

2015

Melbourne Neuroscience Institute Annual Report



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2015

Melbourne Neuroscience Institute

Annual Report

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EXECUTIVE SUMMARIES

Message from the Director

The calendar year of 2015 has been a period of great activity for the Melbourne Neuroscience Institute. Our sponsored themes focusing on Neural Engineering, Imaging, Stem Cell Science and Music Mind and Wellbeing continue to flourish. Work on the 7 Tesla MRI and PET-CT scanners is progressing well and involves a mature synthesis of basic development work and clinical application. The harnessing of stem cell biology to study the function of neural networks in vitro keeps our neuroscientists at the cutting edge, for example those who are studying the pathogenesis of epilepsy and Alzheimer's disease. The Centre for Neural Engineering (CfNE) continues to undertake world leading research in the development of microsensor technology and its application to monitoring the activity of neurological disease. The commissioning of the Helium ion microscope within the CfNE has also provided our investigators with a rare opportunity to visualise the microstructure of the biological and physical systems they work with at unparalleled resolution. The Music Mind and Wellbeing initiative continues to voice the importance of music to the general community, to education and to medical rehabilitation, as well as providing insights into how music education is optimised and how music is appreciated as a key cognitive process.

Linkages with our partner institutes were further enhanced during 2015. In particular, we held a theme-based conjoint workshop with the University of Calgary/Hotchkiss Institute focusing on concussion. The workshop was attended by 33 participants including Professor Sam Weiss, Director of the Hotchkiss and four of his colleagues. The workshop was highly successful and has led to the establishment of key partnerships focusing on paediatric trauma, diagnostic imaging, guidelines for management of concussion and discovery-based research. The two institutes are currently planning a follow-up workshop in 2017. We also fostered a strategic alliance with the Monash Institute for Pharmaceutical Sciences supported via our Indisciplinary Seed Funding Scheme. Two collaborative projects between the two Institutes were supported through this interaction and other concrete interactions have been formulated for mutual benefit.

Looking forward, the vision of MNI is to continue to bring emerging technological developments and the expertise that accompanies those developments to neuroscientists in order to improve outcomes both for the Neurosciences and for the community, in general. To date, this has been achieved in a modular way, for example via sponsorship of the Themes.

However, we are increasingly recognising that, for maximal impact, these initiatives need to be considered in a holistic way, and vehicles need to be developed by which to actively encourage dialogue if not 'collisions' between the Themes.

During the next quinquennium we will also encourage initiatives in the clinical neurosciences. In particular, we will be sponsoring a cohort of young clinical investigators, on the basis that the promotion of clinical translation is a core responsibility of MNI that needs to be nurtured. Commensurate with this, we will provide focused support to key areas of clinical research, for example Alzheimer's disease and traumatic brain injury. We will also explore mechanisms by which to improve our capacity to access and analyse clinical data sets, recognising that there is an opportunity to do this in concert with the recently configured Melbourne Academic Centre for Health. We will also further cement our productive interactions with the Monash Institute for Pharmaceutical Sciences for mutual benefit.

We will continue to nurture strong and productive interactions with the commercial sector, including the pharmaceutical industry, imaging vendors and key partners of the University of Melbourne, such as IBM. We will also nurture our extant interactions with our international academic partners for example the Hotchkiss Institute, Calgary and Université Pierre et Marie Curie, Paris.

The MNI also plans to actively promote ongoing interactions with other University of Melbourne Institutes. We already interact with the Melbourne Social Equity Institute to promote disability oriented research and plan to interact substantively with the Melbourne Networked Society Institute in the area of technological developments for the elderly, in particular to reduce the impact of cognitive decline. Our public seminar program in 2016 will incorporate these themes and will enable interaction with a number of Hallmark initiatives including the Ageing, Disability and Indigenous Research Initiatives.

Finally, I would like to acknowledge the hard work of our Advisory Board and of the MNI team, namely Andrew Metha, Vikki Marshall, Amy Bugeja and Carmel McFarlane. Together, we work as a cohesive group for the benefit of our Affiliates, the University and the community in general. With this in mind, I look forward to an exciting and productive year during 2016.



Professor Trevor Kilpatrick

Professor Trevor Kilpatrick
Director, Melbourne Neuroscience Institute

Message from the Dean

I am pleased to report that 2015 has been another excellent year for the Melbourne Neuroscience Institute (MNI) and for neuroscience-oriented research at the University of Melbourne. The University continues to consolidate its strengths in clinical neuroscience and psychiatry with internationally renowned expertise in areas such as epilepsy, Alzheimer's disease, multiple sclerosis and schizophrenia. Our work in systems neuroscience also continues to flourish and it has been particularly exciting to witness recent advances in the bionic eye project. Links between the Neurosciences and Psychological Sciences continue to strengthen in numerous ways, including in the Neuroscience PhD coursework, cognitive neuroscience oriented programs and in work focusing on the biology of neural networks. Faculty support directed to a complex human data initiative within the School of Psychological Science should also provide a strong foundation for enhanced collaborative interactions in future years.

High quality Neuroscience in the 21st century depends on strong links with engineers, mathematicians, physical scientists and also those involved in the social sciences. It is therefore pleasing that the MNI sponsored themes in Stem Cell Science, Neural Engineering, Magnetic Resonance Imaging and Music not only continue to develop in their own right but that they are inexorably becoming integrated into the activities of the Neuroscience community, in general. Excellent examples of this integration include the application of neural stem cell technology to generate neural networks in vitro to understand epilepsy and the use of the state of the art imaging to further our understanding of the pathogenesis of Alzheimer's disease.

I am particularly pleased that MNI continues to focus on the training of our graduate researchers by delivery of a much valued advanced workshop program and by providing scholarships for secondment to our academic partner, the Hotchkiss Brain Institute in Calgary. At a time of funding challenges in our sector, MNI continues to also provide valuable financial support to test new ideas, as well as fellowships for postdoctoral researchers and student stipends. I also congratulate MNI for assuming a leadership role in establishing concrete links with the Monash Institute for Pharmaceutical Sciences, with several key collaborative projects in medicinal chemistry having already been established.

In summary, I commend the Director and the staff of MNI for their achievements in 2015 and I look forward to another successful year for the Institute in 2016.



Professor Mark Hargreaves

A handwritten signature in blue ink that reads "Mark Hargreaves". The signature is written in a cursive, flowing style.

Professor Mark Hargreaves
Dean, Medicine, Dentistry & Health Sciences

RESEARCH

Music, Mind and Wellbeing

Director: Prof Sarah Wilson

Deputy Director: Prof Gary McPherson

Music, Mind & Wellbeing (MMW) links neuroscience with music and social wellbeing through a unique set of collaborations spanning music, science, health, education, and industry. The year 2015 has been another productive and successful year for MMW, with a range of research and community-based activities receiving ongoing academic and media attention, and promoting public engagement in music within the community.

MMW has three core research strands encompassing (i) music neuroscience, (ii) music education, and (iii) health and wellbeing. Our music neuroscience program incorporates a range of projects relating to the neurobiological basis of hearing, sound recognition and music, as well as the genetic and environmental determinants of music abilities. MMW continues to demonstrate that music is a powerful tool for changing the brain across the lifespan, both in response to training and after recovery from brain injury. Building on this, our music education program is investigating the key factors underlying student engagement in music learning and performance across primary, secondary and tertiary education settings, including the development of highly effective interventions for music performance anxiety in secondary school and conservatorium students. Our health and wellbeing program investigates the use of music to promote the mental health and wellbeing of individuals and communities, and to facilitate recovery following physical or mental illness. These research projects determine the best ways for music to be applied therapeutically with people in hospitals, schools, aged and palliative care facilities, and the community, with important implications for building inclusive communities that embrace diverse and creative participation.



Professor Sarah Wilson

Research

Within the neuroscience research program, recent work includes: (1) a study examining the genetic and environmental determinants of singing ability that is being performed in collaboration with the Australian Twin Registry, (2) investigating the neurobiological and psychological causes of tinnitus (chronic ringing in the ears) and its treatment, (3) examining the cognitive and personality factors that underpin our ability to become absorbed and engaged in music, (4) a systematic review of music abilities in people with epilepsy to

shed light on our understanding of music networks in the brain and to help guide treatment decisions, such as brain surgery in musicians with epilepsy, and (5) using eye tracking to measure visual attention during music therapy.

Within the educational research program, recent work includes: (1) examining the role of music ability in our sense of identity and its impact on child development, (2) identifying early manifestations of musical prodigies, (3) new knowledge of how group instrumental training supports problem-solving abilities, literacy, numeracy and wellbeing in socially disadvantaged primary school students, (4) investigating music performance anxiety in secondary school and conservatorium students, including the most effective psychological strategies to treat it, (5) an ARC-funded study examining motivation and practice quality in elite music performers to determine how best to optimise musical expertise, and (6) building resilient school communities through tailored arts programs. The findings of our team have directly contributed to the Victorian Parliamentary inquiry into music education, and MMW has been approached by the Victorian Curriculum and Assessment Authority (VCAA) to contribute to the development of a series of music programs for the new National Curriculum.

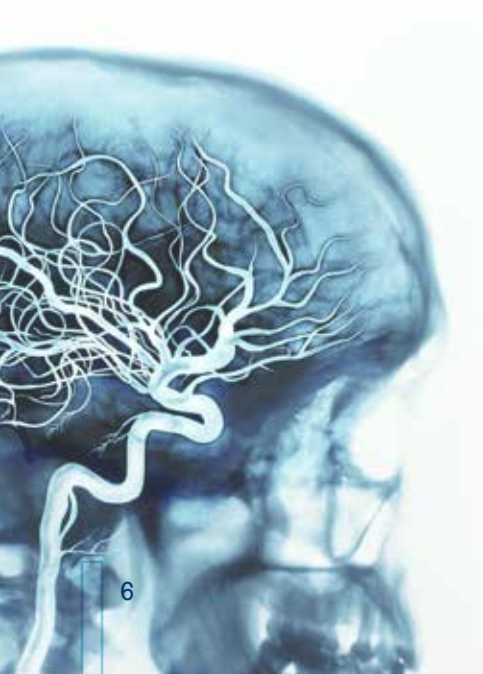
Within the health and wellbeing research program, recent work includes: (1) an ARC-funded multi-site study examining the efficacy of songwriting in the rehabilitation of people with acquired brain injury or spinal cord damage to support changes in personal identity post-injury, (2) investigating self-selected music that enhances exercise capacity and reduces risk factors in older adults with cardiac disease, (3) examining the potential of music-assisted relaxation to help people with motor neuron disease to use non-invasive ventilation, (4) research with people with Parkinson's disease and their caregivers examining the therapeutic effects of singing for speech, wellbeing and relationship quality, (5) the development of innovative telehealth programs providing online music therapy for people with quadriplegia, (6) examining the social benefits of music, particularly the role of music synchronisation for promoting pro-social behaviors and helping people with post-traumatic stress disorder (PTSD), and (7) assessing and enabling music participation for wellbeing across the lifespan, including the promotion of community music participation in people with a disability under the NDIS.

Outreach and education

The MMW community engagement program aims to promote new public attitudes that foster grass roots participation in music. In 2015, it included both public-focused and academic-focused activities that received significant coverage in the print media, radio and television, including a recent feature of our genetic research into singing ability on the SBS television program, 'Insight'.

Public Lecture Series: 'Music on the Mind'

For the fifth consecutive year we co-hosted a popular public lecture series, 'Music on the Mind' with the Melbourne Recital Centre. This series features eminent minds and musicians discussing the relationship between music and



the brain and related links to health and social wellbeing, music participation, learning and development, the role of music in the community and its therapeutic applications. This series has greatly enhanced public engagement in music research through sell-out attendances at the Melbourne Recital Centre, and through interviews and articles in print, radio and online about the lectures and research.

Academic Seminar Series: 'Music, Auditory Cognition and Mind'

Each year, MMW and the Australian Music Psychology Society (AMPS) co-host a series of academically-focused research presentations and discussions showcasing the latest findings in music research. These seminars are attended by international and national researchers from a broad range of disciplines as well as music performers and educators and are designed to promote interdisciplinary dialogue. They are also designed to promote the growth of future research in Australia by engaging student researchers in presentations, discussion and topical debates.

Second Australian Music Research Conference: 'The Art and Science of Music', December 2015

MMW played a vital role in the second Australian music research conference, The Art and Science of Music, which followed on from the inaugural conference co-hosted by MMW with AMPS in 2013. This second conference took place at Western Sydney University and was a huge success, covering topics as diverse as acoustics, rhythm perception, music emotion, music education, music performance, and music therapy. Topics were explored through platform presentations, discussions, panels, mentoring and collaboration sessions, and live music performances, with the event receiving over 100 tweets and featuring a member of the MMW Executive, Professor Jane Davison, as a Keynote speaker.

Partnerships and Goals

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 Bionics Institute, the Melbourne 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 2016, MMW plans to maintain its research and community engagement profile, with public educational events already being arranged, as well as the third national conference in the preliminary stages of planning. Through these

initiatives MMW will continue to develop and apply new knowledge and grow Australian music research in conjunction with its partners.



Professor Roger Ordidge

Melbourne Brain Centre Imaging Unit

Director: Prof Roger Ordidge

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

Chief Molecular Imaging Technologist: Mr Rob Williams

Radiographers: Shawna Farquharson, Claire Mulcahy

The Melbourne Brain Centre Imaging Unit supports a broad spectrum of research focused on understanding the structure of the human brain in health and disease. The Unit hosts two flagship instruments: a PET/CT scanner and a 7T MR Research scanner, both focusing predominately on human-based brain research. This world-class facility was funded by the University of Melbourne, the Florey, the National Imaging Facility (NIF) and the Victorian Biomedical Imaging Capability (VBIC).

Research

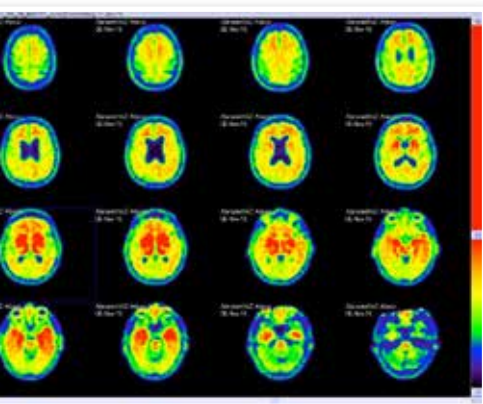
The PET/CT facility has partnered in a diverse range of research projects, many of which are world leading. Last month the Human Amyloid Imaging (HAI) Clark Award at the 2016 international HAI was presented to our research collaborators. This premier award is for overall scientific merit and relevance of the research to the field of human amyloid imaging.

Our Amyloid and Tau PET imaging has progressed quickly and it is expected that this will expand in the upcoming years given that experimental therapies for Alzheimer's disease are now being tested.

Our collaborative work extends to the assessment of new radiopharmaceuticals to be used for enhanced diagnosis of a range of neurodegenerative diseases. Many of our research projects are unique such as our veterans studying into Post Traumatic Stress Disorder and Traumatic Brain Injury, which combines Amyloid PET, Tau PET, and FDG PET imaging and 7T MRI, providing very comprehensive studies. Our other partners have included the Austin Health, Florey, NIH, US Army, Alzheimer's Australia, CSIRO, Monash University, Avid Radiopharmaceuticals, Merck, GE Pharma, and Piramal Pharma.

The 7T MRI scanner became operational in July 2014, and to date, over 140 subjects have been scanned in a variety of collaborative research projects. These pilot projects have been performed together with researchers from several VBIC institutional members.

Studies in Multiple Sclerosis and Alzheimer's Disease will commence in the near future, and further development work to increase the capability of the system will proceed during 2016.



An example of a world-class cutting-edge PET image of the distribution of the tracer THK5351 that attaches to Tau protein (Alzheimer's disease patient). Courtesy of Prof Chris Rowe (Austin Hospital), Rob Williams (UoM)

As an example of the diversity of our research collaboration, the neuroanatomy of cough has been studied. Cough is a critical reflex. Unfortunately, persistent, non-productive cough can occur in some clinical conditions, and treatments for this distressing problem are generally ineffective. Finding an effective treatment is complicated by the need to preserve the vital functions of the cough reflex that keep the airways clear. One strategy is to focus on the sensory processes that accompany irritation of the airways. Stimulation of the airways elicits a perceptible urge-to-cough, and hypersensitivity of this sensation is likely to contribute to frequent coughing in patients with chronic cough. Consequently, understanding the functional neuroanatomy of airways sensations in humans is a priority in the development of potential cough suppressants, and this field of research has received a major boost with the availability of 7T MRI at the Melbourne Brain Centre Imaging Unit. Animal studies of airways sensations have highlighted two parallel pathways in the central nervous system with key nuclei in the brainstem. These nuclei are small, and the measurement of functional responses in these regions is not feasible with standard MRI scanners. Preliminary human experiments involving airway irritation and images acquired with the 7T scanner have been very encouraging, with responses observed in discrete regions of the brainstem.

Outreach and Education

The Imaging Unit hosted a well-attended Imaging Symposium in December 2016. We have also presented a lecture series on MRI as part of the MNI Advanced Workshop series. These lectures were attended by 6 postgraduate students and University staff members and included practical demonstrations of MRI operation. The facility regularly provides tours for University staff, the research community and visiting dignitaries.

Stem Cells Australia

Director: Prof Martin Pera

*Head of Education, Ethics, Law & Community Awareness Unit:
A/Prof 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.

Led by Prof Martin Pera at the University of Melbourne, 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.



Professor Martin Pera

Research

Four main areas of stem cell biology were the focus of SCA's research activities in 2015 – control of pluripotency and reprogramming, regeneration and repair in the brain, regeneration and repair in the heart and the development of blood – with members contributing to over 120 publications in prestigious journals such as Nature, Nature Communications, Nature Medicine, Nature Cell Biology, Cell and Cell Stem Cell.

One SCA discovery that attracted significant media interest was the creation of mini-kidneys from stem cells by Prof Melissa Little and colleagues at the Murdoch Children's Research Institute. By building on their earlier experience, the researchers have been able to grow an organoid in a dish that forms all the different cell types normally present in the human kidney. Key to this breakthrough was adding different concentrations of growth factors at various times, allowing researchers to mimic normal development. Researchers say this discovery will provide a new way to screen drugs either for the treatment of kidney disease or to identify drugs that might pose a risk of kidney damage.

Stem Cells Australia's scientists at The University of Queensland also took part in a discovery that may have implications for the treatment of learning- and mood-related disorders. In research lead by Dr Dhanisha Jhaveri from the Queensland Brain Institute (QBI) two distinct types of cells in a region of the brain known as the hippocampus were identified and examined. While previously it was believed that all progenitors in the hippocampus were identical, this discovery reveals that there are two dormant precursor subtypes. This discovery was made using state-of-the-art cell-sorting and DNA technologies and solves a longstanding mystery about how nerves involved in regulating learning and memory, as well as mood, regenerate.

Outreach and Education

Getting reliable information about stem cell research can be challenging for anyone seeking a solution to troubling health problems, or even those simply interested in learning more about this exciting new area of medical research.

In 2015 Stem Cells Australia supported the International Society for Stem Cell Research (ISSCR) to expand their 'Closer Look at Stem Cells' website (www.closerlookatstemcells.org). Launched in April, this website is a comprehensive destination for those interested in stem cell science and research being conducted across the globe. The site encourages the reader to learn more about the science that underlies a given treatment, as well as the principles and practices that should be followed when taking stem cell research from the laboratory to the clinic.

At a local level we collaborated with the National Stem Cell Foundation of Australia to update 'The Australian Stem Cell Handbook' – an electronic resource designed to help those interested in stem cell science to ask the right questions when researching stem cell treatments – and also partnered with the Australasian Society for Stem Cell Research to develop a multimedia public engagement platform featuring video and the 'Stem Cell Essential' public information site.

For many years Stem Cells Australia has been an outspoken critic of the sale of unproven stem cell treatments. During 2015, we joined colleagues from around the world to update the ISSCR 'Guidelines for Clinical Translation of Stem Cells' and thereby set standards on bringing science from the laboratory to the clinic. Stem Cells Australia also provided a submission to the Therapeutic Goods Administration (TGA) in response to their request for feedback on possible ways to close what we consider to be a loophole in the current Australian regulations that govern autologous cell therapies – where the patient's own cells are used. In addition, recognizing that professional standards are also an important consideration, we have continued to liaise with the Australian Health Practitioner Regulatory Agency and professional bodies such as the Royal Australasian College of Physicians to enhance professional understanding and awareness about these unproven, and in many cases unfounded, practices.

Through MNI, the Melbourne node of SCA continues to offer a workshop in the application of human pluripotent stem cell technology in neuroscience that has been very enthusiastically received. We also continue to support our neuroscience colleagues here through the operation of our Flow Cytometry and Stem Cell Core laboratories.

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, and the CSIRO Material Science Division.

During 2015 SCA received a favourable mid-term review of its operations with the Australian Research Council confirming our ongoing funding to 2018. We were also part of an Australia delegation, led by the Australasian Society for Stem Cell Research that has secured the 2018 International Society for Stem Cell Research conference which is expected to draw over 3,000 researchers and professionals from around the globe to Melbourne.

In 2015, A/Prof Megan Munsie and Prof Martin Pera were invited to sit on the Therapeutic Technologies Research Initiative Steering Committee to help facilitate collaborative and interdisciplinary research by involving research staff from across University faculties, departments, and schools, and by facilitating connections and introductions with external researchers. The Therapeutic Technologies Research Initiative (TTRI) serves to enhance and profile the existing but dispersed groups across the University sector and in Institutes that work in areas related to therapeutics.

Goals for 2016

Having received a favourable mid-term review and approval by the Australian Research Council for ongoing funding until 2018, in the next twelve months SCA will be seeking to:

- Further strengthen the collaborative focus within our current research portfolio
- Expand our 'Affiliate Investigators' and partner network to acknowledge other leading Australian stem cell researchers whose vision and leadership will further strengthen our initiative
- Expand our national and international collaborative networks across bioengineering, nanotechnology, stem cell biology, advanced molecular analysis and clinical research
- 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 UoM and FINMH through:

- Provision of human neural progenitor cells and training to groups wishing to use pluripotent stem cells in functional genomics and disease modeling via our StemCore Facility,
- Access to the latest high-end flow cytometric machinery and services in our 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.



Professor Stan Skafidas

Centre for Neural Engineering

Director: Prof Stan Skafidas

Deputy Director: Prof Steven Petrou

The Centre for Neural Engineering (CfNE) was established by the University of Melbourne as a cross-faculty initiative in response to the developing convergence between the technological and life sciences, bringing together existing strengths in medical, physical and technology research to forge new pathways.

Research within the CfNE operates across discipline boundaries to further our understanding of the brain and neural system. Its multidisciplinary nature, along with the breadth of its collaborative links, provides opportunities for staff and students to develop and utilise expertise from outside their own core area. This environment encourages innovative ideas as participants bring a wide variety of viewpoints and approaches to research problems.

Research

CfNE researchers were involved in a wide variety of projects during 2015, working with fellow researchers, clinicians and industry partners to advance the field of neural engineering.

Working with collaborators, Gursh Chana's Integrative Biological Psychiatry group reported evidence that the decreased expression of the glutamate receptor, mGluR5, and its signalling components represent a key pathophysiological hall mark in mouse models of Autism Spectrum Disorder. This decreased expression of mGluR5 has implications for the regulation of microglial numbers and their activation during brain development. In addition to their major role in the nervous system's immune defences, microglia are thought to play an important role in synaptic pruning, and thus to influence brain connectivity.

Point-of-care diagnostic devices integrating nanoelectronics, microfluidics and functionalised surfaces have been a focus of CfNE work in 2015. Working with collaborators at the Royal Melbourne Hospital, the Victorian Infectious Diseases Reference Laboratory and St Vincent's Hospital, proof of concept devices have been produced for testing applications such as genetic variations associated with epilepsy drug reactions and the identification of species and antibiotic resistance in bacteria. Based on changes to electrical properties following molecular bonding, the devices are able to measure proteins at picogram per millilitre concentrations within 10 minutes, drastically cutting the time traditionally required for doing this testing in the laboratory.

David Simpson, Lloyd Hollenberg, Steve Petrou and colleagues at the University of Melbourne School of Physics have developed a new approach to overcome many of the limitations in current magnetic imaging techniques. Using the magneto-optical response of an array of negatively-charged nitrogen vacancy spins in diamond, they have imaged and mapped the sub-micron stray magnetic field patterns from thin ferromagnetic films. This shows that diamond-based wide-field microscopy can be used as a tool for the rapid, high-sensitivity characterisation and imaging of magnetic samples.

Other projects worked on by CfNE researchers during the year include

- Modelling the Human Nervous System with Human Pluripotent Stem Cells
- New Generation EEG Devices for Improved Mental Health Care
- Next Generation Brain-Machine Interface: Minimally-Invasive Endovascular Stent-Electrode Array for Robotic Limb Control
- Glucose Homeostasis in Epilepsy
- Personalised Prognostic Tools for Early Psychosis Management
- Silicon Photonics Integration for Light Field Microscopy.

Outreach and Education

CfNE continued its association with the *Convergence Science Network* and in September opened the Centre's doors to the public as part of the Network's *Opening the Vault* series. Fifty attendees were provided with a tour of the CfNE's facilities, including the PC2 laboratory and the newly commissioned (and long-awaited) helium ion microscope. Staff and students talked with an eager audience about the work they are doing in understanding brain development and disorders through 3-D Brain-in-a-Dish modelling,



Opening the vault

the use of post-mortem brain tissue to understand the causes of Autism Spectrum Disorder, how advanced biosensors can detect bacteria and how a microscope can be used to both examine biological specimens and to fabricate electrical systems at nanometre levels.

Postgraduate education is an important part of CfNE's activities and during 2015 the Centre provided research higher degree training for almost forty students across three faculties. Eight new students joined the Centre during the year, while six were farewelled after completing their studies. Our new students are working on a variety of projects, including

- Localisation and reconstruction of brain sources from EEG/MEG using beamformers;
- Graphene: a biocompatible scaffold for modelling corticogenesis in three dimensions;
- Laser induced fluorescence detection technology;
- Modelling the sensory nervous system with human pluripotent stem cells;
- High performance printable electronics for biomedical applications; and
- Development of point-of-care molecular diagnostic devices for applications in precision medicine.

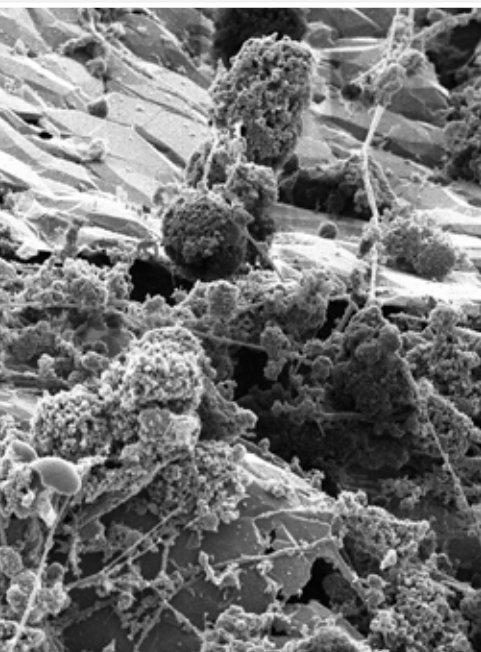
Partnerships & Collaboration

Strong collaborative partnerships are a cornerstone of CfNE's operations, and we would like to acknowledge the vital contributions made by key collaborators, particularly those that bring clinical expertise to projects.

Key partners of the CfNE include the Melbourne Neuropsychiatry Centre, the Bionics Institute, IBM Research, Austin Health, Royal Melbourne Hospital, the Victorian Infectious Diseases Reference Laboratory, the ARC Centre of Excellence for Integrative Brain Function, Duke University, St Vincent's Hospital, the FINMH, Cambridge University, the National Institute of Environmental Health Sciences, Guide Dogs Victoria, the Friedreich Ataxia Research Association, Freedman Electronics, Murdoch Children's Research Institute, Austin Health and the Centre for Eye Research Australia.

Goals for 2016

During 2016 CfNE will continue to expand its collaborative base and engagement with industry, particularly potential partners in point-of-care diagnostics. CfNE will also begin playing a key role in the High Value Product Development program of the new Innovative Manufacturing CRC (IMCRC), developing electronic devices, diagnostic tools, implantable materials and related technologies.



Neurons growing on scaffold- Image from helium ion microscope

Students of Brain Research Professional Development Dinner

SOBR is a not-for-profit, independent organisation that is run by students. Founded in 2011, SOBR aims to connect brain research students from across Victoria. Without sponsors, including the MNI, SOBR would not be able to hold events to provide opportunities for students to network.

Imagine a room filled with 150 brain research students, distinguished scientists, and science communicators from over 15 different institutes and organisations – all gathered together to discuss the future of science in Australia. This sets the scene for the recent Students of Brain Research (SOBR) Annual Professional Development Dinner, held at the Arts Centre, Melbourne, on Tuesday the 23rd of June, 2015.

With keynote speakers Prof Patrick McGorry, Dr Krystal Evans and Dr Andi Horvath, as well as 27 VIP guests and 120 brain research students, the 2015 Professional Development Dinner was a great success. Through the Professional Development Dinner, SOBR continues to provide brain research students opportunities to network and to engage within the scientific community.



Students of the Brain Research Dinner

SOBR Symposium

The second staple event of the year was the Student Symposium, held at the Advanced Technology Centre, Swinburne University of Technology, Hawthorn. Students reap immense benefit from this event via professional development, networking and mentoring. In 2015, the free symposium consisted of 19 oral presentations, over 70 poster presentations as well as 2 plenary lectures from Prof Murat Yücel and Dr Marguerite Evans-Galea.

The most outstanding presentations were awarded research bursaries.

The awardees were:

Oral Presentations:

Convergence Science Network Research Bursary – Louisa Selvadurai (Monash University)

Aaron Warren (The University of Melbourne)

Azu Azhan (Hudson Institute of Medical Research)

Poster Presentations:

Cellular and Molecular Neuroscience

Kathy Sengmany (Monash University)

Estella Newcombe (The University of Melbourne)

David Carter (The University of Melbourne) and Sasha Zaman (FINMH) – draw

Behavioural Neuroscience and Neuropsychology

Aron Hill (MAPrc) and Dylan Fox (Australian Regenerative Medicine Institute) – draw

Stuart Oldham (Monash University)

Neurodegeneration and Brain Injury

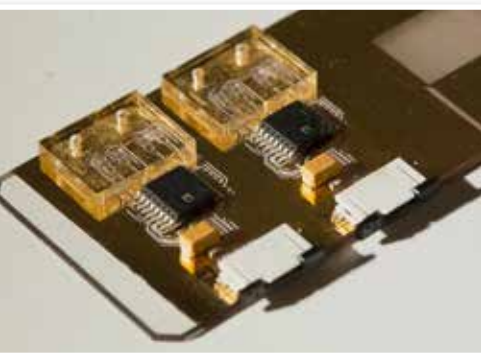
Sanuji Gajamange (The University of Melbourne)

Brett Kagan (FINMH)

Tia Cummins (FINMH)

Clinical Psychology, Psychiatry and Psychopharmacology

Eleni Ganella (The University of Melbourne) and Danielle Amiet (Monash University) – draw



Medical Point of
Care Devices

Research Highlights

Generous gift fires up engineering innovation in healthcare

A major donation to the University of Melbourne's Centre for Neural Engineering (CfNE) will provide critical funds to advance links between life sciences, engineering and physical sciences and drive the next wave of medical breakthroughs in Australia. Mr Leigh Clifford AO, Mrs Sue Clifford and their family are donating \$5 million to the University to endow The Clifford Chair in Neural Engineering.

The new Chair will help facilitate the development of new medical point of care devices, providing clinicians with the information they require to undertake faster, more reliable diagnoses and better management of patients especially those located in Indigenous and rural communities. The findings will also facilitate collaborative interactions across a number of disciplines to deliver new biotechnologies, treatments and improved engineered systems that replicate biological networks.

Mr Clifford, the current Chairman of Qantas Ltd and former CEO of Rio Tinto, is an engineering alumnus from the University and Deputy Chairman of Believe – the Campaign for the University of Melbourne. The Campaign is aiming to raise \$500 million by the end of 2017 to support key research, scholarship and engagement goals.

Mr Clifford supports new and innovative engineering, as he believes this will drive Australia's future, particularly in the area of healthcare. "The Chair will bring together researchers and experts from Engineering, Medicine and Science to improve health outcomes for every Australian not just those living in major metropolitan cities," Mr Clifford said.

“The gift will allow researchers to concentrate on progressing their pioneering and collaborative work ensuring people across Australia, and the region, have equitable access to healthcare. The idea of small, low cost and easy to use devices to optimise patient management is only one example of what is possible in the future,” he said.

Prof Stan Skafidas, Director of the Centre is inspired by the long history of innovative research conducted at the University and is passionate about the interface between engineering, medicine and the future. “This gift will enable us to address some of the long term and complex challenges facing health care. Bringing together interdisciplinary teams, allows them to build technologies that will change lives and help dictate the future of healthcare,” he said. “It will also help CfNE in our work towards addressing some of the major challenges in neuroscience and neurological and psychiatric disorders.”

“This is an exciting challenge as we work together to create not only portable diagnostic tools, but in addition, the next generation of bionic devices and implants.”

Lessons from brain development may help repair myelin in MS

Dr Stanislaw Mitew has made excellent progress in his research looking at myelin repair in the brain. Dr Mitew has recently reported on the results of the first year of his two-year MS Research Australia Post-doctoral Fellowship.

In MS, the insulating myelin layer that surrounds nerve fibres is damaged and lost. The body naturally has the ability to repair and regenerate damaged myelin, but in MS, this repair is often incomplete. Dr Mitew's research is exploring ways to harness the body's natural capacity for myelin repair using a type of stem cell present in the brain. Under normal circumstances these 'precursor' stem cells can mature into oligodendrocyte cells that will produce functional myelin.

Dr Mitew's project has firstly investigated the normal life cycle of these 'oligodendrocyte precursor cells' in the brains of healthy mice, studying the process of how these cells mature into active myelin-producing oligodendrocyte cells. Dr Mitew has been able to demonstrate that the oligodendrocytes in the young adult brain persist well into adulthood and are gradually lost as a normal consequence of ageing. At the same time, new oligodendrocytes are continually being produced in the healthy adult brain to replace older cells at the end of their lifespan, keeping the overall number of oligodendrocytes steady.

This finding is important as it demonstrated that even in some of the very old mice, there was ongoing oligodendrocyte production and replacement, indicating that myelin generation is possible even in old age.

Victorian trial to treat early-stage Alzheimer's by reducing brain's stress hormones

A new drug that could treat early-stage Alzheimer's disease by reducing levels of the stress hormone in the brain is being trialled in Victoria. Patients with the



Dr Stanislaw Mitew

most common form of dementia have been found to have elevated levels of the stress hormone cortisol in the brain, which may accelerate symptoms by promoting build-up of plaque.

Prof Colin Masters, from the FINMH and the University of Melbourne, said the drug Xanamem inhibits an enzyme that makes cortisol. Results of a trial of the safety of the drug in healthy people are expected within months, but there is enough confidence about its effectiveness to plan phase two trials.

“It’s now known that in Alzheimer’s disease cortisol is increased in the brain and it may correlate with rates of cognitive decline in dementia,” he said. “Therefore, lowering levels of the hormone in the brain could have clinical benefit.”

Prof Masters is on the clinical advisory board for the company Actinogen, which is developing the drug. The drug attempts to lower cortisol in the hippocampus and frontal cortex, whilst continuing to enable the body to produce the hormone as a natural response to stress. From next year hundreds of people from Victoria, Britain and the US will test the drug to determine if it can relieve symptoms. “This drug will be trialled on people who are symptomatic because we want to see if it will have an impact on memory loss, disorientation and forgetfulness,” Prof Masters said.

“It’s unlikely that there will be a single magic bullet for Alzheimer’s disease. Like many other chronic illnesses, it’s much more likely there will be a combination therapy, and this drug could form part of that,” he said. If trials succeed, it could be at least four more years before the drug is on the market.

In another important study, healthy Victorians aged 65–85, who are deemed to be at risk of Alzheimer’s. They will be given an anti-amyloid antibody that aims to slow memory loss.



Australian researcher receives international funding

Prof Trevor Kilpatrick, from the University of Melbourne and the FINMH has been awarded a prestigious research grant from the American National MS Society (NMSS). The grant was announced as part of the 2015 NMSS funding round which awarded US\$28 million to 84 new research projects and training awards.

Prof Kilpatrick’s project will look at the role of a specific gene called MERTK in developing MS. Working with a group of international collaborators, Prof Kilpatrick will look at whether abnormal MERTK has an effect on immune cells and their response to inflammation. The team will determine whether the activity of different versions of this gene can modify these effects. They will also examine MERTK in brain tissue from people with MS to see whether its level of expression correlates with disease severity.

Prof Kilpatrick received a project grant over one year to start this work in 2014 from MS Research Australia, with support from the Trish MS Research Foundation.

Dr Matthew Miles, Chief Executive Officer of MS Research Australia said ‘MS Research Australia is pleased to hear of the continued funding of this important

project. I would like to congratulate Prof Kilpatrick on his significant award and look forward to hearing his exciting results’.

Prof Kilpatrick also received an incubator grant in the most recent MS Research Australia funding round to look at a receptor involved in myelination.

Originally published by Multiple Sclerosis Research Australia.

Unlocking the epilepsy puzzle: personalised care and global collaboration

A new international partnership will bridge the gap between patients, doctors and researchers to change the way epilepsy is researched and managed. The Epilepsy Genetics Initiative (EGI) based in the US with the Australian partner at the University of Melbourne, brings together research groups to find cures for people with epilepsy. Epilepsy encompasses a diverse group of neurological disorders of different types and severities, which are united by the occurrence of recurrent seizures.

Prof Ingrid Scheffer AO from the University of Melbourne, Florey and Austin Health said that up until now, epilepsy has been treated by trial and error with no standard of care to determine which of the many treatments might work in combating different types of epilepsy. “Over the past decade however, many genes have been identified that cause epilepsy. Knowing the cause sets the stage for the identification of precision treatments targeted to that cause,” Prof Scheffer said. “For precision medicine to work, we need rapid and thorough genetic diagnosis of patients with epilepsy for the development of their individualised treatments,” she said.

“The EGI has created a central data repository to hold the genetic data of people with epilepsy, with the aim of developing more accurate diagnoses and targeted treatments.”

Prof Stephen Smith, Dean of the Faculty of Medicine, Dentistry and Health Sciences said Melbourne is the only centre outside of the United States to be invited to join this collaboration. “This affirms our expertise in the understanding of epilepsy,” he said.

“Along with our international collaborators, University of Melbourne staff led by Prof Ingrid Scheffer and Laureate Prof Sam Berkovic AC, will open up important lines of enquiry to bring about new and emerging solutions. Such advances are enhanced through new technologies,” he said.

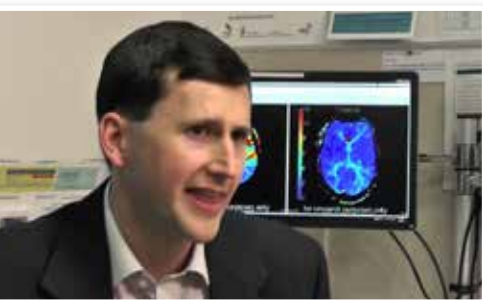
Academic Partners include: Columbia University, Boston Children’s Hospital, Children’s Hospital of Philadelphia, Duke University, The Ann and Robert H. Lurie Children’s Hospital of Chicago, New York University, University of California San Francisco, and the University of Melbourne.

Citizens United for Research in Epilepsy (CURE) is the leading nongovernmental agency in the US fully committed to funding research in the epilepsies. CURE is at the forefront of epilepsy research, raising millions to fund innovative research and other initiatives that will lead the way to a cure.

Originally published by the Melbourne Newsroom.



Professors Sam Berkovic and Ingrid Scheffer



Associate Professor
Bruce Campbell

Stroke treatment pioneered by Royal Melbourne Hospital researchers changing the way doctors approach condition

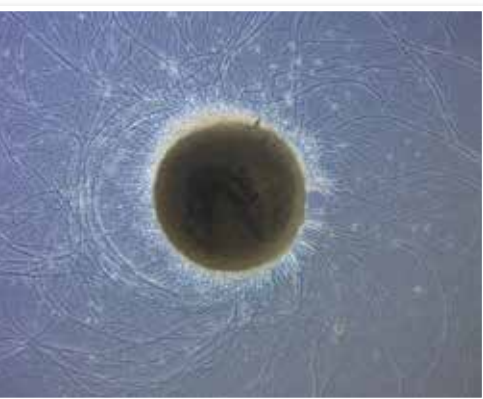
Stroke survivors have described a new treatment Australian doctors have spearheaded as a major breakthrough. Researchers at the Royal Melbourne Hospital announced they had proved the effectiveness of a new technique that almost doubles the chances patients will walk out of hospital. The researchers combined two types of stroke treatment with new technology to improve the outcomes for people with the most severe form of stroke.

William Lo said the development was a major breakthrough. The 21-year-old had a stroke just a week before sitting his final school exams. He lost movement in his left side, spent four months in hospital and a year regaining most movement. He could not walk, eat, drive, play basketball and was in a wheelchair for his 18th birthday.

“My friends from high school had to think what was appropriate to involve me in, going to the beach, going to the city, it was hard.” Three years after the stroke he is still going through rehabilitation.

He said the new research would hopefully prevent many people going through the same difficulties as him.

Under the new approach, doctors used advanced brain imaging to identify which parts of the brain were irreversibly damaged and which parts were salvageable. They then used new stent technology to remove the clot. When combined with traditional clot-busting medication the proportion of patients who did not sustain a significant disability after the stroke went from 40 to 70 per cent. The study involved 14 hospitals in Australia and New Zealand and was published in the *New England Journal of Medicine*.



Organoid

Organoids: the next revolution in human biology has begun

Researchers are growing tiny balls of cells that resemble the features of a variety of different tissues in our bodies and are using them to study a range of developmental disorders like epilepsy, autism and Alzheimer's. University of Melbourne biomedical scientists have joined this biological revolution by growing tiny, immature organs, known as organoids. These lentil-sized balls of cells, which scientists can grow in a dish, resemble the features of our brains, livers, guts, kidneys, prostates and pancreas, with the list rapidly expanding.

Organoids are creating huge interest because they mean we can now study our biology in action outside a patient's body. They are already being used to understand developmental disorders like epilepsy and autism, as well as neurodegenerative conditions such as Alzheimer's and Parkinson's disease.

Currently the organoids can't differentiate into mature organs. They reach a certain size and start to die from the inside because they don't yet have a fully functional blood vessel system for a continuous supply of nutrients and oxygen. But they already have enormous potential both as a research and therapeutic tool.

Stimulating Epilepsy Treatment

Everyone experiences what could be called 'life's little interruptions', but for people with epilepsy, this phrase takes on a whole new meaning. As with many conditions, epilepsy ranges from mild to serious. Even for mild cases, however, epilepsy impacts a person's quality of life; in 1993, the World Development Report assessed the burden of living with epilepsy as being equivalent to having breast cancer for women or lung cancer for men.

The main characteristic of epilepsy is persistent seizures. Apart from the unpleasant experience itself, people with epilepsy are unable to predict when their seizures will happen. This makes it difficult for sufferers to lead a normal life, hinders their ability to attain a driver's licence, and makes activities that the rest of us take for granted – like swimming, cooking or simply crossing a street – potentially dangerous.

Currently, epilepsy treatments include medications, brain surgery or other techniques such as vagal stimulation. None of these, however, have shown to work for all people treated with these methods. And all entail their share of risks, complications and side effects.

Enter Prof Mark Cook who, together with his team at the University of Melbourne and St. Vincent's Hospital, have made significant advances in developing an epilepsy treatment that could be more effective than existing therapies and potentially help more people.

The concept underlying their research was to predict when a seizure was going to occur and then preventing it from actually happening. Prof Cook explains, "Our research involved the design and construction of a system that could detect seizure activity and rapidly respond with a counter-stimulation to prevent the seizure progressing."

They had previously created a system that could do this, but to further validate their system, they needed to create a smaller, more portable system that could be used in different clinical settings. They achieved this through the support of a NHMRC Development Grant. "We successfully built the system and have used it in a clinical setting to show that seizure activity can be effectively treated with direct brain stimulation," he says. "We are now able to engage larger groups of collaborators to help study the best patterns of stimulation, and where to optimally place the electrodes."

Prof Cook and his team's ultimate goal is to create a portable device that can be implanted in people with epilepsy and to prevent them from having seizures. For the more than 225,000 people in Australia who have epilepsy – and millions more worldwide – this could be revolutionary. They could live more active, independent lives and be free of epilepsy drugs. In short: it would give them their lives back. Federal Health Minister, The Honorable Sussan Ley, announced the research funding today.

The collaboration involves researchers from the University of Melbourne, the Florey, Monash University, University of Western Ontario in Canada and the University of California.



Professor Mark Cook

Major research funding to beat Alzheimer's disease announced

A \$6.4 million project to learn more about the biological causes dementia will get researchers closer to finding better treatments and possibly a cure for the debilitating disease. Federal Health Minister, The Honorable Sussan Ley, announced the research funding today.

The collaboration involves researchers from the University of Melbourne, the Florey, Monash University, University of Western Ontario in Canada and the University of California. The research will be led by Dr Amy Brodtmann at Florey and includes Dr Jess Nithianantharajah and Prof Louise Burrell, from the University of Melbourne. It is part of a larger international research effort, which involves the establishment of a \$50 million National Institute for Dementia Research. The project is called Vascular mechanisms of neurodegeneration: drivers and determinants of dementia. Medical researchers will work to understand how impaired blood vessels can cause dementia.

Deputy Vice-Chancellor for Research at the University of Melbourne, Prof Jim McCluskey said this understanding is crucial to therapeutic advances. "By understanding the mechanisms that cause dementia, this research will help to identify ways to prevent and treat the disease," Prof McCluskey said.

"The University of Melbourne and our partners have long been at the cutting edge of medical research in neuroscience and this grant acknowledges the quality of our research.

"We are very pleased the Federal Government has made this commitment to deciphering a disease that will affect 900,000 Australians by 2050.

"There is no doubt that dementia is one of the biggest public health problems we face as our population ages and yet, there is no effective treatment. Our hope is that this work will bring us closer to easing the burden for dementia sufferers and their loved ones, as well as the health system"



New Australian study investigates the effect of genetic change on immune cells

There are now over 110 genetic changes that are known to increase an individual's susceptibility to MS. Current genetic research has now moved on to investigating each of these genetic changes in more detail to try and determine the mechanisms that underlie the MS disease process with a view to identifying new therapeutic pathways.

A new Australian study, led by Dr Judith Field from the University of Melbourne and coordinated through the ANZgene group has recently been published in the medical journal *PLoS One*.

ANZgene is one of MS Research Australia's research platforms which concentrates on the role of genetics in the development and disease course of MS. This collaborative group of researchers from Australia and New Zealand work on a number of genetic studies concurrently and also coordinate the

collation of samples of genetic material and genetic data from people with MS for international collaboration.

The new study focuses on the effects of genetic change in a molecule known as CD40. The CD40 gene has previously been identified as a risk gene for MS as well as a number of other immune related diseases and the molecule functions in a number of immune cell types.

Dr Field and her team showed that the genetic change that increases the risk of developing MS leads to lower levels of CD40 in immune cell subtypes known as B cells and dendritic cells. When the risk gene was present, the ratio of CD40 on the cell surface compared with the secreted form of CD40 was also different in immune cells. This work demonstrates the way that genetic changes in the CD40 gene can affect immune cell function and may impact on the development of MS in individuals.

The research team also showed that irrespective of the form of the CD40 gene, people with MS had lower levels of CD40 in B cells compared with healthy controls. CD40 may be playing a role in the immune regulation that protects against MS and this function is impaired by this genetic change. These types of studies are important because they could uncover the molecular mechanisms underlying MS and through this we could find new pathways for treatment.

Bionic ear could harness brain's 'octopus cells' to improve sound

People who use cochlear implants may one day be able to better understand speech against a noisy background thanks to a new Australian discovery. Biomedical engineer Prof David Grayden, of the University of Melbourne, and colleagues, have identified how the brain uses neurones called 'octopus cells' to pick up the unique rhythm of someone's speech. The findings are published in a recent issue of PLOS ONE.

One of the biggest challenges for people who use a cochlear implant (also called a bionic ear) is picking out particular speech in the presence of background noise, especially in a room full of other people talking. "The worst situation is what's called the 'cocktail party situation'," says Grayden.

Current cochlear implants deal with this problem by using directional microphones pointing to the front of the head. Even then, however, the target speech needs to be 10 to 15 decibels louder than the background sounds in order to be heard properly, says Grayden.

Grayden and colleagues figured that if they could work out how the brain manages this challenge, they could pave the way for improving the performance of bionic ears. Building on previous research, the researchers created a computer model of key parts of the brain's auditory system and looked at what happened when it processed speech-like sounds and random background noise. The model included 'octopus-shaped' neurones that previous research had found are good at detecting speech. In particular, they respond to the series of sound onsets, called "glottal pulses", which are the loudest part of speech, created by puffs of air passing through our vocal cords.

The pattern of these pulses creates a unique signal that a normal hearing system can identify as speech. “The key is that the ‘rhythms’ are different for different voices,” says Grayden.

“The glottal pulses for different speakers will rarely occur at the same time, and the rate (frequency) of these pulses will be different (people speak with different pitches).”

But the question is how exactly normal hearing people use these subtle cues to pick out one person’s speech compared to another. In their computer model, Grayden and colleagues found that a part of the brain called the ‘ventral nucleus of the lateral lemniscus’ (VNLL), integrates signals from octopus cells with other auditory neurons that respond to the volume of each frequency but don’t distinguish at all between speech and noise.

“The brain uses the actual timing of glottal pulses as a cue to decide the most important time to listen,” says Grayden. The researchers tested their model using a 4000 Hertz sound, which was best heard when the VNLL played this role. “When we ran it through the VNLL model this helped the 4000 Hertz sound really stood out,” says Grayden.

This is the first time that this particular mechanism used by the brain to identify speech rhythms has been revealed, he says. It explains how the brain is able to distinguish speech against background noise that is at the same volume. Grayden says the findings could one day help refine the bionic ear speech processor.

And this could make cocktail parties a more pleasant experience for those wearing the devices.

Originally published by Anna Salleh for the ABC.



Discovery prompts rethink on metals and Alzheimer's disease

Researchers at the University of Melbourne have discovered that a protein involved in the progression of Alzheimer’s disease also has properties that could be helpful for human health. The discovery helps researchers better understand the complicated brain chemistry behind the development of Alzheimer’s disease, a condition that affects hundreds of thousands of Australians.

An international team of researchers, led by Dr Simon Drew at the University of Melbourne and Prof Wojciech Bal at the Polish Academy of Sciences, has revealed that a shorter form of a protein called beta amyloid, may act as a sponge that safely binds a metal that can damage brain tissue when it’s in excess.

Researchers have been intensely interested in the role of beta-amyloid in the development of Alzheimer’s disease. This is because clumps of the protein are formed in brains of people with the illness. In the late 1990s, high levels of copper were discovered within these clumps. Copper is essential to health, but too much can produce harmful free radicals. Scientists began to suspect that

this copper might be contributing to the disease. They found that beta-amyloid can bind to copper indiscriminately and allow it to produce these damaging free radicals.

Closer analysis of beta amyloid protein has revealed different sizes. “The shorter form has been overlooked by most researchers since the composition of beta amyloid was first identified 30 years ago,” Dr Simon Drew explains. “We know that the shorter form of beta amyloid is present in both health and in Alzheimer’s disease.

“A small change in length of the various forms of beta amyloid makes a huge difference to its copper binding properties. We found that the shorter form of the protein is capable of binding copper at least 1000 times stronger than the longer forms. It also wraps around the metal in a way that prevents it from producing free radicals.

“Given these properties and its relative abundance, we can speculate that the shorter type of beta amyloid is protective. It’s very different from the current view of how beta amyloid interacts with biological copper.”

So far, therapies aimed at lowering the production of beta amyloid have shown only a modest ability to slow cognitive decline and the number of people affected by the Alzheimer’s disease continues to grow. Dr Drew and the team from Poland are now working to develop a method for identifying the copper-bound form of the shorter beta amyloid in the body. This will enable them to screen how much copper it holds in the brain, whether it safely escorts the copper from one place to another, and how this may change in ageing and disease. “If a beneficial role in copper balance can be established, it’s still possible to have too much of a good thing,” Dr Drew said.

“As the amount of beta amyloid in the brain increases during Alzheimer’s disease, the shorter form can also clump together and this may interfere with its normal function. On the other hand higher levels of the shorter form may further enable it to soak up copper from other places where it is needed. It could be a Jekyll and Hyde scenario.”

Dr Drew’s research was published in Angewandte Chemie.

Published by the Melbourne Newsroom.

New Sub Nanometer Imaging and Fabrication Facilities at the Centre for Neural Engineering

Following a number of “false starts”, the Centre’s new helium ion microscope was commissioned in July-August. This advanced technology allows superior magnification of biological samples. The microscope can attain a resolution of 0.5 nanometres, or one two billionths of a metre! The microscope is already enabling the Centre’s researchers to better understand the brain and brain function through the visualization of cells, neurons and neuronal networks.

The technology can also be used to fabricate devices at nano scale, 10 nanometres, which is very useful in creating prototype devices to enable research and to test ideas. Acquired with the assistance of an ARC LIEF

grant, the Zeiss Helium Ion microscope is a valuable asset for the Centre's researchers and will make an important contribution to furthering our research agenda and in lifting the profile of the Centre through the quality of the publications generated by its use and applications.

Siblings of children with schizophrenia show resilience to the condition as they grow up

Fundamental differences between how the brain forms during adolescence in children with schizophrenia and their siblings has been discovered by researchers from the University of Melbourne and the National Institute of Mental Health in Washington DC.

The study opens up new avenues for researchers to explore how to target treatment to children with this devastating condition. The study used structural brain magnetic resonance imaging (MRI) to map the brains of 109 children with childhood-onset schizophrenia (COS), from ages 12 to 24.

They compared the images with scans taken of the participants' brothers and sisters without COS to see if similar brain changes took place over time. The siblings without COS showed similar delays in brain connectivity while growing up, but these connections tended to normalise or 'catch up' to those of normally developing adolescents. The findings were published in the July edition of a Journal of the American Medical Association Network, *JAMA Psychiatry*.

Lead researcher, Dr Andrew Zalesky is a University of Melbourne electrical engineer who lends his expertise to understanding the brain's wiring. He divides his time between the Faculties of Medicine and Engineering at the Melbourne Neuropsychiatry Centre.

Dr Zalesky indicated that the ability of the siblings to 'catch up' and to develop important brain circuitry means there is a degree of resilience to their risk for schizophrenia. "We've looked at the development of brain networks over the adolescent period, from childhood to early adulthood. Abnormalities detected early in the unaffected children normalise by age 16," Dr Zalesky said.

"The greatest risk for schizophrenia is family history, but the majority of siblings of individuals with the disorder are unaffected.

"So why are these brothers and sisters able to overcome the risk? Looking for these biological factors that protect a person from developing schizophrenia opens up a new direction in the search for treatments."

Co-author, Prof Christos Pantelis, heads the Melbourne Neuropsychiatry Centre at the University of Melbourne. He treats patients with severe forms of schizophrenia at North Western Mental Health.

Prof Pantelis indicated that examining the biological, social and psychological protective factors that can improve resilience to mental disorders will help researchers to develop new approaches to treatment. "Currently available medications can help young patients manage their symptoms, but can have significant side effects. Our work has the potential to open up avenues towards

earlier intervention with fewer side-effects that could potentially improve a child's resilience to becoming ill," Prof Pantelis said.

"This is an interesting new direction, as it suggests the search for targeted psychiatric treatments for schizophrenia and psychosis requires following young people over time."

Originally published by the Melbourne Newsroom.

The silver-lining gene that could help depression

Are you a sensitive soul who takes things to heart but tends to flourish during the good times? New research from the University of Melbourne's Department of Psychiatry suggests you might possess a gene which makes you feel things more deeply. The study shows some people who suffer ongoing depression also have the potential to be happier than most and it all depends on their genetics and their circumstances.

Research Fellow Dr Chad Bousman began studying this gene to answer the question of why only some adults who suffered an abusive childhood develop long-term depression. The research team recruited people with a history of sexual or physical abuse in childhood because it is one of the most severe psychological events a person can experience. "Child abuse occurs during a neurodevelopmental phase, when the brain is making a lot of new connections. Such a terrible thing can disrupt these neural connections," he said.

"But despite this, we know that not everyone who has been a victim of child abuse has depression in adulthood.

Dr Bousman and his team found the answer. People who draw the evolutionary wildcard of a certain type gene are more deeply affected by their life experiences. But swap the traumatic childhood for a good one, and these same people tend to be happier than the rest of us.

Positive psychology expert named among 100 Women of Influence for 2015

Prof Lea Waters has been named as one of Australia's 100 Women of Influence for 2015 in the The Australian Financial Review. She was one of the ten women awarded in the Social Enterprise and Not-For-Profit category.

A registered psychologist, Prof Waters was recognised for her contribution to the youth mental health field and her leadership in establishing the Centre for Positive Psychology at the University of Melbourne. Prof Waters, who has been sharing the benefits of positive psychology for almost 20 years, said she was deeply honoured and affirmed by the award.

"It is wonderful to see the role of women recognised and the positive ripple effect of these women in society," Prof Waters said.

"For me, youth mental health is critical and I am eager to use this award to help raise public awareness. My aim is to ensure every young Australian is



Professor Lea Waters

taught wellbeing skills at school. We need to educate our students about their mind and their heart.”

Suicide is the number one cause of death for Australians aged 15 to 25 years old. Some 25 per cent of young Australians experience symptoms of mental illness and 40 per cent of school students report that they worry a lot.

“The work we are doing at the Centre for Positive Psychology adopts a preventative health approach. We are working with schools all across Australia to support the wellbeing and learning of young Australians,” Prof Waters said.



Shapes, lines and movements are in the eye of the beholder

New thinking about how we perceive shapes, lines and movement suggests this information is first deciphered in the retina of the eye, rather than within the brain's visual cortex as previously thought. Learning more about the circuitry of the sensory systems is essential to making medical advancements in the treatment of conditions such as dyslexia and schizophrenia or even to develop the next generation of bionic eyes.

A new paper in Trends in Neurosciences, authored by University of Melbourne neuroscientist Prof Trichur Vidyasagar at the Department of Optometry and Vision Sciences and Prof Ulf Eysel from Ruhr-University-Bochum in Germany suggests we process orientation and movement of objects in the same way we process their colours.

The vast majority of information about the world around us is processed in the visual cortex of the brain, but it has long been known that colour is a different case. Colour perception is initially processed in the eye itself by three types of receptors within the cone cells of the retina that are sensitive to blue, green and red.

Information sent from the cone cells is measured by the brain's primary visual cortex as a ratio of the activity of the three cone types. Every perceived colour has thus, a unique 'ratio'. “Our sensory world of colour is first painted by only three primary pigments rather than drawn with hundreds of different coloured pencils, which is a very efficient way of processing” Prof Vidyasagar explains.

“But we have found that the way colour is processed may not be unique to colour perception, but may also apply to perception of most sensory stimuli.

“When we observe that the orientation of a line or an edge is vertical, horizontal or oblique, or that one object is larger or darker than another, or how fast an object is moving, our nervous system uses the same simplifying and combining principles as it does when perceiving colours.

“The mechanisms for registering, for example, a line's orientation, are already in the retina in a coarse form. And just like colour, the visual cortex is only required to sharpen these signals.”

The new theory is at odds with the dominant school of thought that sensitivity to lines and edges is first developed only in the brain's cortex.

Are golden pipes passed down generations? Research investigates if twins inherit singing ability

Does singing run in the family? New research is examining the possibility of a so-called 'singing gene' that if proven, it could have broader implications for the field of brain research.

If your twin is a great (or terrible) singer, will you be too?

That seemingly trivial question is at the heart of a new study that could aid understanding of how singing is best taught, and more broadly inform research into brain injury rehabilitation. Lead researcher Prof Sarah Wilson from the University of Melbourne's School of Psychological Sciences describes 'music neuroscience' as her area of expertise. "I am particularly interested in how music can change the brain," says Prof Wilson.

To date, most research in the field has focused on how factors like environment and musical training can be 'powerful determinants of brain plasticity. "We now know that musicians' brains are quite different from non-musicians' brains," she says.

"We don't know anywhere near as much about genes and how they determine our music potential or ability to become an elite musician versus an amateur or fairly ordinary musician."

The study focused on identical twins not only because of their shared genes, but also their similar upbringing and environment; in this case, anything from having the same music teacher to enduring the same family singalongs.

According to Prof Wilson, that sort of exposure is a big variable in shaping children's brains. The early findings of the study are already providing some clear indications. "What we have shown is that the twins that are identical have similar ratings of their ability, so they are more likely to have similar ratings of how good they are."

In short, if your twin is a good singer, chances are you will be too.

The difficulty with such a test, however, is that assessing the quality of someone's singing voice can be a hugely subjective process. To overcome that, Prof Wilson and her team ran a complex acoustic analysis of participant twins' voices, examining tone and timbre qualities of their singing. "When you're miles off the tone, it is painful," she says. "I think most people would agree on that as an objective criterion."

The direct implications of the research are potentially fascinating. "Is there a singing gene? We hope so. That's what the study is all about," she says.

If a singing gene is found, the principle could then be extrapolated to other music-based skills, like the playing of piano or skill with a guitar. There are also potential therapeutic applications. "Singing can be used to rehabilitate language in individuals who have had a stroke," says Prof Wilson.

'So getting down to the nuts and bolts, the genetic components and environmental factors that are most powerful in changing the brain then



**Singers at the
Victorian College of
the Arts**

allows us to have a much better understanding of who might benefit from an educational strategy.”

Originally published by the ABC.



Put forgetfulness down to brain overload not Alzheimer's, doctors say

SCORES of the ‘worried well’ fear they have degenerative memory conditions such as Alzheimer’s disease when the problem is just brain overload. The director of Austin Health’s department of neuropsychology, Prof Michael Saling, said at least one patient a week was convinced that forgetting things such as their car keys, or to collect their children, was the result of a serious brain condition. The department is preparing to study the prevalence of the phenomenon.

“Because the (computerised) devices we use have perfect memories, there is almost an expectation building that we too should have perfect memories,” Prof Saling said.

“This expansion of information in our age has happened so fast ... it’s bringing us face to face with our brain’s limitations,” he said.

The working memory can hold only about seven things at one time, Professor Saling told a Melbourne University forum at the Melbourne School of Psychological Sciences. “We’ve lost sight of the fact that forgetfulness is a normal and necessary phenomenon,” Prof Saling said.

“We must keep pushing information out so that our brains can deal with information coming in, and if it gets overloaded people become forgetful,” he said.

“When people vehemently complain their memory is totally gone, we know we’re not dealing with the most serious memory problems.

“In Alzheimer’s, the first you see is forgetting arbitrary things and daily living activities are beginning to slip.

“But then they develop amnesia. They have very muted memory complaints.

“People with the most serious amnesias stop complaining,” Prof Saling said.

Predicting Risk of Disability in MS

Two articles published recently by Australian and international investigators using the MSBase database provide insight into several factors that most strongly predict the risk of accumulating MS-related disability. MSBase is an international database that records clinical data on tens of thousands of MS patients from around the world. It allows valuable analysis and understanding of factors affecting disease and the ‘real world’ use of treatments outside of clinical trials.

In the first study, led by Dr Vilija Jokubaitis from the University of Melbourne, the researchers aimed to understand the factors associated with worsening symptoms over time in people who had experienced a first demyelinating event, often a precursor to a diagnosis of MS, known as Clinically Isolated Syndrome (CIS).

Published in the journal *Annals of Clinical and Translational Neurology*, the team looked for the factors that were different between those whose symptoms did not change over a 12 month period, compared to a subset of people whose symptoms worsened during the study period. In a group of 1989 people with CIS they identified 391 individuals who had a recurrence of their symptoms resulting in increased disability within the first three months of the study. On average, this group of individuals had an older age at the first onset of symptoms, more difficulties with motor function and movement as the first symptom, a higher number of relapses in a 12 month period, and a greater delay in receiving treatments.

The researchers also showed that over a 12 month period, disease modifying medications were a significant protective factor associated with a reduced risk of disease worsening. This may have important implications for the future management of people presenting with CIS as in most countries they are not routinely prescribed disease modifying medications.

ENGAGEMENT

Public Outreach

Melbourne Neuroscience Institute Public Seminar Program

The MNI has had an exceptionally successful year hosting a number of free public seminars on a diverse range of topics. This year's series saw a more engaged and diverse audience with a number of the seminars being subscribed to capacity. The MNI hosted some of the seminars outside of the Kenneth Myer Building including in the City of Melbourne in order to increase our accessibility and to broaden our audience thereby facilitating outreach.

The sharp increase in attendance can be attributed to an excellent array of interesting and engaging local and international speakers who focused on topics that are both relevant and important to society in general.

Our 2015 seminars were as follows:

'Zap my Brain'

Zap my Brain audience members were treated to a demonstration of Transcranial Magnetic Stimulation (TMS) and heard how scientists are using TMS and transcranial Direct Current Stimulation (tDCS) to study the brain. The panel debated the ethics of "electrodoping" and explored how brain stimulation is currently being used to treat disorders like depression.

MNI proudly organised this event alongside The Brain Dialogue, an initiative of the ARC Centre of Excellence for Integrative Brain Function and the Monash Alfred Psychiatry Research Centre.

'Positive Psych: What's the hype?'

The Centre for Positive Psychology has recently developed the +S3 model which extends Positive Psychology in Education to three levels of analysis: students, schools and systems. The group symposium showcased the innovative research methods used by the team at the Centre, such as mobile experience sampling, biodata, and big data system modelling, as well as work with the undergraduate and postgraduate students at The University of Melbourne. These methods provide comprehensive insights guiding the

development of more refined well-being programs aimed at reducing the incidence of mental illness and promoting resilience in young Australians.

‘When art and science collide: In conversation with Daniel Glaser, Director of the Science Gallery at King’s College’

Dr Daniel Glaser is a neuroscientist who has worked for many years promoting public engagement with science. Most recently, Daniel has taken on the role of Director of Science Gallery London at King’s College London. Prof Kilpatrick moderated this intimate conversation with Daniel, that explored how art and science can collide to bring the public a new and innovative way of experiencing knowledge.

‘Brainoids: Growing a Brain in a Dish’

The human brain is a complex thing, and scientists are trying new and innovative techniques to unravel its mysteries. Most recently, researchers have been growing brain-like organs called ‘brainoids’ in their labs using induced pluripotent stem cells (iPSCs). These pieces of tissue, called brainoids because they mimic some of the structure and function of a real brain, are furthering our knowledge of human development, serving as disease models and drug-screening platforms, and might eventually be used to rescue damaged tissue. Researchers spoke on how brainoid-based research might be applied to Autism and Epilepsy research.

‘Understanding Autism: Implications for Research’

What is Autism? How are we advancing knowledge on the nature and causes of Autism Spectrum Disorders? From early and accurate diagnosis to effective translation, these multidisciplinary researchers are committed to improving the quality of life for children and adults with autism.

The MNI convened a panel of experts from education, engineering, neuroscience, health and behavioural sciences, to explore our understanding of autism and the future of autism research in Australia.

‘Is Proof Overrated?’

The Melbourne Research Institutes joined forces with the Wheeler Centre to debate the concept of scientific proof. Policy-makers often cite research as providing proof on contested issues. But whether or not overwhelming evidence necessarily leads to evidence-based policy is another question. Is proof overrated? How does Australian society use research to inform its decisions?

The indomitable Sally Warhaft hosted this spirited debate, while our panellists – with a wealth of experience in both policy-making and research – debated the idea, and importance, of proof in Australia today, each referring to their individual areas of expertise.

Stem Cells Australia’s A/Prof Megan Munsie joined Prof Peter Doherty, Dr Ranjana Srivastava, Prof Kate Auty, and Dr Sara Bice for a discussion of the role of research in the choices we make about everything from energy



Judges and MC at the No-Bell Prize



Winners and Judges of
the No- Bell Prize

technologies, social equity, environmental policies to our use of medical breakthroughs and new communication technologies.

‘The No-Bell Prize’

The No-Bell Prize is a hilarious science communication competition that challenges academics to present their research to a public audience without using jargon. In 2016, we once again welcomed Dr Shane Huntington from Triple R’s Science Program as our formidable Chair, and Dr Mel Thompson (Scientists and Science Communicator) and Dr Adam Bandt MP (Federal Member of Melbourne) as our tenacious judges. Our top secret judge was 12 year old, Rowan – who better to judge if our contestants are presenting in lay speak, than a 12 year old lay person with a keen interest in science?

Our contestants were Dr Mirella Dottori (stem cell researcher in the Centre for Neural Engineering), Dr Christine Nguyen (Research Fellow in Ocular Physiology and Neurodegeneration), Prof Dennis Velakoulis (Clinical Director of the Melbourne Neuropsychiatry Centre), Dr Toby Merson (Laboratory Head and Myelin Biologist, Florey) and our winner, Dr Isabel Lopez Sanchez (Research Fellow in the Mitochondria and Neurodegeneration Research lab at the Centre for Eye Research Australia).

MNI wishes to thank all involved in this fantastic event.

Melbourne Brain Symposium

On Tuesday 13 October, the MNI and the Florey hosted the annual Melbourne Brain Symposium.

We would like to express our gratitude to the distinguished medley of local and international research leaders who spoke so eloquently at the 2015 symposium. The speakers were:

- Prof Kathryn North, Director, Murdoch Children’s Research Institute and the David Danks Prof of Child Health Research at the University of Melbourne.
- Associate Professor Bruce Campbell, Consultant Neurologist and Head of Hyperacute Stroke, Royal Melbourne Hospital
- Prof Bill Charman, Dean, Faculty of Pharmacy and Pharmaceutical Sciences and Director, Monash Institute of Pharmaceutical Sciences
- Prof Pam McCombe, Neurologist, Head of Royal Brisbane Clinical School and co-Head of the Brain and Mental Health Theme at the UQ Centre for Clinical Research
- Prof Julie Bernhardt, Head of Stroke Division and Senior Principal Research Fellow, the Florey
- Prof John Collinge, Prof of Neurology and Head of the Department of Neurodegenerative Disease at the UCL Institute of Neurology, and Director of the MRC Prion Unit

Education

PhD Coursework and Advanced Research Workshops in Neuroscience

The 4-week PhD structured coursework program is taken over the first month of candidature and includes stepped assessment designed to provide a sound basis on which the dedicated PhD research project can be built and conducted more efficiently. The University of Melbourne and the Florey have joined forces to develop this inspiring doctoral research program which aims to provide a broad oversight of the different disciplines, approaches and methods encompassed by the Neurosciences.

In 2014, the MNI developed a pilot program of advanced research workshops for graduate students as a complementary experience to the existing introductory neuroscience coursework program. These advanced workshops provide graduate students with the opportunity to gain practical skills in key areas that relate directly to their research project. The skills gained will enhance the research that the student is conducting, assist in timely completion and enhance the marketability of RHD graduates in both the academic and commercial sectors.

The workshops are developed by senior neuroscientists and each runs for around 20 hours, with a mixture of theory and practical activities.

The following workshops were conducted in 2015:

Introduction to Bioinformatics for Neuroscientists

Workshop leader Dr Vicky Perreau led weekly two hour sessions for eight weeks. Six students participated in the workshops, culminating in student presentations. The workshop was extremely successful, and over-subscribed.

One of the students, Mike Notaris from the Florey commented that “The MNI ‘Bioinformatics for Neuroscientists’ workshop was, unequivocally, the most rewarding extra-curricular experience that I have undertaken during my PhD. Vicky Perreau ran an inspired and impassioned workshop, and tailored the content to the needs of the student cohort. Vicky’s experience as a wet-bench scientist led to the course being delivered with a practical focus, with all students developing and presenting a short bioinformatics project as part of the workshop which, in my case, has lead to an experiment that is likely to be included as part of my thesis.”

Mike went on to state that “The skill set taught in this workshop is of broad relevance, and is likely to not only facilitate the completion of my PhD but also the way that I conceptualise and approach research questions well into the future.”

Fundamentals of Ion Channel Function in the Brain

Workshop leader Associate Prof Steve Petrou with Dr Chris Reid presented two six-hour theoretical and three eight-hour practical sessions in August, with



Symposium

pre-reading material provided. Five students attended what was another highly successful workshop.

Human Pluripotent Stem Cells in Neuroscience Research

Prof Martin Pera and Dr Anna Michalska led a highly effective workshop in early September. The workshop was attended by eight students who participated in six one-hour tutorials, two one-hour literature reviews and four five-hour hands on work in the Stem Cell Core laboratory.

Magnetic Resonance Imaging Workshop

Prof Roger Ordidge led this workshop on the principles of MRI, the design of the MRI scanners and the use of contrast to distinguish between abnormal and normal brain tissue. A scanner was used to explore MRI contrast differences between various liquid samples.

MNI is truly grateful to all workshop leaders for their hard work and commitment to making the Advanced Workshops in Neuroscience a huge success.



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 may 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, but also learn about the scientific process, obtaining grants and science in the 'real-world'.

The MNI work experience program received excellent feedback in 2015, with one student commenting 'I utterly loved working in the laboratory, surrounded by such knowledgeable scientists. Being able to observe them at work was a privilege and such an amazing sight to see. I was able to learn so much more than I expected and I've seen and participated in several experiments along the way'.

Elizabeth Blackburn School of Sciences Extended Investigation Program

In 2015, over 45 volunteer mentors from The University of Melbourne supported the Elizabeth Blackburn School of Sciences Extended Year 11 Extended Investigation students in their year-long, independent research projects.

Mentors and matched students met regularly to discuss the various phases of the research process.

Here is a sample of some of the research questions which the students pursued:

Anita	Depending on age, to what extent does the use of colour impact one's short-term memory in teenagers' aged 15 to 17 years old?
Jacqueline	Does high intensity background music affect the short-term memory capacity of teenagers?
Shaun	IQ or EQ, which is more important for people working in the scientific research and education fields?
Abbie	What is the Frequency of Psychopathic Trends in Adolescents Aged 15 to 18?
Amity	Which of the two treatments: medical hypnosis or lucid dream therapy is more effective in treating post-traumatic stress disorder (PTSD)?
Adem	Does high blood pressure influence working memory of adolescent students in Victoria?
Shirleen	Does multidisciplinary non-pharmacological rehabilitation have any effect on the progression of Huntington's disease?
Carine	Which is more efficacious in the treatment of mild to moderate pain, ibuprofen or paracetamol?

Highlights of the year included the yearly poster-symposium, at which students, mentors, teachers and family members met to view and discuss the cohort's research posters, and also a visit by Prof Elizabeth Blackburn.

Australian Brain Bee Challenge

On 17th June, 250 year 10 students and accompanying teachers from 48 secondary schools across Victoria, as far as Ouyen and Tallangatta, participated in the Australian-New Zealand Brain Bee Challenge State Final. It was hosted and sponsored by the Florey and the MNI.

The event was officially opened by the State MP for Melbourne Ms Ellen Sandell, who reflected on her own experiences in science training, and



Brain Bee how that helped her perspectives as a politician as well as a person. Nobel Laureate Prof Peter Doherty then asserted that being a scientist is not about accumulating a great deal of ‘stuff’ but is really about seeing the universe with an unbiased clear lens, even when what you see is against what you and others believe.

A highlight of the day was the tours of the Anatomy museum, the DAX gallery and neuroscience laboratories, during which students showed a newly discovered interest in basic science.

The McRoberston Girls’ High School cleaned up this year winning all three individual places (Champion: Nebula Chowdhury) as well as the Team 1st prize. Runners up for the team final were John Monash Science School and the Methodist Ladies College. The prizes included a giant 14-pieces model of the brain, trophies, and Elsevier books.

The success of the event was very much dependent on the efforts of volunteers for the day, which included over 50 scientists from the Florey and the University of Melbourne. We also acknowledge the tireless efforts of the Victorian committee coordinating the administration and logistics of Brain Bee, which included Dr Jee Hyun Kim (Coordinator), Ms Jan Morgan (University of Melbourne), Dr Thomas Keeble (Florey), A/Prof Andrew Metha (University of Melbourne), and Dr Carli Roulston (St Vincent’s Hospital/University of Melbourne).

Mindfields

The ongoing, year-round Mindfields program, run in conjunction with Florey and the Dax Centre, gives Year 12 students an insight from UoM and FINMH scientists into the biological processes underpinning brain function, and what happens to the brain during mental illness. Students and scientists also hear from a speaker who has experienced mental health problems.

Think About It

International Brain Awareness Week took place in March and MNI partnered with FINMH for the “Think About It” School Outreach Program. We sent over 50 scientists out to over 20 Melbourne high schools, from Werribee to Frankston. Students heard from experts on topics such as drugs and adolescence, neurodevelopmental disorders, advanced imaging and a wide range of research subjects undertaken by our scientists.

Scientists in Schools

Scientists and Mathematicians in Schools (SMiS) is a national program managed by CSIRO on behalf of the nation. It provides skilled volunteers the opportunity to have a positive impact and 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 for this program.

Focus on Dr Chad Bousman

Dr Chad Bousman leads the Gene-Environment Neuropsychiatry (GENe) research group within the Melbourne Neuropsychiatry Centre. Through the Scientists in Schools program, Chad was paired with Penola Catholic College in Glenroy.

Chad assisted in a special program aimed at understanding the function of the brain. The program involved all Year 10 students at Penola and was designed using a problem-based learning pedagogy.

Students worked in groups of 3–4 over the course of a semester. Their task was to identify and then explain how a specific behaviour (e.g. sleep, drug use, exercise) or condition (e.g. depression) impacted on the function of the brain. This involved looking at scientific and online literature and then collating this information into a short film that was shown to all year 10 students and family members at an end of semester evening screening.

Chad was on hand weekly during this period to assist students in identifying appropriate literature, assisting with interpretation of that literature, and providing feedback on their storyboards for their films.

Chad's ability to engage with the students on their level assisted in this successful partnership 'I don't think I fit most students' picture of a scientist as I'm not old and I don't have grey hair! They were also often surprised that I was quick to admit I didn't have the answer to all their questions and soon came to realize that I was keen to lead them to the answer rather than just tell them. I think this approach was successful because by the end of the semester most groups were quite efficient at finding answers to their questions and required very little assistance from me. I learned quite a bit as well!'



Dr Chad Bousman

PARTNERSHIPS



Melbourne Brain Centre and the Florey Institute of Neuroscience and Mental Health (FINMH)

We continue to work with our partner organization, the FINMH. The MNI and the FINMH 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 FINMH on a number of key initiatives. These initiatives include:

- course work and advanced workshops for our graduate researchers
- outreach to secondary schools
- 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 to 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 University of Melbourne hosted a workshop focused on 'Applying advanced technology to advance Precision Neuroscience'. The workshop catalysed interactions between the University and IBM and lead to a pragmatic perspective which resulted in IBM developing five discrete potential collaborative projects to move forward with. These include cognitive computing, emergency logistics to optimise acute stroke care and the utilisation of data sets in epilepsy, MS and schizophrenia to optimise management and to limit disease progression.

Traumatic Brain Injury Initiative

The MNI continues to coordinate the University engagement in Traumatic Brain Injury research. During 2015, Neurosciences Victoria established the Centre for Brain Injury, an unincorporated joint venture for which the University of Melbourne is a key partner.

The Centre has already developed a focus on the development of novel imaging techniques to optimise the diagnosis and management of TBI, reflecting the dedicated input of Siemens into the initiative. It is envisaged that the University and its partners will submit an application to the Federal government's Cooperative Research Centre scheme in 2016 to further enhance our activities in this area in order to minimise the impact of Traumatic Brain Injury in the community.

Hotchkiss

A Memorandum of Understanding between the Hotchkiss Brain Institute (HBI), University of Calgary and the University of Melbourne, as well as with the FINMH, has been established to foster the partnership between the Institutions and will include student and academic exchanges, symposia and research collaborations. It is reviewed annually by all partners. Collaborative activities undertaken in 2015 are renewed below:



International visits

Dr. G. Campbell Teskey, HBI Education Director, visited the University of Melbourne in April, 2015. During his visit, Dr. Teskey met with Prof. Janet Keast and Prof. Andrew Metha, Deputy Director of the MNI.

Symposium – Future Directions in Sport Concussion Research

The MNI hosted a joint symposium on 22 August 2015 on the topic of sports concussion. A total of 33 participants included researchers from the Hotchkiss Brain Institute, University of Melbourne, the Florey Institute, and a small number of additional participants from Deakin University, Neurosciences Victoria, Monash University, the Australia Football League, Siemens, University of Newcastle and The Royal Melbourne Hospital. This event included discussion of the global state of sport concussion research, presentations on the concussion-related research programs from 15 of the participating researchers, and roundtable discussions of approaches to advance collaborative projects.

A key outcome of the 2015 symposium was the recognition that the MNI and the HBI have great opportunity for collaboration in a wide spectrum of trauma-related projects, including but not limited to sports concussion in elite athletes.

Collective interests also include mild traumatic brain injury (TBI) across the life span, with particular interests in the pediatric/adolescent age group. Research into TBI in this age group holds broad community importance and represents an area of mutual strength between the HBI and the MNI.

Several other areas of mutual interest were identified as promising areas to pursue research collaborations moving forward. These include:

- Preclinical TBI Studies in University athletes
- Establishment of an international sports concussion Group/Society
- Advanced Neuroimaging methodologies (Prof. Roger Ordidge, Head of the Melbourne Brain Centre Imaging Unit that houses an ultra-high field 7T MRI scanner, will visit the HBI to assist in knowledge transfer and collaborations when a 7TMRI Scanner is installed at the HBI).

The Rebecca Hotchkiss International Scholar Exchange (RHISE)

The Rebecca Hotchkiss International Scholar Exchange (RHISE) program has been developed by the Hotchkiss Brain Institute (HBI) at the University of Calgary with the primary aim to develop new interactions and strengthen existing ties between the HBI and international centres of neuroscience research and training excellence including Oxford and the Karolinska. Secondary goals of the RHISE program include opportunities for trainees to learn new skills and to explore future career possibilities in Calgary and/or Melbourne.

The RHISE program commenced in 2015. An exchange takes place over a period of four to eight weeks. Applications for the first round opened in October 2014, with 3 PhD students awarded funding for 2015 exchanges, one taken in early 2016.

The successful PhD students/trainees from the inaugural round are:

Mr. Cary Zhang, PhD student from the FINMH (Peptide neurobiology laboratory) visited the laboratory of Prof. Jaideep Bains at the HBI from June 20–18 August, 2015. Cary undertook collaborative research work investigating ‘Neuromodulatory control of stress: Interactions between corticotrophin-releasing factor (CRF) and relaxin-3 systems?’

Mr. Jeff Kenzie, PhD student from the HBI, visited the FINMH from August 10–5 October 2015, in the laboratory of Prof. LeeAnne Carey (Melbourne Brain Centre, Austin Campus). The goal of this project was to ‘identify the extent to which interruption to brain networks, determined from advanced neuroimaging, predicts proprioceptive impairment and recovery following stroke’.

Mr. Nick Ryan from the University of Melbourne (Department of Child Neuropsychology) visited the HBI from January 11th to 22nd February 2016, in the laboratory of Prof. Keith Yeates undertook collaborative work on ‘Predicting longitudinal outcome and recovery of social and behavioral functioning after pediatric traumatic brain injury (TBI): a multicenter, cross-national comparative analysis.’



All three exchanges were highly successful with collaborative links enhanced and new ones established, and with the opportunity greatly appreciated by all students. Mr. Jeff Kenzie from the HBI, University of Calgary noted: "This exchange offered me a different perspective on conducting research (i.e. subject recruitment, lab management, MRI scanning protocols, data analysis) that I would otherwise not have access to at the HBI."

Overall feedback from international exchange students in the inaugural round has enabled us to plan an expansion of benefits from the program, including pre-arranged visits with key scientists in the destination city of the exchange (other than those of the University of Melbourne and FINMH) as well as more structured opportunities for social interaction with other PhD students in the destination city. These initiatives will be implemented in the 2nd round of the HISE program in 2016.

FUNDING INITIATIVES

Grants and External Funding

Active in 2015

Administered through Engineering

Integrated Interconnects in Data Centres and High-Performance Computing

Australian Research Council – Discovery Early Career Researcher Awards (DECRA)

\$375,000

2015–2017

Wang

Silicon Photonics Integration for Light Field Microscopy

University of Melbourne – Early Career Researcher Grant

\$40,000

2015

Wang

New Generation EEG Devices for Improved Mental Health Care

Institute for a Broadband Society – Seed Grant

\$49,420

2015

Skafidas, Pantelis, Qiu

Modelling the Human Nervous System with Human Pluripotent Stem Cells

Australian Research Council – Future Fellowship

\$755,320

2014–2018

Dottori

Australian Research Council – Discovery Projects

Computational Neural Modelling of Bottom-up Information and Top-Down Attention in Auditory Perception

\$360,000

2014–2016

Grayden

Australian Research Council – Centres of Excellence

ARC Centre of Excellence for Integrative Brain Function

\$1,032,913

2014–2020

Director – Gary Egan (Monash); Petrou, Skafidas, et al

Modelling Freidreich's Ataxia Neurodegeneration using Induced Pluripotent Stem Cells

Freidreich's Ataxia Research Alliance, USA

\$261,277

Oct 2013–Sept 2015

Dottori

Augmented White Cane Proof-of-Concept Prototype

Guide Dogs Victoria

\$62,230

Skafidas, Boyd

System-on-Chip Compression for High-End Wireless Audio

Freedman Electronics

\$662,000

Skafidas

Administered through Medicine, Dentistry & Health Sciences**Personalised Prognostic Tools for Early Psychosis Management (PRONIA)**

National Health & Medical Research Council – European Union Health Collaborative Research Grant

\$386,686

2014–2018

Pantelis, Skafidas, Velakoulis, Everall

Rapid Point-of-Care Detection of Genomic Variations for Personalised Medicine

Australian Research Council – Discovery Projects

\$303,000

2014–2016

Kwan, Skafidas, Todaro

Candidate Genes for Classifying Autism Spectrum Disorders (ASD) – Do They Contribute to the Brain Pathology?

University of Melbourne

\$45,000

2014–2015

Chana, Everall, Skafidas, Pantelis, Testa, Zantomio

Next Generation Brain-Machine Interface: Minimally-Invasive Endovascular Stent-Electrode Array for Robotic Limb Control

NHMRC – Project Grant

\$1,651,686

2014–2018

Oxley, Burkitt, Davis, Grayden, Mitchell, Horne, Opie

Advanced Epileptic Seizure Warning Methods

NHMRC – Project Grant

2014–2016

\$410,179

Cook, Grayden, Burkitt, Kuhlmann, Freestone

Developing a Prototype of a Next Generation Brain Computer Interface

NHMRC – Development Grant

2014–2016

\$810,382

Oxley, Burkitt, O'Brien, Grayden, Davis, Opie

Muscarinic Receptors in the Human Brain: In Health and in Sickness

National Health & Medical Research Council – Project Grant

\$382,637

2013–2015

Scarr, Dean, Everall, Hanssen, Chana, Aumann

Monitoring cortical excitability using a probing stimulus for epileptic seizure anticipation

National Health & Medical Research Council – Project Grant

\$380,360

2013–2015

Cook, Grayden, Nesic, McDermott



Glucose Homeostasis in Epilepsy*National Health & Medical Research Council – Project Grant*

\$301,931

2013–2015

Petrou, Reid, Hildebrand

Administered through Science**New Views of Life: Quantum Imaging in Biology***Australian Research Council – Australian Laureate Fellowship*

\$3,110,000

2014–2018

Hollenberg

Administered Externally**Black Out Advisory System – Development of Implantable Sub-Scalp Seizure Monitor***NHMRC – Development Grant*

\$840,175

2014–2016

Williams, Cook, Seligman, Grayden

Defining the Cellular Determinants that Drive Dynamin Inhibitor Induced Cell Death and in vivo Efficacy Against Glioblastoma*Cancer Council NSW – Project Grants*

\$360,000

2014–2018

Chirop, McCluskey, Jones, Sakoff, D'Abaco

Awarded in 2015 for Future Funding***Administered through Engineering*****Transplantation Studies of Sensory Neurons Derived from Freidreich Ataxia Induced Pluripotent Stem Cells into the Dorsal Root Ganglia***Freidreich's Ataxia Research Alliance, USA*

\$360,000

Jan 2016–Dec 2017

Dottori



Prediction Models for Neurological Outcomes

National Institute for Environmental Health – National Toxicology Program

\$105,000

Jan 2016–Dec 2016

Dottori

Beating the Chu Limit

Lockheed Martin

\$150,000

2016

Skafidas, Evans

Administered through Medicine, Dentistry & Health Sciences

Human Epilepsy: Understanding Biology to Improve Outcomes

NHMRC – Program Grants

\$16,110,300

2015–2020

Berkovic, Schiffer, Petrou, *et al.*

Interdisciplinary Seed Funding

The neural basis of moral decision-making

CI: Stefan Bode

Team Members: Simon Laham, Carsten Murawski (PhD student: Damien Crone)

Research Project Detail

This project, a collaboration between the interdisciplinary Decision Neuroscience Lab (DNL; Melbourne School of Psychological Sciences and Department of Finance) and the Melbourne Moral Psychology Lab (MMPL, Melbourne School of Psychological Sciences), aims to investigate the neural correlates of foundational moral values (e.g. care, fairness, loyalty). Specifically, by examining brain activity in response to the presentation of morally-loaded stimuli, the project aims to shed light on the cognitive processes underlying moral perception and judgment in a way that (1) addresses theoretically interesting questions in moral psychology (e.g. How rapidly/automatically are specific kinds of moral content processed? To what extent do representations of different kinds of moral content overlap?), and (2) provides the necessary foundation for building more accurate models of moral judgment and moral behaviour.

The project is divided into two parts. The first part involves development of a novel, theory-driven image set representing foundational moral values that will serve as the stimulus set for subsequent electroencephalography (EEG) and functional magnetic resonance imaging (fMRI) studies. The second involves EEG and fMRI studies in which participants are presented with the aforementioned images, eliciting neural activity that is analysed using novel multivariate pattern analysis methods (MVPA). In both neuroimaging studies, an attempt will also be made to predict moral value processing from local patterns of brain activity, as well as to link brain activity patterns to moral preferences and behaviours with questionnaires and ecologically valid economic decision tasks.

Outcomes

Image set development

Image set development is complete. A pool of over 3,000 images has been constructed from which to draw stimuli that have been validated by a sample of over 2,000 people. Moreover, the image set has now been accepted for two conference presentations, and has received a best-poster award (see below). A manuscript is in preparation.

EEG and fMRI studies

The EEG and fMRI studies are ongoing. Initial data acquisition was delayed by allowing for a prolonged stimulus optimisation phase, which has since led a tripling of the size of the image pool, targeting under-represented content categories. With these issues now resolved, the EEG and fMRI studies proceed as originally planned. Data acquisition for both studies will be completed in early 2016, and data analyses will continue until June/July 2016. Outcomes of this work will be presented at several national and international conferences in 2016, with intent to publish at least two peer-reviewed research articles in international journals.

New collaborative links

The work has already created new collaborative links to Dr Pascal Molenberghs (Monash University Senior Lecturer; current president of the Australasian Society for Social and Affective Neuroscience).

Conference presentations

Crone, D. L., Bode, S., Murawski, C. & Laham, S. (2015, April). Development and validation of a Moral Foundations Picture Set. Poster presented at the Society for Australasian Social Psychologists Annual Conference, Newcastle.

- Recipient of SASP 2015 Best Poster Award

Crone, D. L., Bode, S., Murawski, C. & Laham, S. (2016, January). Probing moral perception with a novel moral image set. Poster accepted for presentation at the Society for Personality and Social Psychology, San Diego, CA, USA.

Goals for 2016

It is expected that EEG data acquisition will be completed during January 2016, with the results of the EEG study determining specific parameters of the fMRI study. Completion of data collection for the fMRI study is expected in the first half of 2016. It is also planned to use the results of the present project for a Project grant application to the Australian Research Council in 2017.

Development of electroceutical technology: vagal nerve stimulation for anti-inflammation therapy.

CI: Rob Shepherd

Team Members: John B Furness, Robin McAllen

Research Project Detail

A promising new method to treat inflammatory diseases such as arthritis and inflammatory bowel disease is electrical stimulation of the vagus nerve. Long-term electrical stimulation would be required for such a treatment to be effective. However, investigations to date have been limited by only studying stimulation periods. This project set out to investigate the nerve pathways that control inflammation in the intestine, to determine the sites most likely to be used for control of intestinal inflammation, and to design electrodes and the surgical approach required for long-term electrical stimulation.

Issues/Outcomes

The MNI funding has been critical for establishing this collaboration. With the funding, the investigators have set up a rodent model to determine the circuitry of the anti-inflammatory reflex pathways for the intestine. It has been possible to inflame a defined length of small intestine (8–10 cm, length depending on positioning of vascular arcades). The investigators have established methods of recording nerve activity from branches of the vagus nerve and mesenteric nerves in anaesthetised rats, and have quantified the innate inflammatory response using a stain for neutrophils. They have also assessed the degree of inflammation and proliferation of lymphocytes using conventional histology. It has been established that afferent nerve activity travels by both the hepatic and celiac branches of the vagus, and efferent activity travels in the mesenteric nerves. There is a rapid innate immune response and infiltration of lymphocytes within an hour of inducing inflammation with trinitro benzene sulfonate (TNBS). The investigators are in the process of designing electrodes for chronic studies.

Goals for 2016

The MNI Interdisciplinary Seed Funding was the springboard for a successful application to the Defense Advanced Research Projects Agency (DARPA) which will allow the research to not only continue but to expand. The award



is for \$6.07 million over 4 years, beginning in November 2015. It is planned to complete the rat work begun with MNI funding and then to proceed to studies in sheep. This will form a bridge to a clinical trial, which will require design of a fully implantable, externally controlled, stimulator.

Developing biomarkers of proteostasis decline for translational medicine in neurodegenerative diseases

CI: Yuning Hong

Team Members: Danny Hatters, Dennis Velakoulis, and Trevor Smith

Research Project detail

Maintaining protein homeostasis (proteostasis) in cells is highly important for cell health. The main system in cells ensuring proteostasis is the quality control mechanisms that are in charge of protein synthesis, folding and degradation. A loss of proteostasis capacity is predicted to occur in neurodegenerative diseases such as Huntington's disease and will promote the latent capacity of misfolding proteins to accumulate as aggregates.

New approaches to identify the efficiency of proteostasis are needed in order to track the risk of cells suffering the damage from protein misfolding and aggregation. This project involves the construction of a biochemical fluorescent sensor, TPE-MI, as a probe to detect the proteostasis capacity in cells or patients, samples under different stress conditions. Results so far suggest that in cells expressing mutant aggregation-prone Huntingtin protein there is a large increase in TPE-MI fluorescence prior to inclusion formation, providing insight into the relationship between protein misfolding, aggregation and proteostasis. The investigators will next apply the method to patient samples and investigate the correlation between the proteostasis decline and disease progression.

Issues/Outcomes

1 The results have been presented at conferences:

'Quantification of the Protein Folding Capacity of a Cell', Presented at Gordon Research Conference – Proteins, Holderness, NH, USA, June 14–19, 2015 by Danny Hatters

'Revealing Proteostasis Capacity in Cells by a Fluorescent Sensor', Presented at Biophysical Society Thematic Meeting – New Biological Frontiers Illuminated by Molecular Sensors and Actuators, June 28–July 1, 2015, Taipei by Yuning Hong

'Probing Protein Misfolding and Aggregates by Novel Aggregation-Induced Emission Luminogens', Presented at ComBio, September 27–October 1 2015 by Yuning Hong

- 2 The findings have been submitted to the Technology Licensing Services team at the University for technology assessment for a patent application.
- 3 The findings also evoked the interest of many other research groups and new collaborations are being established. These include collaboration with Prof Leann Tilley (Bio21) focusing on the investigation of the effect of antimalarial drugs on parasites, Dr Mahmoud A. Pouladi (National University of Singapore and A*STAR) enabling access to Huntington's disease neural stem cells, and Prof Hideki Mochizuki (Neurology, Osaka University) to enable the application of the technology to Parkinson's disease cell models.

Goals for 2016

Further work will involve the synthesis of more variants of the probes and their application in order to better understand the quality control machinery in cells, to study effect of regulators/drugs on the proteostasis system in cells, and to establish simple methods for disease diagnosis. The CI is applying for an ARC fellowship based on this project in 2016. Our team plans to collect more clinical data and apply for an NHMRC Project Grant.

A new prognostic tool for cochlear implantation using functional near-infrared spectroscopy (fNIRS).

CI: Dr Abd-Karim Seghouane

Team Members: Abd-Krim Seghouane, Colette M. McKay, and Adnan Shah

The aim was to recruit 10 existing cochlear implant (CI) users with variable outcomes and up to 10 candidates on the waiting list for a CI in addition to 10 normally hearing people for comparison. For the major study involving auditory stimulation concatenated with resting state, a total of 15 NH and 18 CI users were imaged. Overall, the aim of the project has been achieved successfully making a productive year for our cross-disciplinary collaboration.

After finalising the experimental protocol for auditory stimulation, 15 NH and 18 CI participants were recorded for hemodynamic neuroactivation during the course of the year 2015. These experimental sessions involved concatenated resting-state and task-related functional sessions. Based on this neuroimaging data, a manuscript demonstrating the differences of auditory stimulation in NH and CI groups is in the final stages of development to be submitted soon [6]. This manuscript describes the brain dynamics of auditory function in response to acoustic chirp stimulation. Upon finalizing this manuscript, there is pending work, analysing imaging data sets of the 15 NH and 18 CI participants. This study will investigate resting state functional connectivity in the two groups.

Published/accepted to appear:

- 1 "Brain plasticity due to deafness as revealed by fNIRS in cochlear implant users," Conference on Implantable Auditory Prostheses (CIAP).



- 2 “Resting state connectivity in language areas: an fNIRS study of normally-hearing listeners and cochlear implant users,” Conference on Implantable Auditory Prostheses (CIAP).
- 3 “Connectivity in language areas of the brain in cochlear implant users as revealed by fNIRS,” 17th International Symposium on Hearing (ISH), pp. 267–274, Chapter 34, Talk Thursday, June 15–19, 2015.
- 4 “Using fNIRS to study speech processing and neuroplasticity in cochlear implant users,” 17th International Symposium on Hearing (ISH).
- 5 “Functional connectivity assessment of language areas in CI users using fNIRS” Australian Biomedical Engineering Conference (ABEC).

In preparation:

- 1 “Investigating brain dynamics of auditory function in cochlear implant users with fNIRS”, to be submitted to Neuroimage.
- 2 “An fNIRS based assessment of resting-state functional connectivity in bilateral auditory areas in cochlear implant users and normal hearing listeners”.

Modelling the generation of oligodendrocyte cell topography in white matter

CI: Barry Hughes

Co-Investigators named on grant: Tobias Merson, Kerry Landman

Other participants: Philipp Röth, Darragh Walsh

Research project detail

Myelination of central nervous system (CNS) axons by oligodendrocytes is critical for rapid and efficient neural processing. Until recently, myelination was thought to be restricted to early postnatal life. Recent research shows that myelin is laid down throughout adult life and is thought to be an important mechanism for activity-dependent plasticity, learning and memory, as well as for enabling recovery from demyelinating disease. Since only a subset of CNS axons become myelinated, synchronous activation of target nuclei in the brain that are innervated by common groups of axons that fasciculate together requires that these axons must be myelinated to a similar extent and tight regulatory mechanisms must exist to ensure this. A striking feature of oligodendrocyte development within white matter is that the cell bodies of many oligodendrocyte progenitor cells become organised into discrete linear arrays of three or more cells before they differentiate into myelin-producing oligodendrocytes. These linear arrays align parallel to the direction of the axons within white matter tracts.

Guided by experimental data on the abundance and composition of linear arrays in the corpus callosum of the postnatal mouse brain, we have

constructed discrete and continuous models of linear array generation to investigate the relative influence of cell migration, proliferation, differentiation and death of oligodendroglia upon the genesis of linear arrays during early postnatal development.

Issues/outcomes

We have found that only models with significant cell migration can replicate all of the experimental observations on number of arrays, number of cells in arrays and total cell count of oligodendroglia within a given area of the corpus callosum. These models are also necessary to accurately reflect experimental data on the abundance of linear arrays composed of oligodendrocytes that derive from progenitors of different clonal origins. In related work, we find compelling evidence from probabilistic modelling that the selection of axons for myelination by adjacent oligodendrocytes is a cooperative phenomenon.

This work contributes to our understanding of the regulation of myelination on a system-wide level and will inform future studies of normal and pathological myelination.

Tracking the Dynamics of Information Processing in Cortical Circuits

CI: Hamish Meffin

Team Members: Michael Ibbotson, Paul Martin, Joseph Lizier, Michael Wibral

Research Project Detail

The brain is segregated into functional regions: some which process sensory inputs, and others which create perception and actions. Understanding the principles of information processing in microcircuits of neurons in the brain would lead to a major advance in our fundamental understanding of brain function.

This project aims to develop the methodologies required to quantify information processing in and between microcircuits of neurons in the brain. These methods will enable for the first time, quantitative tracking of the storage, transfer and modification of information within and between brain microcircuits.

The signals from multiple neurons are recorded simultaneously using arrays of electrodes implanted in the visual cortex, as they respond to visual stimuli. The aim is to track the flow of information from the stimuli to the neurons and between the neurons themselves as they perform processing.

Initially, a computational method to track information storage and transfer using computer models of the neurons in the visual system has been developed. The information transferred via the (model) visual pathway from the image to the model neuron consists of both positive information, which the neuron correctly predicts, and negative information which the neuron cannot correctly predict.

From recordings of single neurons in visual cortex it has been possible to recover their spatial receptive fields to create models of their response to visual stimuli, similar to the models we use to perform the analysis of information storage and flow. It is planned to use these results to track the flow of information from the presented images to these neurons.

Issues/Outcomes

The recovery of receptive fields from recordings of visual cortical neurons will provide important preliminary data for an ARC Discovery Project Grant in the forthcoming 2016 ARC grant round concerning the formation of receptive fields during early development of the visual system.

Melbourne Neuroscience Institute (MNI) Fellowships

The MNI awarded Fellowships to Dr Alexandra Grubman, Department of Pathology and Dr Andrew Watt, FINMH, to promote the University's interdisciplinary research projects in the Neurosciences.

Dr Alexandra Grubman

Brain inflammation is an important feature in Alzheimer's disease, however, whether this is a beneficial or detrimental component in Alzheimer's disease pathogenesis remains controversial. Microglia, the key cells involved in neuroinflammatory responses, are diverse – microglia protect neurons through the capacity to degrade toxic beta-amyloid (Ab) but can also damage neurons via chronic production of toxic pro-inflammatory mediators. Alterations in the metabolism and location of biological metals such as copper are also detected in the brains of Alzheimer's disease patients. The overall objective of this fellowship is to understand how microglia contribute to inflammation and impaired metal metabolism in Alzheimer's disease, and to develop effective therapeutics that promote beneficial microglial pathways, while dampening toxic pathways. The work will involve use of cells from mice modeling Alzheimer's disease and human stem cell models to investigate the action of neuroprotective metal-complexes on various microglial functions, including the production of toxic factors, the digestion of A β , and modulation of microglial genes that are associated with increased risk of late-onset Alzheimer's disease.

This work will involve the optimisation of cell sorting approaches to isolate live microglia from the brains of adult mice in order to investigate age-dependent microglial dysfunction in mouse models of Alzheimer's disease. Human neural progenitor cell-derived cultures are also being generated. These cultures contain astrocytes and neurons, and contain cell subsets that respond to dopamine, glutamate and cholinergic agonists. The cultures are being grown in high-throughput microfluidic perfusion bioreactors in 3D. Using models to screen novel complexes for modulation of microglial functions, it has been possible to identify an A β -targeting compound that affects microglia. Specifically, this compound regulates the expression of several genes



2016 Fellows

associated with risk of late onset Alzheimer's disease that are involved in microglial phagocytosis, and reduces the production of pro-inflammatory factors in primary mouse microglia. Investigation of the molecular mechanism by which this compound modulates microglial activity is proceeding. The fellowship has also resulted in an NHMRC Dementia Research Development Fellowship.

Dr Andrew Watt

A common feature of neurodegenerative diseases is the spread of misfolded proteins throughout the brain as the disease progresses. In Alzheimer's disease, the misfolded protein is called β -amyloid ($A\beta$) which aggregates to form $A\beta$ clusters known as plaques. The presence of these $A\beta$ plaques in the brain is characteristic of AD; however, the process by which they spread throughout the brain remains unclear. The fellowship has focused on whether the $A\beta$ is being trafficked through the brain via small vesicles called exosomes. Exosomes can be thought of as microscopic packages that are transported between cells to deliver messages in the way of proteins, DNA and other chemicals. Exosomes had previously been isolated from blood and cerebrospinal fluid, but not from frozen human brain samples.

Previous work from my collaborators has enabled me to apply a methodology in order to identify an exosome rich fraction in the human brain samples taken at autopsy from neurologically normal individuals and individuals with AD. The analysis of these fractions indicated that $A\beta$ was enriched within the exosome-rich fraction of the AD samples, suggesting that as the disease progressed, $A\beta$ was being shunted towards the exosome system and spread from cell to cell. These early results indicate that the exosome system may be one of the means by which $A\beta$ spreads throughout the AD brain; further work is needed to unravel what factors are driving the $A\beta$ down this pathway. Ongoing work is looking at other markers of cell stability and trafficking pathways to determine whether other non-exosome pathways are also being utilised to traffic $A\beta$ between cells or whether disruption to these alternate pathways and damage to the cells are driving the $A\beta$ towards exosomes like rats racing to the lifeboats on a sinking ship.

Strategic Research Australian Postgraduate Awards

In 2014, the MNI conducted an Expression of Interest for up to 3 Strategic Australian Postgraduate Awards (STRAPAs) to support cross-disciplinary graduate research in the Neurosciences and related disciplines, for commencement in 2015. The MNI STRAPAs are designed to attract outstanding graduates who have demonstrated excellence in neuroscience, science, biomedical science, chemistry or other related disciplines.

MNI STRAPA recipients receive an additional support package for their research of \$5,000 per annum from the MNI for 3 years. These funds are allocated as follows:

- \$3,000 per annum stipend top-up

- \$2,000 per annum to be held by the supervising laboratory and used for direct research costs for the student's project and attendance at conferences.

The recipients of the MNI Strategic APAs for 2016 commencement are:

Name	Project Title
Samuel Titchener	Bionic Eyes: enhancing perception in retinal prostheses using low-power eye tracking
Peter Eli Yoo	A real-time 7T-fMRI pre-diagnostic tool for an invasive motor-restorative brain machine interface
Lucy Oehr	Does microstructural brain damage contribute to poor outcome following Mild Traumatic Brain Injury (MTBI)?

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 in the private, public and non-government sectors and act as advocates on behalf of the MNI.

The MNI would like to extend thanks to Prof Mark Hargreaves who was Chair of the Advisory Board for the first half of 2015 before being recruited as acting Dean of the Faculty of Medicine, Dentistry and Health Sciences. MNI welcomes back Prof Liz Sonenberg as Chair who will continue in the role through to 2016. Both Professor Hargreaves and Professor Sonenberg have provided impeccable oversight and guidance to the MNI.

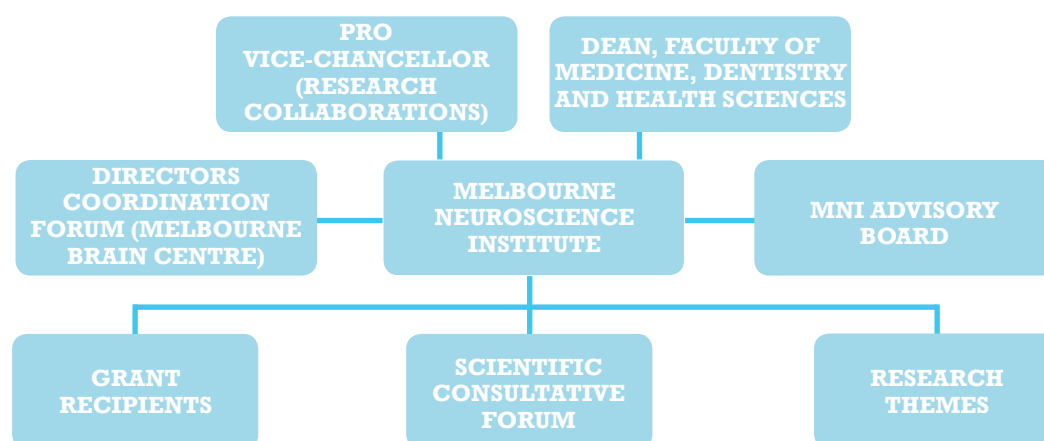
2015 Board Membership

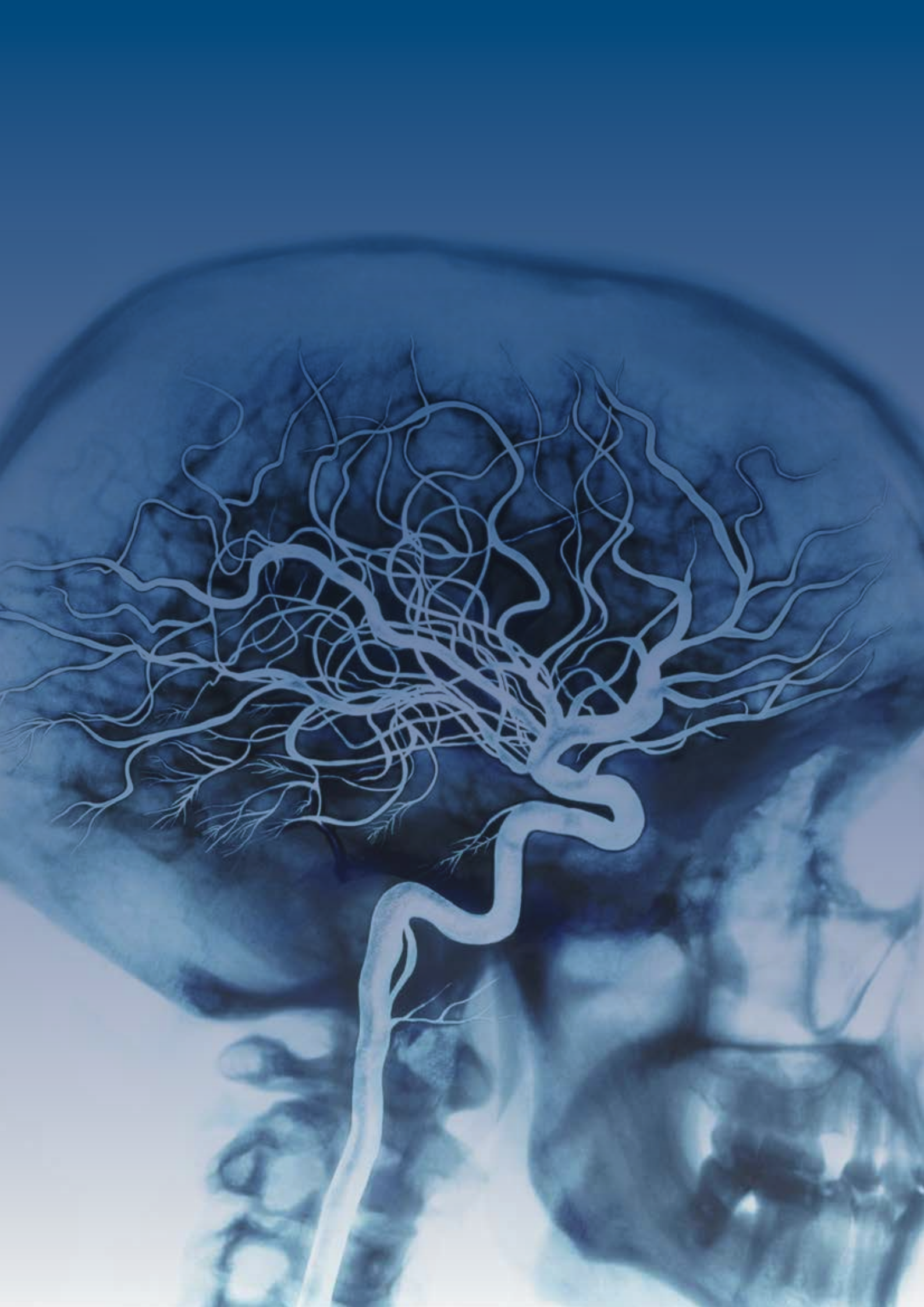
Name	Title
Prof Liz Sonenberg (Chair)	Pro Vice-Chancellor (Research Collaboration & Infrastructure), UoM
Prof Trevor Kilpatrick	Director, Melbourne Neuroscience Institute, UoM
Prof Mark Hargreaves	Dean, Faculty of Medicine, Dentistry and Health Sciences, UoM
Prof Greg Qiao	Assistant Dean (Research), Melbourne School of Engineering, UoM
Prof Karen Day	Dean, Faculty of Science, UoM
Dr Andrew Milner	Chief Executive Officer and Managing Director, Neurosciences Victoria
Prof Richard Head	Deputy Vice Chancellor & Vice President: Research & Innovation, University of South Australia
A/Prof Andrew Metha	Deputy Director, Melbourne Neuroscience Institute
Prof Glenn Bowes	Associate Dean (External Relations), Faculty of Medicine, Dentistry and Health Sciences, UoM
Prof Bob Williamson	Chief Scientific Officer, Yulgilbar Foundation, Ex-Secretary for Science Policy, Australian Academy of Science, Faculty of Medicine, Dentistry and Health Sciences, UoM
Dr Keith McLean	Theme Leader: Biomedical Materials and Devices, CSIRO

Scientific Consultative Forum

The Scientific Consultative Forum comprises Heads or 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.

Governance Structure





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