer Building
(Melbourne Brain Centre, Parkville)
30 Royal Parade, Parkville, Vic 3010
University of Melbourne

Telephone: 03 8344 1804
www.neuroscience.unimelb.edu.au