2014

Melbourne Neuroscience Institute

Annual Report

THE UNIVERSITY OF MELBOURNE

MELBOURNE NEUROSCIENCE INSTITUTE

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info-mni@unimelb.edu.au

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Editor: Amy Bugeja
Designer: Ali Edmonds Graphic Design

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

2014

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Annual Report

contents

Executive Summaries	2
Research	5
Engagement	24
Partnerships	36
Funding Initiatives	39
Governance	53

1 EXECUTIVE SUMMARIES

Message from the Director

The calendar year of 2014 has been an important and successful one for MNI. The four foundation themes supported from the outset by the Institute continue to flourish. Stem Cells Australia completed a successful 3-year review by the Australian Research Council. The Melbourne Brain Centre Imaging Unit commissioned the 7T MRI that now sits beside a PET-CT instrument to provide our researchers with state of the art capability to assess the structure and function of the human brain in health and disease. The Centre for Neural Engineering continues to excel and in particular is focusing on the development of an effective point of care nano-sensor which could revolutionise the assessment of health and wellbeing. The Music, Mind and Wellbeing initiative has continued its successful partnership with the Melbourne Recital Centre to deliver the 'Music on the Mind' seminar series. Plans for the establishment of a Music Garden in collaboration with the City of Melbourne are also well advanced.

Important links with other academic institutions with prominent neuroscience programs have also been forged. These include partnerships with the Salpetriere in Paris and the Hotchkiss Institute in Canada, resulting in the genesis of student exchange programs and planning for theme-based conjoint workshops to commence in 2016.

The MNI spearheaded an important new initiative for our graduate researchers in 2014 designed to enhance expertise in areas relevant to their PhD projects. The initiative comprised four advanced workshops devoted to advanced neural imaging, stem cell science, ion channel recordings and live-cell microscopy. Feedback from students, supervisors and coordinators of the workshops was very encouraging and, in response to this the program will be expanded in 2015.

As in previous years, we offered a series of interdisciplinary seed funding grants as well as postgraduate fellowships. We are pleased to report that our internal auditing has identified that a significant number of previous recipients of these awards has been successful in obtaining subsequent peer-reviewed funding for their work.

Thanks to the sterling work of our project officer, Amy Bugeja, our outreach program continues to expand. The activities range from a vibrant public seminar program to a series of opportunities offered to high school students that provide insight into the importance of Neuroscience to the community and what a career in the Neurosciences entails. Importantly, we now have a portal

to enable those who wish to donate to Neuroscience-focused research at the University do so in a directed manner and I suspect that this facility will be increasingly used as people become familiar with the opportunity.

Highlights also included a series of visits by high profile dignitaries. These included Mr John Berry, US Ambassador to Australia who discussed ways in which we could potentially optimise links with US researchers for mutual benefit under the umbrella of President Obama's BRAIN Initiative. The UK Minister for Higher Education Mr Peter Willett provided a vision of how government can assist in optimising research translation. The UK PM's Special Envoy for Dementia Research Dr Dennis Gillings discussed ways in which we can work together to accelerate the global fight against dementia.

I was also appointed as a scientific adviser to the Yulgilbar Alzheimer Research Program (YARP) which is Chaired by Mrs Samantha Ballieu. Mrs Baillieu and her father Mr Baillieu Myer have established the YARP with the aim of assisting researchers who are working to produce drugs that will either prevent, slow down or cure Alzheimer's disease. This is an important initiative that I am pleased to be involved with and it comes at an important time for research into Alzheimer's disease given that the Commonwealth government has also pledged $200 million for dementia research over 5 years.

The MNI is currently involved in crafting several important new initiatives, the majority of which are being fashioned as multi-centre collaborative interactions. Of particular importance is the Centre for Brain Injury which should fundamentally transform the coordination of traumatic brain injury-related research in the State of Victoria, this Centre will also provide a focus for community engagement to promote prevention and to improve outcomes after traumatic injury. We are also engaging with the Monash Institute of Pharmaceutical Sciences to scope an initiative with the long-term aim of promoting drug development for neurological diseases, recognising our complementary talents in this arena, and with the ultimate aim of developing interactions with commercial partners. It should be acknowledged that these initiatives have been very much facilitated by ongoing productive engagement with Neurosciences Victoria, which has played a key role in catalysing the relevant interactions.

Finally, I am most grateful to the office of the Deputy Vice-Chancellor (Research) and to the Dean of the Faculty of Medicine, Dentistry and Health Sciences for their wise counsel and continued support of MNI. I would also like to sincerely thank the MNI staff namely Associate Professor Andrew Metha, Deputy Director, Trish Weston (Operations Manager), Amy Bugeja (Project Officer) and Carmel McFarlane (Office Administrator) whose tireless work has ensured the success of MNI for the benefit of the University and the community at large.

Professor Trevor Kilpatrick
Director, MNI

Below: Professor Trevor Kilpatrick, Associate Professor Andrew Metha, Ms Trish Weston, Ms Amy Bugeja and Ms Carmel McFarlane.

Message from the Dean

It is a pleasure to provide this perspective on the activities of the Melbourne Neuroscience Institute (MNI) during 2014. The University of Melbourne has the ambition of becoming one of the truly great Universities of the world and in order to achieve this goal it must focus on big picture science in areas of research where it can excel and contribute to outcomes relevant to the community at large. The MNI provides an important opportunity for the University and the Faculty of Medicine Dentistry and Health Sciences to consolidate and focus its activities in the Neurosciences, a research discipline that we collectively identify as a priority.

Most importantly, the MNI has acted as a catalyst to promote important collaborative links both within the University and with external partners. Important initiatives with prominent overseas institutions have been forged for the benefit of both our students and staff. I am particularly supportive of developments that are being brokered by MNI in neurotrauma research and in the application of pharmaceutical science to the treatment of neurological disease. These initiatives are important goals for MNI and I look forward to working with the Director to bring them to fruition during 2015.

Professor Stephen Smith

Dean, Faculty of Medicine, Dentistry and Health Sciences

Above: Professor Stephen Smith.

RESEARCH

2

Music, Mind and Wellbeing

Director: Professor Sarah Wilson

Music and Education: Professor Gary McPherson

Music and Audition: Associate Professor Neil McLachlan

Music and Wellbeing: Associate Professor Kat McFerran

Research Theme

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 2014 has been highly productive and successful for MMW, with a range of research and community based activities receiving significant academic and media attention, and promoting broad public engagement in music within the community.

MMW have three core research strands encompassing music neuroscience, education and health. The neuroscience program incorporates a range of projects relating to the neurobiological basis of hearing, sound recognition, music and speech processing, including how these can change in the context of training or disease. MMW continues to demonstrate that music is a powerful tool for changing the brain across the lifespan. Building on this, our educational research program is investigating the key factors underlying student engagement in music learning and performance in Australian primary and secondary schools. It has led to the development of new pedagogical approaches and instrument ensembles for teaching and learning music in primary schools, and recently demonstrated highly effective interventions for music performance anxiety in secondary school and conservatorium students. The health research program investigates the use of music to promote the mental health and wellbeing of individuals and communities, as well as to facilitate recovery following physical or mental illness. Among other things, MMWs recent research investigates the ways that music is applied by music therapists with people in hospitals, schools, aged and palliative

Below: Harmonic gongs and bells and percussion seats installed behind the Grevillea bells.

Above: Detail of a sculptural bell installation inspired by Grevillea flowers; Music, Mind and Wellbeing Team.

care facilities, and the community. Research findings have important new implications for people with physical and mental health problems, as well as for building inclusive communities that embrace diverse creative participation.

Research

Within the neuroscience research program, recent work includes: (1) a comprehensive review of the genetic basis of music abilities, including ways in which the environment and genetic factors interact to produce changes in the brain, (2) new cognitive and computational models of speech and sound recognition mechanisms and speech de-noising, including their application to analysing vocalisations as behavioural markers of genetic disorders in humans and mouse models, (3) new brain-based theories of pitch and dissonance perception, and (4) advances in our understanding of pervasive developmental and psychological disorders, including new methods for their detection based on auditory perception and vocal production tasks.

Within the educational research program, recent work includes: (1) pilot programs of innovative technologies and approaches to maximise engagement in classroom music education in primary schools, (2) new knowledge of how group instrumental training supports problem-solving ability, literacy, numeracy and wellbeing in socially disadvantaged primary school students, and (3) multiple studies investigating music performance anxiety and the efficacy of psychological strategies to optimise music performance in secondary school and conservatoire students. MMWs findings 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 plan a series of music programs for inclusion in the Victorian teaching support materials for the new National Curriculum.

Within the health research program, recent work includes: (1) investigations of music therapy with young people who have intellectual disabilities to facilitate their communication and engagement, (2) investigations of music therapy with people who have mental health problems, including a study showing that listening to sad music significantly increases depressive symptoms in people with anxiety, and (3) investigations of music therapy with adults in rehabilitation hospitals, including the use of song writing to facilitate emotional recovery in

people with acquired brain injuries or spinal cord injuries. MMW also recently completed a review of the way that certain forms of music therapy work, including its neurobiological, cognitive, and emotional mechanisms.

Outreach and Engagement

The MMW community engagement programs aim to promote new public attitudes that foster grass roots participation in music. Illustrating this, in 2014, researchers from MMW created the 'Music Garden' at the Docklands that will be officially opened in March 2015. In 2014 MMW again ran a series of high-profile, public events that have been booked to capacity, highlighting the success and broad appeal of these events.

Opening of the Music Garden at the Docklands

The Music garden features innovative harmonic bells and gongs designed by Neil McLachlan at the University of Melbourne. The commercialisation of these instruments led to the creation of a joint venture spin-off company, Harmonix Instruments in 2011 that was contracted to produce the instruments and music sculptures with artist (and graduate of Victorian College of the Arts) Emilia Storm and Landscape architect Simon Ellis. The Music Garden is a highly innovative project funded by property developer Mirvac in collaboration with The City of Melbourne and Places Victoria to create a playground for all ages in a landscaped garden on the Docklands waterfront. The instruments are intended to foster spontaneous cooperative play among visitors to the park, and thereby build stronger social bonds between residents who have all just arrived in the new apartments. Musical play in public places is an exciting new concept that must address the challenge of creating visually exciting, vandal and weatherproof instruments that can be easily used to make beautiful sounds. This project has achieved all these aims and we hope is the forerunner for many more interventions to further build community interactions and to promote mental wellbeing.

Public Lecture Series: 'Music on the Mind'

For the fourth 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 social wellbeing, music participation, learning and development, and the role of music in our contemporary communities. This series has greatly enhanced public engagement in music research and its applications 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 co-host a series of academically focused research presentations and discussions showcasing

ENGAGEMENT WITH THE MEDIA

Over 2014, MMW researchers have engaged the public and explored a range of issues relating to the benefits of music for mood, memory, health and wellbeing. This has included numerous radio interviews around the country, including special commentary during Mental Health Week on the relation of music to depression, and contributing to a short documentary on the benefits of music in education. Our neuroscience research program was also featured in Australian Geographic, while members of MMW have attended film screenings at the Human Rights Arts and Film Festival and at the premiere of 'Alive Inside' to provide public commentary and debate. The latter film examined the benefits of music for patients and families coping with the significant challenge of dementia.

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.

Forthcoming Symposia: 'Dance, Song, Ceremony and Wellbeing in Australia'

In May 2015, Sally Treloyn and Penelope Smith (Australian Catholic University) will convene a panel 'Dance, song, ceremony and wellbeing in Australia' at the forthcoming conference 'Creating Futures 2015: Practice, Evidence and Creativity in Tropical and Remote settings' (Cairns), bringing together four collaborative presentations on music and wellbeing in Indigenous Australian communities from the Kimberley (Western Australia), Alice Springs, Darwin and Goulburn Island (Northern Territory). This panel represents the second of two meetings supported by a University of Melbourne Engagement & Partnerships Grant, 'Indigenous musical arts and wellbeing: Promoting knowledge and building dialogue for future research'.

Partnerships and Goals for 2015

It is essential to attract philanthropic support and sufficient Government and Industry engagement for MMW to influence education, health policy and public attitudes. 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 (FINMH), the Centre for Neural Engineering (CfNE), and the Bionics Institute. MMW also disseminates research and engages the public in collaboration with the Australian Music Centre, The Music Trust, The Centre for Cultural Partnerships (VCA), the Australian Music Therapy Association, The City of Melbourne, Places Victoria and The Melbourne Recital Centre, and provide ongoing advice and consultancies for the Victorian State Government (VCAA) and the Federal Government.

In 2015, MMW plans to maintain its research and community engagement profile, with public educational events already being arranged, as well as the second national 'Music, Mind and Health' conference to be hosted in Sydney, December 2015. Through these initiatives MMW will continue to develop new research initiatives with its partners.

Melbourne Brain Centre Imaging Unit

Director: Professor Roger Ordidge

Senior Molecular Imaging Technologist: Mr Rob Williams

Manager of Research Computing and IT Infrastructure: Dr Neil Killeen

Senior Research Fellow: Dr Brad Moffat

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 focussing predominately on human-based research. This world-class facility was funded by the University of Melbourne, FINMH, the National Imaging Facility (NIF) and the Victorian Biomedical Imaging Capability (VBIC).

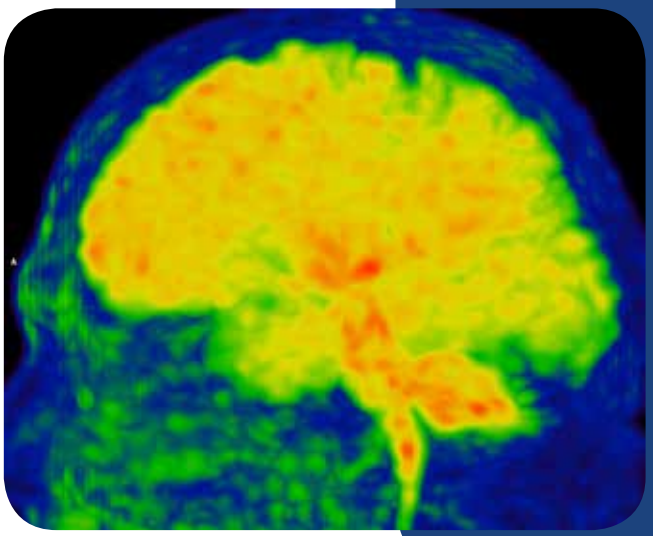
Research

The PET/CT scanner has attracted a range of research projects emanating from within the University of Melbourne and FINMH, as well as from external research institutions. Projects range from measurement of beta-amyloid (Aβ) plaques acting as sentinel for the development of Alzheimer's disease, to trials of new radiopharmaceuticals and CT on animal and human anatomical samples.

Research studies facilitated by our PET imaging in Alzheimer's Disease have received the 2012 and 2013 de Leon Prize in Neuroimaging. This award, presented by the International Society to Advance Alzheimer's Research and Treatment (ISTAART) Neuroimaging Professional Interest Area (NPIA), acknowledges the best papers published in any peer-reviewed journal.

With respect to the Alzheimer-based research, it is noteworthy that is has now been shown that PET tracer studies reveal changes up to 30 years before symptoms of dementia. This study has attracted funding from the international pharmaceutical company GE and has collaborators from the Austin Hospital, Cyclotek and the Commonwealth Scientific and Industrial Research Organisation (CSIRO).

The quality and low noise of the data has meant that the investigators have been able to identify meaningful changes earlier and at lower levels than at other international research sites. For example, using a radioactive fluorine-labelled compound (Flutemetamol) tracer we have shown that a higher burden of



Below: A Flutemetamol tracer image of a normal human brain.

Above: The Melbourne Brain Centre Imaging Unit team.

amyloid is associated with subjective memory complaints.

The 7T MRI scanner became operational in July 2014. Development of operating protocols has progressed well with the first pilot projects to commence in December/January 2014/15. The pilot projects have been offered to researchers from all VBIC institutional members which includes a reduced cost for scans to enable the collection of comparative data (3T verses 7T) by researchers for use in submission to major grant rounds in 2015.

Studies in Multiple Sclerosis and Alzheimer's Disease will also commence next year and development work to increase the capability of the system will proceed during 2015.

Outreach and Education

The Imaging Unit has hosted three symposia in 2014, two of which were in association with VBIC and Siemens Medical Systems, and the other associated with the opening ceremony for the 7T MR scanner. We have also presented a lecture series on MRI as part of the MNI Advanced Workshop series. These lectures were attended by 17 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.

Partnerships

- FINMH
- The National Imaging Facility (NIF)
- The Victorian Biomedical Imaging Capability (VBIC)
- Siemens Medical Systems
- Cyclotek Ltd
- Monash University

- The Royal Melbourne Hospital (Melbourne Health)
- Austin Health

Goals for 2015

Our goals for 2015 include:

- Expansion of research studies for both PET/CT and 7T MRI scanner.
- Research and development of new techniques for high field MRI scanning.
- Testing of new radiotracers for the PET/CT scanner.

Stem Cells Australia

Director: Professor Martin Pera

Head of Education, Ethics, Law & Community Awareness Unit: Associate Professor Megan Munsie

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

Led by Professor 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.

Research Highlights

Four main areas of stem cell biology were the focus of SCA's research activities in 2014 – control of pluripotency and reprograming, regeneration and repair in the brain, regeneration and repair in the heart and the development of blood – with members contributing to over 140 publications in prestigious journals such as *Nature, Nature*

LAUNCH OF 7T MRI

The new ultra-high field 7 Tesla human MRI machine is used to analyse and understand dementia, stroke, multiple sclerosis, epilepsy, post-traumatic stress and other neurological disorders. Conventional machines used in hospitals rely on 3 Tesla; a less powerful magnet.

Senator Scott Ryan, Parliamentary Secretary to the Minister for Education represented Prime Minister to officially launch the new machine.

The MRI offers unprecedented clarity of the brain's workings, according to Professor Roger Ordidge, the Chair of Imaging Science at the University of Melbourne. "The difference between the 7 Tesla and the more common 3 Tesla is extraordinary and demonstrates how quickly technology advances for improved results," says Professor Ordidge.

Chairman of the FINMH, Harold Mitchell AC, welcomed the machine's capacity to diagnose diseases of the brain. "The human b rain is the most complex living structure. To be able to view its workings without the need for surgery is fascinating," says Mr Mitchell.

Above: Professor Roger Ordidge and Senator Scott Ryan.

Above: Claire Cuddy, Research Assistant for the Pera Laboratory, Stem Cells Australia.

Communications, Nature Medicine, Nature Cell Biology, Cell and Cell Stem Cell.

One discovery that attracted significant media interest was the contribution of SCA's researchers to Project Grandiose – the international effort that used a variety of very sophisticated approaches to interrogate genes and proteins involved in the process of reprogramming including the identification of a new type of artificial stem cell.

Stem Cells Australia's scientists were also part of a discovery that revealed that heart muscle cells retain the ability to replicate long after birth. This finding overturning centuries old scientific theory and opens the possibility for repair of the hearts of babies born with heart defects, or even to reactivate heart muscle cells damaged after a heart attack in adults.

Outreach and Education

During 2014, we continued our focused on bringing stem cell science to high school students and their teachers across Australia. We provided unique educational events for over 400 students in Melbourne, Brisbane and Perth through partnerships with the Gene Technology Access Centre (GTAC), The University of Queensland and the Harry Perkins Institute of Medical Research. A highlight was the Melbourne Stem Cells: Transforming Science, Medicine and Society event where Year 8 students got the chance to don lab coats and conduct experiments alongside real stem cell scientists in the GTAC laboratories.

Throughout 2014, SCA also held workshops for patients and the general public including a series of workshops in Melbourne and regional Victoria with the Centre for Eye Research Australia where the latest research on eye disease using stem cells was discussed.

Stem Cells Australia also continued to raise concerns about the sale of unproven, and in many cases unfounded, treatments alleged to involve the patient's own stem cells. In particular we have called for immediate action to tighten the regulatory loophole that allows these practices to be offered in Australia. We strongly believe that evidence that the practices are safe and effective should be required before stem cell therapies are offered to the community.

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 2014, SCA entered into a Memorandum of Understanding with the Canadian Centre for Commercialisation of Regenerative Medicine to increase the translation of stem cell research in the two countries. Exploring the potential of stem cells and their regenerative capacity has been a core focus of medical research in Canada and Australia for many years. Recognising the need to accelerate the translation of such findings into real benefits, this agreement will enable an international cluster of scientific excellence to be built.

Above: Melbourne Stem Cells: Transforming Science, Medicine and Society.

Goals for 2015

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
- Establish 'Affiliate Investigators' 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.

ADVANCED WORKSHOP IN STEM CELLS AND NEUROSCIENCE RESEARCH

As a part of The University of Melbourne Advanced Research Workshops in Neuroscience, scientists from Stem Cells Australia's Pluripotency and Cell Reprogramming program and our Stem Cell Core facility ran a week long workshop for scientific colleagues wanting to know more about how to grow and use stem cells in their research.

The aim of this workshop was to familiarise participants with the application of human pluripotent stem cells to problems in neuroscience, including the study of brain development, functional genomics and disease modeling. Both embryonic stem cells and the more recently discovered induced pluripotent stem cells were featured in the workshop.

Over five days of lectures and practical classes, eight PhD students from the University of Melbourne, FINMH, Monash University and Ludwig Institute for Cancer Research had the opportunity to develop skills in pluripotent stem cell science directly related to their research project. Students also discussed the important regulatory, ethical and societal impact of pluripotent stem cell research during the workshop.

The workshop was very well received, particularly in relation to the opportunity to get into the laboratory environment, with one student commenting, "It's difficult to set up a prac class for stem cell culture – as the cells are difficult to grow up in bulk – as such the prac classes were excellent. We all had cells to play with so we got an excellent overview of the techniques required."

Please contact Dr Anna Michalska at our Melbourne StemCore Facility if you are interested in finding out more about training opportunities in stem cell science at The University of Melbourne.

Centre for Neural Engineering

Director: Professor Stan Skafidas

Deputy Director: Professor Steven Petrou

Research

A wide range of research activities occur under the auspices of the Centre for Neural Engineering: quantum diamond magnetometers; point of care diagnostic devices; genetic markers for autism; retinal implants; 3-dimensional cell culture techniques; dielectric spectroscopy; quinidine treatment for epilepsy; improved signal processing for cochlear implants; biological sensors; neural network connectivity; the role of mGLuR5 in autism spectrum disorder; and many more. Activities are grouped in two disorder flagships – Epilepsy and Autism Spectrum Disorder – and two technology flagships – Sensing and Neural Modelling. This work is undertaken both within the CfNE itself and as collaborative projects with colleagues locally and internationally.

Two particular highlights for 2014 relate to the Epilepsy and Neural Modelling flagships. With colleagues at the FINMH and internationally, Steven Petrou has been working on demonstrating the efficacy of quinidine as a potential treatment for certain epilepsy types associated with KCNT-1 gain-of-function mutations. The team have shown that by identifying individual mutations through exome sequencing of epileptic encaphalopathies it is possible to determine the electrophysiological and pharmacological characteristics of these mutations and from there to develop targeted therapies for individuals. After demonstrating in mouse models that quinidine can reduce the frequency of seizures associated with KCNT-1 mutation epilepsy of infancy with migrating focal seizures (EIMFS) it has now been shown to also hold true in a three year old child, affected with the disorder. This work has suggested a translational paradigm where in vitro studies inform novel, individually targeted therapies for sufferers of neuropsychiatric diseases.

Bringing together molecular biologists, stem cell scientists, materials scientists and electrical engineers, the three dimensional cell-culture project

being driven by Giovanna D'Abaco also embodies the multi-disciplinary and paradigm-shifting approach that CfNE is enabling. The development of three-dimensional cell culture models is a rapidly emerging field with the potential to dramatically change the ways in which cellular and tissue processes are studied, disorders and diseases are modelled, and potential treatments tested. In 2014 the team were able to demonstrate, for what is believed to be the first time, that 3D cell culture techniques have the potential to provide effective models of networks of human neuronal cells and processes. The team has successfully maintained and supported the growth of SH-SY5Y neuroblastoma cell lines and neurons derived from human embryonic stem cells in a 3D culture environment. A number of candidates are being assessed for use as scaffolds in three-dimensional cell cultures and it is being actively interrogated as to whether there are links between particular scaffold types and optimal models for particular cell and tissue types. The team have also shown that off-the-shelf graphene foam is a viable scaffolding material, providing a high surface to volume ratio, porosity and conductivity to allow for improved accuracy in modelling of the in vivo cellular environment.

Above: Dr Chathurika Abeyrathne and the CfNE team.

Some other projects worked on during the year by CfNE researchers include:

- Identification of Additional Novel and Specific Cell Surface Markers of Human Neural Crest Progenitors that can be used to Isolate these Cells by Fluorescence Activated Cell Sorting (FACS)
- Rapid Point-of-Care Detection of Genomic Variations for Personalised Medicine
- Computational Neural Modelling of Bottom-up Informational and Top-Down Attention in Auditory Perception
- Advanced Epileptic Seizure Warning Methods
- Personalised Prognostic Tools for Early Psychosis Management (PRONIA)
- A Virtual Reality Environment for Real-Time Analysis of Brain Function in Rodents
- Blackout Advisory System – Development of an Implantable Sub-scalp Seizure Monitor

In 2014 some 75% of CfNE's research output appeared in peer-reviewed journals across a variety of disciplines. Researchers affiliated with CfNE produced 77 research publications during the year, with a number accepted for publication early in 2015.

Outreach & Education

The CfNE provided research higher degree training for almost forty students during 2014. With its cross-disciplinary focus, the CfNE is developing the new generation of convergence researchers, providing valuable exposure to activities and personnel outside their home discipline. Almost half of CfNE's students have formal supervisors from two or more faculties. In addition, CfNE hosted a number of undergraduate students through programs such as UROP and Faculty schemes.

Throughout 2014 the CfNE continued its involvement with the Convergence Science Network and its events, promoting an understanding of the convergence of life, physical and engineering sciences to improve our lives.

Partnerships

The CfNE's key collaborators include the FINMH, the Bionics Institute, Murdoch Children's Research Institute, the Institute for Integrated Cell-Material Sciences at Kyoto University (iCeMS), Duke University, CSIRO, MIT, RIKEN Brain Science Institute, Edinburgh University, National Vision Research Institute, Monash University, the Eccles Institute of Neuroscience and the University of Adelaide.

During 2014 CfNE researchers Stan Skafidas and Steven Petrou became part of the ARC Centre of Excellence for Integrative Brain Function, led by Monash University, with partners at the University of Sydney, the University of Queensland, the Australian National University and the University of NSW.

Neurosciences and Behavioural Sciences Domain

Research in the Faculty of Medicine, Dentistry & Health Sciences is encompassed in eight broad Research Domains, incorporating discipline and disease focuses. The Research Domains aim to increase opportunities for researchers to conduct research on common themes.

The Neurosciences & Behavioural Sciences Research Domain is led by Professor Andrew Allen who is charged with developing, facilitating and supporting events and activities that provide opportunities for researchers to connect, collaborate and communicate with one another.

The research interests of researchers in the Neurosciences & Behavioural Sciences Research Domain are grouped into four broadly interrelated groups that provide participants with the opportunity to engage more closely with people who share similar interests. These four groups are Neurological Disorders; Behavioural Neurosciences/Psychology and Mental Health; Basic Neurosciences; and Advanced Technologies.

In 2014, the *Neurosciences & Behavioural Sciences* Research Domain supported the following activities:

Melbourne Social Neuroscience Symposium

Wednesday 5 March – Thursday 6 March 2014

A team of enthusiastic researchers came together to launch the University's Inaugural Social Neuroscience Symposium, supported by the Melbourne School of Psychological Sciences, the Department of Psychiatry and the Neurosciences & Behavioural Sciences Research Domain. The event was held at the Melbourne Brain Centre.

Social neuroscience is a field of research that aims to understand how the brain mediates social cognition, social interactions and relationships, and group social dynamics. It also covers related topics that deal with social/ personality psychology and neurobiology.

The two day event included keynote talks from leaders in the field of social neuroscience, including Professor Martin Reuter (University of Bonn, Germany), Professor Eddie Harmon-Jones (University of New South Wales) and Associate Professor Tom Denson (University of New South Wales).

Over 200 attendees listened to presentations by local researchers. There was also a series of Q&A panels led by students and early career researchers.

Genome Engineering of Cells and Organisms: CRISPR and TALENs Workshop

Wednesday 21 May 2014

More than 230 researchers from across the University of Melbourne packed into the auditorium of the Melbourne Brain Centre to attend this workshop.

Co-presented by the Biomedical Sciences Academic Centre (BSAC) and the Neurosciences & Behavioural Sciences Research Domain, attendees heard from five speakers with demonstrated success in CRISPR and TALENs. They presented their recent findings using these new genome editing approaches, considered one of science's top ten breakthroughs of 2013.

The speakers included Professor Paul Gleeson, chair of the Biomedical Sciences Academic Centre Research Committee and Head, Department of Biochemistry & Molecular Biology at the University of Melbourne, Professor Paul Thomas, School of Molecular & Biomedical Science at the University of Adelaide, Associate Professor Ernst Wolvetang, Australian Institute for Bioengineering and Nanotechnology at the University of Queensland, Professor Mike Ryan, La Trobe Institute for Molecular Science at La Trobe University, Dr Mirana Ramialison, Australian Regenerative Medicine Institute at Monash University and Dr Marco Herold, The Walter and Eliza Hall Institute of Medical Research.

Students of Brain Research Professional Development Dinner

Tuesday 1 July 2014

For the third year running, the Neurosciences & Behavioural Sciences Research Domain provided sponsorship support to the Students of Brain Research (SOBR) Professional Development Dinner.

SOBR is a social and academic network designed to facilitate knowledge transfer to students and between students with an interest in brain research in Melbourne.

More than 120 graduate medical research students from across the University's centres, departments and affiliated institutes attended the sold out dinner which this year focused on 'Science and Politics'. The event also attracted a number of VIPs including scientists, media and government representatives.

Over the course of the evening, attendees heard from three high profile guest speakers as they discussed the future of science in Australia and the interplay between science, communication and policy. The speakers included Dr Adam Bandt MP, Deputy Leader of Australian Greens Party, Penny Wright, Senator for South Australia with the Australian Greens Party and Dr Andi Horvath, Senior Curator and Science Communicator at Museum of Victoria and Science Communications Media Officer at the University of Melbourne.

SOBR Symposium

Thursday 30 October 2014

The *Neurosciences & Behavioural Sciences* Research Domain was pleased to once again support the Students of Brain Research's annual symposium at the Melbourne Brain Centre.

Research Highlights

New genetic discovery shed light on causes of developmental delay and autism

An international study published in *Nature Genetics*, researchers have used a new gene discovery approach to identify genes causing developmental delay and autism.

Co-author of the study, Professor Ingrid Scheffer, based at the University of Melbourne, FINMH and Austin Hospital said that the study used a large data set of almost 30,000 affected children and as such provided a novel integrative

approach to gene discovery to produce a more effective way to find genes. The findings would contribute significantly to developing new targeted therapies for autism spectrum disorders, intellectual disability and developmental delay.

The research was led by the Eichler group in Seattle who collaborated with Victorian researchers at the University of Melbourne, Barwon Health and FINMH. Other collaborators included the Murdoch Children's Research Institute and The Royal Children's Hospital.

New insights into degenerative disease

Researchers from the University of Melbourne have established how two diseases that present in similar ways are in fact quite different.

Progressive Supranuclear palsy (PSP) and Parkinson's Disease (PD) have overlapping symptoms but can remain difficult to distinguish clinically.

A first-ever paper on the topic published in the *Journal of Neuropsychology* from the British Psychological Society now suggests that people with early stage PSP experience more severe and extensive cognitive impairments including difficulties in planning, abstract thinking, memory retrieval than those with PD.

Lead researcher Dr Young-Eun Claire Lee said the two conditions are so similar to standard neurological examination that in some cases, patients with PSP often go undiagnosed for the main part of their illness.

"Parkinson's disease and PSP are the two of the most common forms of neurodegenerative disease, resulting in loss of balance and deterioration in mobility. Telling these conditions apart can be challenging because most patients with PSP do not develop distinctive symptoms distinguishing them from patients with PD such as paralysis or weakness of the eye muscles and episodes of frequent falling until later stages."

The results indicate that undertaking detailed cognitive profiles could aid in the distinction between these important conditions which will have important prognostic and therapeutic implications.

New genetic cause for rare form of epilepsy identified

An international research team that includes the University of Melbourne's Professor Sam Berkovic (AC/FRS) has identified a new gene for a progressive form of epilepsy. The findings of this international collaboration have been published in *Nature Genetics*.

Progressive myoclonus epilepsies (PME) are rare, inherited, and usually childhood-onset neurodegenerative diseases whose core symptoms are epileptic seizures and debilitating involuntary muscle movements (myoclonus).

Professor Berkovic said that progressive myoclonus epilepsy is one of the most devastating forms of epilepsy.

"In this study, we used modern DNA sequencing technologies, which have revolutionised genetic research focused on rare, severe diseases of this nature. The study revealed a single mutation in a gene that explains the underlying cause of a significant proportion of unsolved PME cases. The new mutation identified in the study disrupts the function of a pathway that has a central role in signal transmission in the brain."

The likely consequence of the mutation is that signals in certain parts of a patient's brain are compromised, which makes patients susceptible to both epileptic seizures and involuntary muscle movements starting in childhood.

The mutation also causes degeneration of the cerebellum and subtle cognitive decline in some of the patients.

Last drinks: brain's mechanism knows when to stop

A recent study published in the *Proceedings of the National Academy of Sciences* has provided insight into the human instincts that determine survival behaviour and are also of medical importance. The study used magnetic resonance imaging to scan the brain during two physiological states, firstly during the experience of thirst and secondly following satiation and 'overdrinking'. Commenting on the work, Professor Derek Denton from the Faculty of Medicine, Dentistry and Health Sciences at the University of Melbourne indicated "Different areas of the brain involved in emotional decision-making were activated when people drank water after becoming thirsty and when study participants followed instructions to keep drinking when no longer thirsty. The brain regions determining the signals to stop drinking have not previously been recognised in this context. It identifies an important component in regulation and this 'stop mechanism' may prevent complications from excessive water intake."

Over drinking can reduce the salt concentration of the blood that can result in cerebral swelling, a potentially fatal condition. Also known as polydypsia, it has been found in some patients with schizophrenia and in some marathon runners.

Professor Denton believes the findings could be applied to other aspects of human gratification.

"This is a study of elements of gratification and how the body programs accurate behaviour. In revealing aspects of gratification control, the data are relevant to study the gratification of other instincts, such as food intake, salt intake and sexual behaviour."

The study was undertaken in collaboration with the Baker IDI Heart and Diabetes Institute and Monash Biomedical Imaging.

Australian researchers closing in on therapy for Motor Neurone disease

A well-known copper containing compound may help treat motor neuron disease (MND). In Australia, MND, also known as amyotrophic lateral sclerosis (ALS) or Lou Gehrig's disease, kills roughly two people every day.

Using animal models, an international team including researchers from the University of Melbourne and the FINMH, have shown that swallowing a cheap copper containing compound can improve movement and significantly extend life. To date, no therapy for human ALS has ever been discovered that could extend lifespan more than a few additional months.

Dr Peter Crouch, from the Department of Pathology at the University of Melbourne, said the new approach has great potential.

"We believe that with further improvements, and following necessary human clinical trials for safety and efficacy, this could provide a valuable new therapy for ALS and, in addition, possibly Parkinson's disease. The compound has previously been studied for use in some cancer treatments, and is inexpensive to produce."

Amyotrophic Lateral Sclerosis was first identified as a progressive and fatal neurodegenerative disease in the late 1800s and gained international recognition in 1939 when it was diagnosed in American baseball legend Lou Gehrig.

It's known to be caused by the degeneration of motor neurons in the spinal cord, and in a subset of cases its aetiology has been traced to mutations in the copper, zinc superoxide dismutase, or SOD1. When SOD1 is mutated and the binding of its metal co-factors altered, it "unfolds" and becomes toxic, leading to the death of motor neurons.

Dr Crouch says ALS occurs in a sensitive and relatively inaccessible part of the human body, making it difficult to identify and implement treatments that alter the pathogenesis of the condition.

"The damage from ALS is happening primarily in the spinal cord and that's also one of the most difficult places in the body to absorb copper. Copper itself can be toxic, so its levels are tightly controlled in the body. The therapy we're working toward delivers copper selectively and safely into the cells in the spinal cord that actually need it."

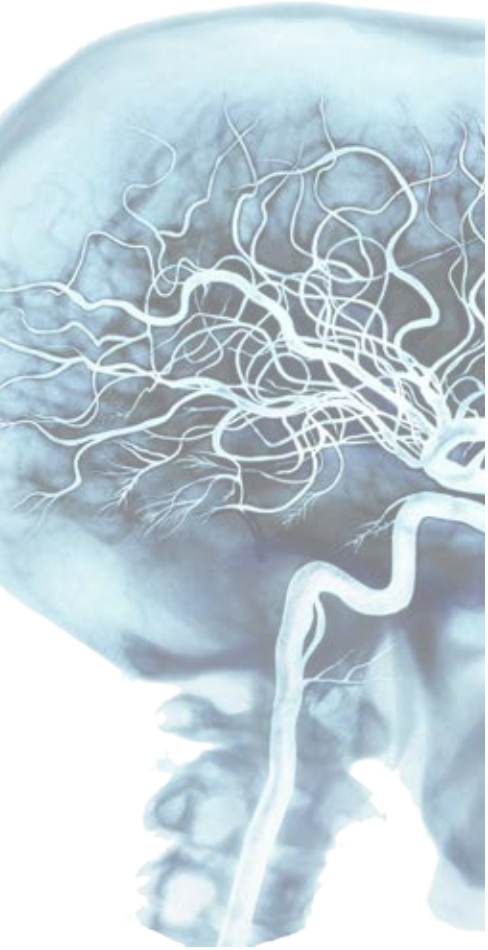
By restoring a proper balance of copper into the brain and spinal cord, scientists believe they are stabilising the superoxide dismutase in its mature form.

"In this case, the result was just the opposite of what one might have expected," said Blaine Roberts, lead author on the study and a research fellow at FINMH.

"The treatment increased the amount of mutant SOD, and by accepted procedures, this means the animals should get worse. But in this case, they got a lot better. This is because we are providing targeted delivery of copper just to the cells that need it. This study opens up a previously neglected avenue for new disease therapies, for ALS and other neurodegenerative disease."

The research has been published in the *Journal of Neuroscience*.

Potential for Traumatic Brain Injury Sufferers



Eight Melbourne-based scientists have discovered that copper induces the relocalisation via nerve axons of a key protein in the brain, Amyloid Precursor Protein (APP). This is of potential significance to traumatic brain injury given the neuroprotective role of this protein in such injury.

The team, made up of researchers from the partners of the Melbourne Brain Centre led by Professor James Camakaris and Dr Karla Acevedo, published their findings in the prestigious *Journal of Biological Chemistry*.

"Understanding the role copper plays in regulating APP function in normal neuronal cells will also provide insight into the interplay between copper and APP in normal and pathological conditions such as Alzheimer's disease. The brain must maintain a healthy "copper balance" given the deleterious effects of either too little or too much copper.

Brain development provides insights into adolescent depression

A new study led by the University of Melbourne and Orygen Youth Health Research Centre is the first to discover that the brain develops differently in adolescents who experience depression. These brain changes also represent possible risk factors for developing depression during teenage years.

Lead research Professor Nick Allen from the Melbourne School of Psychological Sciences said, "It is well known that the brain continues to change and remodel itself during adolescence as part of healthy development. In this study, we found that the pattern of development (such as changes in brain structure between ages twelve to sixteen) in several key brain regions differed between depressed and non-depressed adolescents."

The brain regions involved include areas associated with the experience and regulation of emotion, as well as areas associated with learning and memory.

"The findings are an important breakthrough for exploring possible causes of depression in adolescence. They also suggest that both prevention and treatment for depression (even for early signs and symptoms of depression)

in adolescence is essential, especially targeting those in the early years of adolescence aged twelve to sixteen."

"We also observed some differences between males and females. For males, less growth in an area of the brain involved in processing threat and other unexpected events that is a critical part of the brain's fear circuitry, was associated with depression. On the other hand, for females, greater growth of this area was found to be associated with depression."

"This is important information because depression becomes much more common amongst girls during adolescence, and these findings tell us about some of the neurobiological factors that might play a role in this gender difference."

Professor Allen says adolescence is a period during the lifespan where risk for developing depression dramatically increases.

The study examined eighty-six adolescents (41 female) with no history of depressive disorders before age 12 by using a Magnetic Resonance Imaging (MRI) scanner, which allowed researchers to measure the volume of particular brain regions of interest. Participants underwent an MRI scan first at age twelve and again at age sixteen, when rates of depression were beginning to increase. Researchers also conducted detailed interviews with each of the participants at four different time points between age twelve and age eighteen. Thirty participants experienced a first episode of a depressive disorder during the follow-up period.

These findings have recently been published in the *American Journal of Psychiatry*. The longitudinal study was conducted in collaboration with the Melbourne School of Psychological Sciences and the Melbourne Neuropsychiatry Centre, all at the University of Melbourne.

The Brain Research Institute and Royal Children's Hospital also provided support in acquiring the neuroimaging data.

3 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 so as 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.

Below: Professor Sam Gosling spoke on 'The Structure and Personality Correlates of Music Preferences'.

Below: Professor David Forbes led the seminar on 'Not All Wounds Are Visible – Researching and Treating Post-Traumatic Stress Disorder'.

Our 2014 seminars were as follows:

'The Structure and Personality Correlates of Music Preferences'

The MNI proudly co-hosted this event alongside Music, Mind and Wellbeing. The seminar was presented by Professor Sam Gosling from University of Texas, Austin.

At this very moment, in homes, offices, cars, restaurants, and clubs around the world, people are listening to music. Despite its prevalence in everyday life, the sound of music has remained very much mute within social and personality psychology and its impact is only now starting to be explored in a dedicated way.

'Not All Wounds Are Visible – Researching and Treating Post-Traumatic Stress Disorder'

This seminar featured presentations by Professor David Forbes, Director, Australian Centre for Posttraumatic Mental Health, Ms Jane Nursey, Neuropsychologist, Australian Centre for Posttraumatic Mental Health (ACPMH), Dr Andrea Phelps, Deputy Director, ACPMH and Professor Mal Hopwood, Director of Professorial Psychiatry Unit Albert Road Clinic.

The impact of trauma on a person can have significant effects on their mental health. Three out of every four Australians will be exposed to a traumatic event in their lifetime, in the form of serious accidents or injuries, war, natural disasters or sexual and physical assault.

Traumatic events are common and most people will recover on their own, however some will develop long-lasting problems and need help to come to terms with what they have encountered.

'Stem cells: the potential, the reality and the dangers'

This seminar was presented by Professor Irv Weissman, Stanford University in California and Dr Ann Tsukamoto, Stem Cells Inc.

When will stem cell medicine deliver on its promise for challenges like cancer, neurological diseases and tissue regeneration?

What's holding us back after the years of hype?

Why is it a bad idea to pursue unproven stem cell treatments?

'PhD Up and Comers'

This exciting public lecture featured four research higher degree students who each presented a compelling oration on their thesis research.

Presentations:

Neural processes underlying information sampling in uncertain environments
Daniel Bennett

Stem Cell tourism to China
Jane Brophy

Stimulation control of the bionic eye
Matias Maturana

The Sound of 'Silence': Exploring the psychological and neurobiological mechanisms underlying the experience of tinnitus
Krysta Callander

'Unravelling the Mysteries of Human Consciousness'

Baroness Professor Susan Greenfield returned to the MNI in 2014 to take part in a panel discussion on consciousness. Joining Professor Greenfield on the panel were Dr Laura Schroeter (School of Historical and Philosophical Studies), Dr Scott Kolbe (Department of Anatomy and Neuroscience) and Dr Olivia Carter (Melbourne School of Psychological Sciences).

What is it to be aware? What makes us conscious? The complexities of consciousness have intrigued philosophers and scientists for thousands of years. But can modern neuroscience ever hope to understand this phenomenon?

Below: Dr Ann Tsukamoto and Professor Irv Weissman (not pictured) spoke at 'Stem cells: the potential, the reality and the dangers'.

Below: Krysta Callander speaking at 'PhD Up and Comers'.

Below: Baroness Professor Susan Greenfield spoke at 'Unravelling the Mysteries of Human Consciousness'.

Above: Dr Shane Huntington and Dr Emma Burrows at the 'The No-Bell Prize'.

Neuroscientist and synaptic pharmacologist Professor Baroness Susan Greenfield discussed how neuroscience sheds light on our understanding of consciousness. A panel of philosophers, ethicists and neuroscientists were then invited to discuss this challenging topic.

'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.

The event was expertly hosted by Dr Shane Huntington, Principal Strategy Adviser to the Dean of the Faculty of Medicine, Dentistry and Health Sciences and Host of the 3RRR Science radio program. Our three judges were Associate Professor Megan Munsie, Policy and Outreach Manager and Head of Education, Ethics, Law & Community Awareness Unit Head, Stem Cells Australia, Dr Lauren Ayton, Vision Researcher and Science Communicator, Centre for Eye Research Australia and Bionic Vision Australia, and Eric van Bemmel, Senior producer and co-creator of Up Close.

Our spirited and adept researchers included Dr Emma Burrows, Research Officer, Behavioural Neuroscience, Associate Professor Helmut Butzkueven, Deputy Director of the Melbourne Brain Centre at the Royal Melbourne Hospital, Dr Simon Murray, Laboratory Head, Department of Anatomy and Neuroscience, Dr Michele Veldsman, Postdoctoral Research Fellow, Stroke and Professor Stan Skafidas, Director, Centre for Neural Engineering.

Congratulations to Dr Emma Burrows who narrowly took away the gong for the No-Bell Prize!

Melbourne Knowledge Week

On the 27 October, 20 members of the public were invited to go behind the scenes at the Melbourne Brain Centre as part of the 2014 Melbourne Knowledge Week Tours of the Parkville Biomedical Precinct.

Attendees were given the opportunity to visit the laboratories and meet scientists who work on diagnosing and treating brain disorders such as stroke, multiple sclerosis, mental illness and dementia. The tour group visited a research laboratory, the Melbourne Brain Centre Imaging Unit and the Histology unit.

Melbourne Knowledge Week (MKW) is an initiative of the City of Melbourne and forms an integral part of the Knowledge Melbourne program of activities. Melbourne Knowledge Week supports and celebrates the innovation, creativity, idea-sharing and thought-leadership that contributes to Melbourne being one of the leading knowledge cities in the world.

The fifth annual MKW was held from Monday 27 October to Sunday 2 November 2014. The program featured over 60 events showcasing Melbourne's diverse and innovative knowledge sectors.

Melbourne Brain Symposium

The University of Melbourne's MNI and the FINMH share a proud history of hosting the annual Melbourne Brain Symposium.

This symposium program is a testament to the remarkable breadth of neuroscience focused research occurring both in Melbourne and internationally. Our speakers for the 2014 program were Professor Perry Bartlett, Professor Chris Pantelis, Professor Robyn Guymer, Professor Seth Grant, Professor Heather Young and Professor Lawrence Wald. Their excellent contributions made for an outstanding event.

Above: Melbourne Brain Symposium speakers; Professor Trevor Kilpatrick and Associate Professor Andrew Metha at the Melbourne Brain Symposium.

Presentations:

Adding new neurons to the adult hippocampus: How is it regulated and what is its function?

Professor Perry Bartlett, Director, Queensland Brain Institute, University of Queensland.

Understanding Brain Changes in Schizophrenia: Impact of Stress, Drugs and Inflammation on the Adolescent Brain

Professor Chris Pantelis, Foundation Professor of Neuropsychiatry and Scientific Director of the Melbourne Neuropsychiatry Centre, University of Melbourne.

Age-related macular degeneration – the accumulation of too much debris

Professor Robyn Guymer, Deputy Director, Centre for Eye Research Australia, Deputy Head of Department of Ophthalmology, University of Melbourne, Synapse Proteome Complexity; Professor Seth Grant, Centre for Clinical Brain Sciences and Centre for Neuroregeneration, Edinburgh University.

Generating a nervous system in the gut during development and disease

Professor Heather Young, Department of Anatomy and Neuroscience, University of Melbourne.

New directions for brain MRI hardware and acquisition

Professor Lawrence Wald, Associate Professor in Radiology, Harvard Medical School, Associate Biophysicist, Massachusetts General Hospital, Director, MGH NMR Core, Martinos Center.

Frontotemporal Dementia: Towards better diagnosis and management

Professor John Hodges, Professor of Cognitive Neurology, NeuRA and UNSW.

Students of Brain Research Symposium

Students of Brain Research (SOBR) provides a social and academic network designed to facilitate knowledge transfer both directed to students and between students across Melbourne who share an interest in brain research. SOBR hosted the annual SOBR Student Symposium on Thursday 30 October at the Melbourne Brain Centre.

This free symposium provides students with the invaluable opportunity to present their research (either via poster or oral presentation), to hear from prestigious guest speakers and to network with other young brain researchers from across Melbourne. Many excellent prizes were awarded to a series of outstanding young researchers. The MNI is proud to be a foundation sponsor and to continue to sponsor this event on an annual basis.

The speakers for 2014 were Professor Doug Hilton (Director, WEHI), and Professor Christine Kilpatrick (CEO, Royal Children's Hospital).

Prize winners were:

Oral Presentation

1st: Dean Wright, 2nd: Yea Seul Shin, 3rd: Nirma Perera

Poster Presentations

Behavioural Neuroscience & Neurophysiology:

1st: Nicola Chen, 2nd: Isabel Zbukvic, and 3rd: Durgesh Tiwari

Cellular & Molecular Neuroscience

1st: Estella Newcombe, 2nd: Metta Jana and 3rd: Amber Ou

Computational, Neuroengineering & Neuroimaging

1st (thanks to Victorian Life Sciences Computation Initiative): Shawna Farquharson, and 2nd: Phillip Ward

Psychology & Psychiatry

1st: Simone Hearps, and 2nd: Eleni Ganella

High profile visits

UK Minister of State for Science and Universities

The MNI hosted a visit by Rt Hon David Willetts, UK Minister of State for Science and Universities on Friday 28 February 2014. The focus of the visit was science innovation. The delegation included:

- Liam Izod, Private Secretary to Mr. Willetts
- Professor Nigel Thrift, Vice Chancellor, University of Warwick
- Libby Hackett, Chief Executive, University Alliance
- Callista Thillou, Assistant Director, HE International Unit, Universities UK
- Matthew Hilton, Director of Higher Education, Department of Business, Innovation and Skills
- Nick Hillman, Director, Higher Education Policy Institute
- HE Paul Madden, British High Commissioner to Australia
- Dr Svetozar Kovacevic, UK Science and Innovation Network, Australia

Above: Rt Hon David Willetts.

In a public lecture that evening, Rt Hon David Willetts presented his vision of 'The Critical List' – The vital research streams governments need to invest in now. The Minister spoke alongside the Chief Scientist of Australia, Professor Ian Chubb and leading academics from the University of Melbourne. The Director of RiAus, Dr Paul Willis, facilitated the lively discussion on research priorities and the role of government in the research agenda in the UK and Australia.

US Ambassador to Australia

On Wednesday 9 April, MNI welcomed the United States of America Ambassador to Australia Mr John Berry and his delegation to the University of Melbourne and specifically to the Melbourne Brain Centre

Professor Kilpatrick indicated, "We are honoured to welcome the ambassador to the University of Melbourne and are keen to explore further engagement with the United States, particularly on Brain Research via the Advancing Innovative Neurotechnologies (BRAIN) Initiative that is part of the US's focus aimed at revolutionising our understanding of the human brain. As an internationally focussed University we look forward to further strengthening our links with American organisations and Universities."

Above: Mr John Berry, Professor Trevor Kilpatrick and Professor Martin Pera.

The Chair of Imaging Science, Professor

Roger Ordidge hosted a tour of the Melbourne Brain Centre Imaging Unit by Ambassador Berry and the delegation saw first hand the advanced imaging technologies available to researchers.

Internationally renowned stem cell scientist, Professor Martin Pera, Chair of Stem Cell Science guided the delegation through the world class facilities of the Stem Cells Australia laboratories within the Kenneth Myer Building.

The delegation also met with Dr Andrew Milner, CEO of Neurosciences Victoria to learn more about the continued development of the neuroscience cluster in Melbourne which encourages international collaborations and partnerships leading to strategic investment in the sector, including collaborative interaction with the commercial sector to enhance both research and development and its applications for community benefit.

Neuroscience Downunder 2014

In 2014, the Melbourne Chapter of the Society for Neuroscience organised a successful function at the Australian Embassy in Washington DC during the Annual Meeting of the Society for Neuroscience. The function was attended by almost 300 neuroscientists and guests and was a marvellous display of neuroscience research from the University of Melbourne and Australian SfN members.

This event was hosted by the Ambassador the Hon Kim Beazley and was jointly sponsored by the Department of Industry and Science, the Australasian Neuroscience Society, the MNI, University of Melbourne and FINMH.

Below: From left – Mr Michael Schwager (Minister Counsellor (Education, Science, Technology), Australian Embassy), the Hon Kim Beazley (Australian Ambassador to the United States), Associate Professor Peter Crack (SfN Melbourne Chapter President), Professor James Vickers (President of Australasian Neuroscience Society); Open to Business Forum.

Australian Neuroscience research was profiled by presentations from Professor James Vickers, President of the Australasian Neuroscience Society and Professor Moses Chao, a Past President of the Society for Neuroscience. A slide loop highlighting Australian neuroscience research institutions was presented.

Open to Business Forum

On Tuesday 23 September, the MNI hosted an industry partnerships forum that saw around 80 guests participate in a half day forum.

The forum explored opportunities for collaboration between the University's neuroscience research community and industry partners in order to further foster innovative research partnerships and, ultimately, commercialisation.

The program featured presentations on how to build successful partnerships and reflections on recent successes. A number of industry representatives discussed their perspectives concerning the

benefits of collaboration. Industry speakers included representatives from Pfizer, Medtronic, Fibrotech, Siemens, Cyclotek and IBM.

The forum also featured presentations by our academic leaders on research with the potential for industry engagement. Topics highlighted the breadth of neuroscience-related research at the University of Melbourne, and included 'New translational opportunities in Epilepsy' by Professor Sam Berkovic, 'Stem cell discovery platforms for human neurogenetics and disease modelling' by Professor Martin Pera and 'Micro-nano electronic devices for neural applications' by Professor Stan Skafidas.

Helmholtz Association

On Tuesday 21 October, the MNI participated in a visit by the Helmholtz Association. With almost 35,000 collaborators in 18 Research Centres, the Helmholtz Association is Germany's largest scientific organisation. It is dedicated to pursuing long-term research goals of state and society, and carries out top-level research to identify and explore the major challenges facing society, science and economy.

The MNI provided the delegation with a tour of the Melbourne Brain Centre and facilitated meetings with some of MNI's key research leaders to explore the common scientific interests from both groups and to draw up options for intensified future collaborative interactions.

UK Prime Ministers World Dementia Envoy

The World Dementia Envoy, Dr Dennis Gillings CBE visited the MNI, FINMH and Alzheimer's Australia to discuss how our nation can optimise its role in the global fight against dementia. During his visit, Dr Gillings presented a public lecture entitled 'Towards an Action Plan for a Cure for Dementia.'

Dr Gillings was appointed as World Dementia Envoy by the Prime Minister of the United Kingdom David Cameron, on behalf of the G8 group of nations in 2014.

The role of the Envoy is to reduce barriers to investment in research, to speed up drug development and to bring together ideas from around the world in order to improve the lives of people living with dementia. The ultimate goal is to find a cure or an effective disease modifying therapy by 2025.

Speaking at a Global Dementia Legacy Event in June 2014, Dr Gillings said "Let us be an international team, collaborating, sharing knowledge, investing and innovating so that we win the prize of success together."

Below: Dr Dennis Gillings CBE, World Dementia Envoy.

Dr Gillings has a prestigious biopharmaceutical background and has worked with a diverse array of health organisations. In addition, he held the role of Professor of Biostatistics at the University of North Carolina and was awarded a CBE in 2004 for services to the pharmaceutical industry. Dr Gillings' mother lived with dementia for 18 years until her death in 2013.

During his time in Australia, Dr Gillings met with senior Commonwealth Government Ministers, relevant Departments and Agencies, representatives from Alzheimer's Australia and people living with a diagnosis of dementia, to discuss how Australia can best contribute to the international effort to find a cure.

The Australian Government's legacy contribution to dementia research includes a $200 million commitment to dementia research over the next five years, and the establishment of a National Dementia Research Institute. Discussions will focus on these initiatives and how they can be maximised to best complement work happening internationally.

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 PhD research project can be built and conducted more efficiently. The University of Melbourne and FINMH 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 opportunity 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.

Four senior neuroscientists were invited to develop a workshop that would each run for around 20 hours, with a mixture of theory and practical activities. The workshop pilot program consisted of:

WORKSHOP	COORDINATOR	OTHER PRESENTERS
Magnetic Resonance Imaging	Professor Roger Ordidge	Dr Brad Moffat
Human Pluripotent Stem Cells in Neuroscience Research	Professor Martin Pera	Dr Anna Michalska Associate Professor Megan Munsie
Fundamentals of Ion Channel Function in the Brain: Intracellular and Extracellular Recordings	Associate Professor Steve Petrou	Dr Chris Reid
Fundamentals and Future of Advanced Live Cell Imaging	Associate Professor Andrew Metha	Dr Paul McMillan Mr Ben Hibbs

Following a competitive application process, 35 students were offered places in the workshops. The feedback from students, workshop coordinators and supervisors of the students was encouraging. There is broad support for continuing and expanding the advanced workshop concept in the future and 6 workshops will be offered in 2015.

Quotes from students:

- 'It shows how it can be easy to work with stem cells and how FACS is a quick high-throughput system for screening'
- 'I enjoyed the practical exercise with the 7T and the opportunity to plot the data to increase my understanding of how to calculate T1 and T2 values'

Feedback from students' supervisors:

- 'I would definitely suggest to any students in my group working or considering working with stem cells to apply for the course. It seems very complementary to many neuroscience related research projects- especially as stem cells become more accessible to the broader research community.'
- 'I think the Advanced Research Workshop was an excellent experience for my student. She learned a great deal about the theory of MRI and she will be able to read the MRI papers with a much more critical and understanding eye. The practical experiment using the new magnet was a great idea and she really learned a lot from that.'

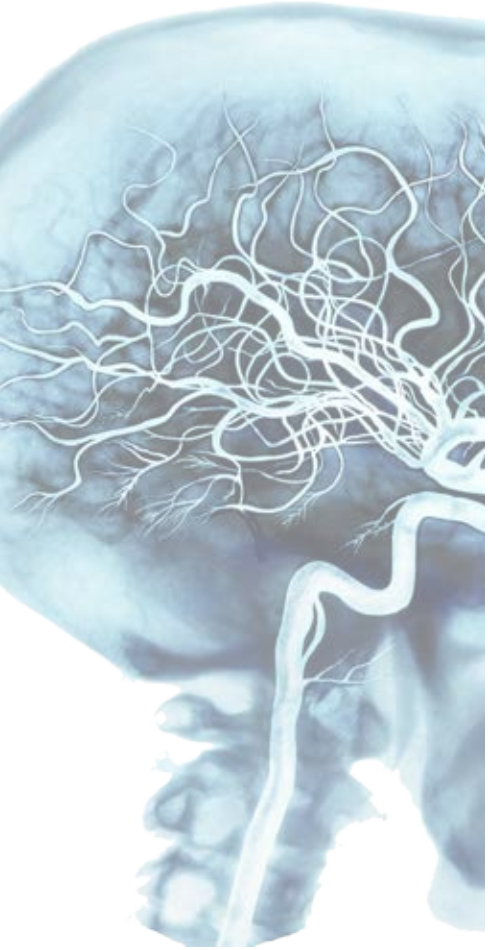
Secondary Schools Work Experience

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
- Demonstrate the wide variety of interesting careers available within neuroscience-related research.

The MNI work experience program received excellent feedback in 2014, with one student commenting 'Work experience at the MNI was extremely rewarding, and I would definitely recommend it to other students in the future. During my placement, I not only learned countless new things, for example the fascinating history of and controversy surrounding stem cell research, but also got to witness the daily routine of a scientist, and had the opportunity to discuss with a wide variety of people their jobs, the reason why they chose to do what they do and how they got there. The placement was also extremely fun, as we had the opportunity to do hands on tasks and mini experiments on several occasions.'



Elizabeth Blackburn School

In 2014, the Elizabeth Blackburn School of Sciences (EBSS) was launched as a branch of the University High School. The school provides a specialist maths and science program for VCE students who intend to pursue study/research into maths and sciences at university.

As part of the program, all of the year 11 EBSS students undertake a new VCE subject entitled Extended Investigation. The students formulate their own research question and then conduct research for 9 months. The culmination of the work is a 4000 word written report and an oral presentation to an external panel. This year several researchers from the University of Melbourne participated as Research Mentors. Over twenty-five neuroscience-related researchers took part in 2014 and mentors found the experience to be very rewarding for both themselves and the EBSS students.

Australian Brain Bee Challenge

On 4th June, 250 year 10 students and accompanying teachers from 39 secondary schools across Victoria, as far away as Ouyen, participated in the Australian-New Zealand Brain Bee Challenge State Final. It was hosted and sponsored by the MNI, University of Melbourne and FINMH. Other major sponsors included Monash University and Deakin University.

The event was officially opened by the Parliamentary Secretary of Education Mr Clement Newton-Brown representing the Minister Hon Martin Dixon, and by Professor Geoffrey Donnan, Director of FINMH. During the day, the students participated in a quiz about the brain given by the quizmaster Dr Thomas Keeble from FINMH. They also listened to globe-trotting and cross-disciplinary experiences selected from a lifetime of science by Professor Sandra Rees. Students agreed that the highlight of the day was the tour which included the Anatomy Museum, the DAX gallery and neuroscience laboratories.

The individual champion of the event was Rajan Venkatraman from John Monash Science School, and the winning team was from Melbourne Grammar School. The prizes included a giant 14-pieces model of the brain, trophies, and Elsevier books presented by Professor Trevor Kilpatrick, Director of the MNI and Dr Christopher Reid, Victorian representative of Australian Neuroscience Society.

Media Training

The MNI coordinated a half day professional media training course specifically for neuroscience-oriented researchers. The MNI worked with various Departments and Schools of the University to sponsor ten professional development places. The sponsors included the Melbourne School of Engineering, the Faculty of Medicine, Dentistry and Health Sciences, FINMH, the Music, Mind and Wellbeing initiative, the Centre for Neural Engineering and the Melbourne Brain Centre Imaging Unit.

This training assisted academic staff prepare for interviews about their research, learning and teaching activities. Professional media trainer Doug Weller provided a general introduction to the media, with advice on interview techniques and direct experience of being interviewed in front of a camera. Participants were also introduced to the university's on-campus TV studio.

Mindfields

Mindfields is an innovative program integrating art, mental health and neuroscience aimed at secondary school students.

The session includes:

- A Presentation by a neuroscientist (Year 12)
- A presentation by a mental health advocate
- A tour of the current exhibition at the Dax Centre
- This popular extended program for students of psychology caters for both regional and metropolitan schools.

4 PARTNERSHIPS

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

We continue to have a strong working relationship with our partner organisation, 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
- our public seminar program
- 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.

Traumatic Brain Injury

Together with Neurosciences Victoria and Monash University we are taking a lead role in the development of a Centre for Brain Injury. This Centre will aim to promote better outcomes for those suffering from traumatic brain injury (TBI)

across a range of circumstances whether on our roads, on sporting fields or for those involved in defence related activities. The Centre plans to focus on a number of key areas in particular concussion, the development of paraclinical, including imaging-based markers, as predictors of outcome and strategies to minimize the long-term societal impact of severe TBI. Potential partners in the initiative include the TAC, the Australian Football League and Siemens.

Siemens

A Master Research Agreement was signed with Siemens Medical Systems to cover the performance of joint research and MRI applications. As part of the agreement, Dr Sonal Josan will be a Siemens Applications Scientist based at the Melbourne Brain Centre for four years. The Melbourne Brain Centre Imaging Unit is also developing research projects with Siemens focusing on the interrogation of Traumatic Brain Injury.

Salpetriere

Our partnership with the University Pierre et Marie Curie continues to develop. Student exchange is being encouraged and we shared a submission for combined funding to the International Progressive MS Alliance.

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 to develop new interactions and strengthen existing ties between the HBI and international centres of neuroscience research and training excellence. 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.

The RHISE program will commence in 2015. Travel and accommodation expenses will be funded by the RHISE program, with a contribution towards direct research costs to be provided by the University of Melbourne (MNI) and the FINMH. Applications for the first round opened in October 2014, with 3 PhD students awarded funding for 2015 exchanges. A second round will be advertised in mid-2015.

The successful applicants for the inaugural RHISE are:

STUDENT	DEPT.	SUPERVISOR	HOST LABORATORY
Nicholas Ryan	Department of Child Neuropsychology, MCRI	Vicki Anderson, MCRI	Keith Yeates, Dept of Psychology, University of Calgary
Cary Zhang	FINMH	Andrew Gundlach, Neuropeptides Division, FINMH	Jaideep Bains, Cumming School of Medicine, HBI
Jeffrey Kenzie	University of Calgary	Sean Dukelow MD, Calgary Stroke Program, HBI	Leeanne Carey, Stroke Division, FINMH

5

FUNDING INITIATIVES

NHMRC Success

The latest round of competitive research funding from the National Health and Medical Research Council included the following successful applicants in the Neurosciences and related disciplines.

PROJECT GRANTS		
Professor Heather Young	Cell therapy for enteric neuropathies – the essential next steps	Anatomy & Neuroscience
Professor John Furness	Neural control of colorectal function and identification of sites of drug action	Anatomy & Neuroscience
Professor Paul Gleeson	Membrane trafficking of BACE1 and amyloid precursor protein in primary neurons and the production of Abeta amyloid peptides	Biochemistry and Molecular Biology
Doctor Michael Hildebrand	Exploring Somatic Mutation in Focal Epilepsies	Medicine – Austin
Professor Terence O'Brien	How does chronic epilepsy result in cardiac electrophysiological dysfunction?	Medicine – Royal Melbourne Hospital
Doctor Tomas Kalincik	Treating progressive multiple sclerosis	Medicine – Royal Melbourne Hospital
Doctor Anneke van der Walt	Predicting treatment response to onabotulinumtoxin-a in MS-related tremor: a combined clinical, electrophysiological and neuroimaging approach	Medicine – Royal Melbourne Hospital

Doctor Allison McKendrick	Cortical excitation in migraine: using vision to understand and track brain excitability	Optometry & Vision Sciences
Doctor Sarah Whittle	Pubertal timing, brain development and mental health in adolescence	Psychiatry
Associate Professor Atte Meretoja	STOP-AUST: The Spot sign and Tranexamic acid On Preventing intracerebral haemorrhage growth – AUStralasia Trial	Medicine – Royal Melbourne Hospital
EARLY CAREER FELLOWSHIPS		
Associate Professor Atte Meretoja	Acute Stroke Care: rapid unblocking of vessels, mending ruptures, and recovery	Medicine – Royal Melbourne Hospital
Dr Bridget Callaghan	Human neural development in the absence of species-expected stimuli: The effect of maternal or social deprivation on maturation of emotion circuitry during critical periods of development.	Anatomy and Neuroscience
CAREER DEVELOPMENT FELLOWSHIPS		
Dr Adam Vogel	Communication and swallowing outcomes in patients with acquired and progressive neurological disorders	Audiology and Speech Pathology
Dr Mario Alvarez-Jimenez	Connecting the Dots: Novel Social Media Technologies for Long-term Functional Recovery in First Episode Psychosis	Centre for Youth Mental Health
Dr Peter Crouch	Harnessing the consequences of impaired mitochondrial function to treat and image motor neuron disease	Pathology
Dr Sandy Shultz	Investigating treatments and biomarkers of brain concussion	Medicine – Royal Melbourne Hospital
PRACTITIONER FELLOWSHIPS		
Associate Professor Helmut Butzkueven	Predicting and Improving Multiple Sclerosis treatment outcomes	Medicine – Royal Melbourne Hospital

ARC Future Fellowships

Dr Olivia Carter

2014–2018

Project Summary

This project aims to use a multi-disciplinary approach to investigate the factors influencing human perception and cognition – from the level of basic neuroscience, through to the wider impact felt by individuals and society when these functions are either impaired or enhanced. This will inform the basic research question of how the brain generates a conscious experience, identify the relationship between altered visual cognitive function and clinical symptoms of psychosis, and determine the current prevalence and neuroethical issues associated with the non-medical use of drugs to enhance cognitive or perceptual function within Australia.

Dr Alice Pebay

2014–2018

Project Summary

This project aims to dissect the roles of lipids in cell fate. The study of lipids, or lipidomics, is an emerging and exciting area of biological science. The fundamental roles of lipids in development remain vastly understudied. This project will look at reprogramming of somatic cells into stem cells, their pluripotency and differentiation. This will be complemented with studies in the zebrafish, which permits the direct study of cell fate in vivo. This approach is a powerful way to unlock major events involved in development and to unmask the roles of lipids in these fundamental mechanisms.

Discovery Projects

Professor Nick O Haslam; Dr Stephen Loughnan

2015–2017

Project Summary

Violence and discrimination are serious problems facing women in Australia. This project examines how sexual objectification contributes to these problems, investigating the process from both the perpetrator's and the victim's perspectives. Using a multi-method approach, the project is expected to show how objectification hampers women in their personal and professional lives. Importantly, the project aims to go beyond identifying the harm caused

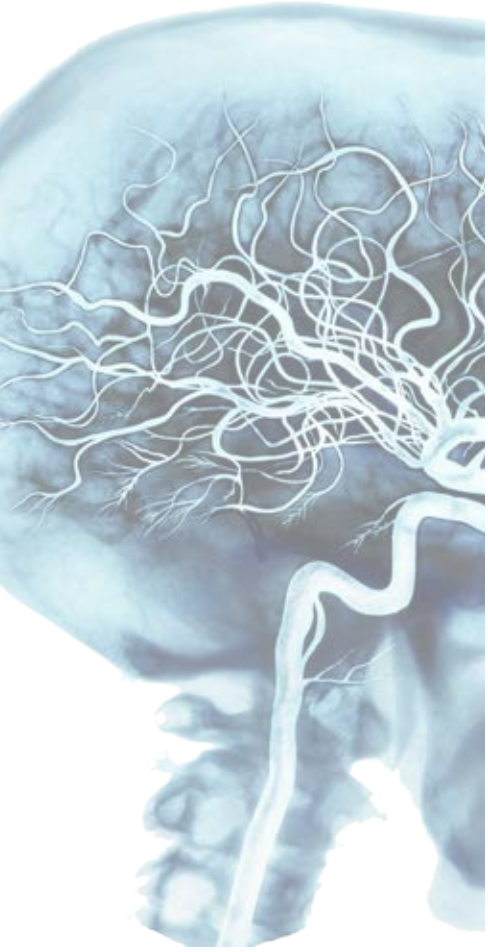
by objectification to start examining ways in which it can be reduced and women can protect themselves from its effects. This is expected to provide insight into a previously unstudied psychological cause of violence and discrimination against women, and map ways of reducing its harm.

Professor Gordon S Lynch; Dr James G Ryall

2015–2019

Project Summary

The project aims are to identify the metabolic factors that regulate muscle stem cell identity and to examine how changes in the local metabolic environment can influence how stem cells respond to biological perturbations. One of the most important and unresolved issues in skeletal muscle biology is understanding the role of muscle stem cells in the regulation of growth and development, adaptation and plasticity. We have identified that the local skeletal muscle metabolic milieu may regulate the activity of skeletal muscle stem cells. This project could reveal novel mechanisms by which skeletal muscle stem cells can be regulated. This information is crucial for our fundamental understanding of stem cell biology and its future applications



A/Professor Anthony R White; Dr Elizabeth J New

2015–2017

Project Summary

Copper (Cu) plays essential roles in the functioning of brain cells, but the regulation and activity of this metal is poorly understood. This project aims to map sub-cellular Cu pools in brain cells, with particular emphasis on the effects of cellular stresses on these pools. These studies are expected to contribute important new methods for the study of Cu biology, and could provide valuable information about how Cu homeostasis is maintained or perturbed under various stresses. In the future, this work is expected to form the basis of studies of brain Cu pools in neurodegenerative diseases.

Professor Heather M Young

2015–2017

Project Summary

This project aims to examine the neural crest cells that colonise the developing gut and to identify why some cells advance while others stay behind to populate a region. Directed cell migration is essential for normal development, including for the nervous system. In most of the migratory cell populations that have been analysed to date, all of the cells migrate as a collective from one

location to another. However, there are also migratory cell populations that must populate the areas through which they migrate, and thus some cells get left behind while others advance. The planned data are likely to be relevant to other cell populations that also populate the areas through which they migrate, including neural crest-derived melanocytes and Schwann cell precursors.

Outcomes from Prior MNI Funding

Research Theme Grant Report

Recreating Disease in a dish – Pre-clinical testing of novel therapeutics using 3-D cell culture systems

Investigators: Dr Giovanna D'Abaco, Dr Mirella Dottori, Prof Stan Skafidas, Dr Gursh Chana, Dr Babak Nasr.

In 2014 the team was able to demonstrate, for what is believed to be the first time, that three-dimensional (3D) cell culture techniques have the potential to provide effective models for human neuronal cells and processes. They have successfully maintained and supported the growth of SH-SY5Y neuroblastoma cell lines and neurons derived from human embryonic stem cells in a 3D culture environment. A number of candidates are being assessed for use as scaffolds in three-dimensional cell cultures and it is yet to be seen if there will be links between particular scaffold types and optimal models for particular cell and tissue types. The team demonstrated that off-the-shelf graphene foam is a viable scaffolding material, providing a high surface to volume ratio, porosity and conductivity to allow for improved accuracy in modelling of the in vivo cellular environment. The ability to produce viable 3D cell cultures of human neural cells is an important step towards improved testing of therapies for use in treating neuronal conditions.

Developing Diagnostics towards Neurodegenerative Diseases with Nanowire Technologies

Investigators: Dr Babak Nasr, Dr Chathurika Abeyrathne, Dr Giovanna D'Abaco, Dr Mirella Dottori, Prof Stan Skafidas.

Work undertaken by the team in 2014 focused on the development of vertical nanowire based immunosensors, with the potential to measure protein levels directly inside a living cell. Nanowires are single dimensional structures which have excellent electronic transport properties. Functionalsed nanowires can be used to measure the concentration of target molecules based on changes they make to the surface potential of the nanowire. This sensor functions without the need for target labelling or to employ secondary processing.

Interdisciplinary Seed Funding

Since its inception MNI has supported a competitive Interdisciplinary Seed Funding Scheme. The purpose of this funding is to provide short-term (up to one year) support for exciting and high return projects in the Neurosciences and related disciplines that will lead to new collaborations and develop opportunities for future external funding.

2014 Project Reports

Poverty, Family Chronic-Stress, and Children's Development (Co-funded with the Melbourne Social Equity Institute)

Lead investigator: Francisco Azpitarte, Melbourne Institute of Applied Economics and Social Research

Co-Investigators: Dr Eric Dommers, School of Social & Political Sciences; Dr Nicholas Allen, Faculty of Business & Economics; Dr Sophie Havighurst; Department of Psychiatry; Fatou Roost, Brotherhood of St Laurence

Funding amount: $10,000 (MNI)

Background and purpose of project

Research over the last fifty years has provided consistent evidence about the importance of early environmental conditions for children's social, emotional, and cognitive development. Recent psychology and neuroscience research finds that the relationship between family environment and children's development is partially mediated by children's exposure to chronic stress.

This project aims to investigate the relationships between chronic stress experienced by children, parental stress, and parenting behaviours, in the context of highly disadvantaged families in Australia. The project also aims to analyse how the quality of parent-child interactions are related to the level of stress experienced by family members, and the extent to which parent-child interactions mediate the effects of disadvantage on children's experiences of stress.

To our knowledge, this is the first project aimed at understanding how children's chronic stress is determined in disadvantaged families in the Australian context. Results from this research will contribute to our understanding of the negative impact of poverty on children's development and the intergenerational transmission of poverty. Further, the insights derived from this research will inform the design of interventions in the early years of life aimed at improving family environments and the cognitive and non-cognitive development of children from highly disadvantaged families.

Progress report 2014

The project is in progress with 20 families recruited out of the 60 required to complete the research. Interviews are proceeding with the current recruits and will be completed by October 2015.

Correlating membrane binding and toxicity of amyloid beta peptide from Alzheimer's disease

Lead investigator: Dr Guiseppe (Joe) Ciccotosto, Department of Pathology, Bio21

Co-Investigators: Dr M Akhter Hossain, FINMH; Professor Frances Separovic, School of Chemistry & Bio21

Funding amount: $30,000

Background and purpose of project

Alzheimer's Disease (AD) is the most frequent cause of dementia in our aging population. While the rapid advances in health and medical treatments have resulted in dramatically increased life spans, a consequence of this is that age-related neurodegenerative diseases including AD will become more prevalent and will present a greater medical and health care problem. Presently, there are limited therapeutic treatments and no cure for this disease to date. The key protein causing AD is called amyloid beta (Aβ). This protein is destructive to brain neurons in the aging brain. To better understand what makes this protein neurotoxic, we hypothesise that its toxicity is correlated with binding to the lipid components of the plasma membrane. Further, we have identified the specific amino acids, glutamine (Q), at position 15 and lysine (K) at positions 16 and 28 in Aβ that may have a critical role in mediating the binding to lipid membranes. This project, which combines the strengths of peptide chemistry, structural biology, and neuroscience, investigates the biophysical, cell binding and toxicity properties of mutated Aβ peptides with the aim of identifying a possible therapeutic target to treat AD.

Progress report 2014

In 2014, we successfully completed part1 – The synthesis of the different Aβ peptides that will be used for our investigations. The peptides synthesised include the full length wild type human Aβ peptide sequence (Aβ42) and the three peptide mutants, Aβ42(Q15A), Aβ42(K16A), and Aβ42(K28A). We also had each peptide synthesised to contain an N-terminal fluorescein tag. Part 2, involves the downstream biophysical experiments and will commence in January 2015. In Part 3, the cell biology experiments, we have some preliminary data. We have tested the neurotoxicity of the mutant peptides and we observed that the wild-type, K16A and K28A species were toxic but the Q15A peptide was not toxic in our cell culture model (67.5, 78.5, 75.7, and 102 % cell viability respectively after 96 hours of treatment at 15 μM concentration). This is an important result as it demonstrates that the Q15A mutant lacks neurotoxicity, thereby suggesting that this site is important in mediating the neurotoxic effects for Aβ. We have performed preliminary cell binding experiments and we identified that these peptides bind to primary cortical neurons at different levels.

Deciphering the language of mice

Lead investigator: Associate Professor David Grayden, E&E Engineering & Centre for Neural Engineering

Co-Investigators: Dr Emma Burrows, FINMH; Associate Professor Anthony Hannan, FINMH; Associate Professor Neil McLachlan, Melbourne School of Psychological Sciences

Funding amount: $30,000

Background and purpose of project

Until recently, it was not known that mice communicate in social contexts using ultrasonic vocalisations (USVs). The genetic factors that underlie variation in USVs could provide insight into mechanisms underlying communication disorders associated with Autism Spectrum Disorder (ASD). There is evidence to suggest that patterns of calls influence behaviour and so likely constitute meaningful communications. The major challenge for quantitatively assessing differences in vocalisations lies in the quantity and complexity of data to be analysed. Current methods for classifying USVs involve protracted manual analysis, splitting ultrasonic vocalisations into call types based on visual inspection of spectrograms for the duration and shape of frequency changes of tonal components in the call (pitch contours). Visual estimation of acoustic variables from spectrograms by eye leads to uncertainty about which variations between calls represent differences in call categorisation, and, in consequence, problems of poor standardisation and replication. Classifying USVs by using just median pitch and call rate addresses the problems inherent in visual inspection but fails to capture the information-rich pitch contours present in USVs. This project focuses on the development of a novel algorithm for assessing USVs based on principles of human speech recognition. The algorithm enables investigation of putative communication impairments in a genetic mouse model of ASD.

Progress report 2014

Using the algorithm, we have recently shown that mice containing an ASD-associated gene mutation in neuroligin-3 (NL3) show altered communication. The automated approach was able to generate templates representative of the waveform of USVs that were activated by wild-type (WT) and NL3 mice, demonstrating that NL3 mice use a completely different repertoire compared to WT mice. We have shown that NL3 mice demonstrate aberrant social behaviour towards both male and female mice and alterations in their use of USVs could underlie this phenotype. Validation of this automated data gathering against manually classified data is ongoing. Investigation of the novel sound templates associated with NL3 mouse communication is currently underway.

Elucidating speech disorders by genetic analysis and imaging of neural pathways in twins

Lead investigator: Dr Michael Hildebrand, Department of Medicine (Austin)

Co-Investigators: Professor Alan Connelly, FINMH; Dr Angela Morgan, Department of Audiology & Speech Path., MCRI; Professor Ingrid Scheffer Medicine, Paediatrics RCH & FINMH

Funding amount: $40,000

Background and purpose of project

Speech disorders are one of the most common reasons for paediatric referral with an annual cost of > $3,000 per patient [1], and significant impact on self-esteem and learning. Clinical and genetic evidence suggests a strong genetic contribution as twin studies show a > 70% concordance for speech disorders in monozygotic (MZ) twins compared to < 50% in dizygotic twins (reviewed in [1]). Overall speech disorders have a high heritability of > 90%. Little is known about the genes contributing to speech production apart from one gene, *FOXP2*, first identified in a large family with very severe speech impairment rendering them almost unintelligible [2]. Although a number of large families have been ascertained, the vast majority of cases are sporadic suggesting *de novo* mutations are likely to be involved, an increasingly recognised occurrence in other neurodevelopmental disorders [3].

This project investigates a rare cohort of MZ twins discordant (only a single twin in each pair is affected) for speech disorders. It involves a pilot study of 10 pairs collected through the Australian Twin Registry using exome sequencing to identify genes. The key advantage of this strategy is the ability to eliminate background genetic variation, critical given little is known about the genetic architecture of speech disorders. In a multi-faceted and complementary approach genetic analysis is combined with imaging techniques to elucidate the neural pathways perturbed in speech disorders.

Progress report 2014

Detailed clinical speech pathology assessment of 13 twin pairs is being undertaken to determine their suitability to be included in the study. Exome sequencing will commence early in 2015.

In vivo photoreceptor and retinal capillary flow imaging to study neurovascular coupling in human diabetes, thalassemia, optic neuritis, benign intracranial hypertension and progressive retinal dystrophies

Lead investigator: Associate Professor Andrew Metha, Department of Optometry and Vision Sciences

Co-Investigators: Associate Professor Andrew Symons, Department of Optometry and Vision Sciences; Dr Phillip Bedggood, Department of Surgery, RMH

Funding amount: $21,000

Background and purpose of project

New optical methods borrowed from advances in astronomy now enable us to take movies of the retina within the living human eye with unprecedented clarity. We are now able to resolve individual photoreceptor (cone) cells and watch them as they respond to light. We can also track individual red and white blood cells as they traverse the minute capillary networks lining the inside of our eyes. Thus we are able to provide both structural and functional imaging of the eye's retina at cellular scales. With this ability comes an opportunity to study cellular level neurovascular function non-invasively in people who have interesting pathologies hypothesised to affect the way blood flows in response to stimulation. By characterising their neurovascular responses, and comparing these to normal cases, we are learning more about how blood flow in the eye is regulated in health and disease. Further, because the retina is a genuine extension of the brain, this research exploits the "eye as a window to the brain" concept to inform us about blood flow and regulation within the central nervous system in general, and how metabolic needs of neural tissue is met on demand.

Progress report 2014

To date, 11 patients have been identified as suitable candidates and have undergone extensive imaging with our device. Image analysis is currently underway using this patient data.

Exploring the function of the Parkinson's protein, alpha synuclein, in the cardiovascular system

Lead investigator: Associate Professor Christine Wright, Pharmacology/ School of Biomedical Sciences

Co-Investigators: Dr Scott Ayton, FINMH; Dr Peng Le, FINMH

Funding amount: $40,000

Background and purpose of project

Alpha synuclein (asyn) is considered a principal protein implicated in the pathogenesis of Parkinson's disease (PD) protein and lowering its expression is a prominent therapeutic strategy. But the normal function of asyn in the brain and periphery is unknown. Cardiac dysfunction is a feature of PD, and asyn pathology is observed in cardiac tissue in PD and other disease. Lack of asyn (asyn KO mice) causes altered cardio physiology, suggesting a functional role of this protein in the heart. Given this, the project involves a series of experiments to comprehensively explore cardiac functions of asyn KO mice.

Progress report 2014

We have comprehensively characterised the cardiovascular system of asyn KO mice over their lifetime. Our techniques ranged from in vivo measurements of cardiovascular physiology, to ex situ experiments on isolated heart and blood vessels. We explored baseline performance between wild-type and asyn KO mice, and also relative changes in output in response to selected drugs.

This approach allowed us to characterise the precise changes that occur in the cardiovascular system as a result of loss of asyn. We found that asyn KO mice had selectively impaired nitric oxide signaling, and no change to a broad range of other cardiovascular parameters. This result agrees nicely with a recent report from CIs Ayton and Lei regarding altered nitric oxide signaling in Parkinson's disease.

2015 Recipients

LEAD INVESTIGATOR	DEPARTMENT	FACULTY	TEAM MEMBERS	PROPOSAL TITLE
Dr Yuning Hong	Chemistry	Science	Danny Hatters (Biochemistry) Dennis Velakoulis (Psychiatry) Trevor Smith (Chemistry)	Developing biomarkers of proteostasis decline for translational medicine in neurodegenerative diseases
Dr Peregrine Osborne	Anatomy and Neuroscience	MDHS	Scott Mueller (Microbiology & Immunology), Erica Fletcher (A&N), Holly Chinnery (OVS)	Sensory innervation of the cornea: A new approach for visualising neuron-immune and neuron-virus interactions.
Dr Stefan Bode	Melbourne School of Psychological Sciences	MDHS	Simon Laham (MSPS), Carsten Murawski (Finance, Business & Economics)	The neural basis of moral decision-making.
Prof Rob Shepherd	Medical Bionics	MDHS	John Furness, Robin McAllen (both Anatomy & Neuroscience)	Development of electroceutical technology: vagal nerve stimulation for anti-inflammation therapy.
Dr Hamish Meffin	Optometry and Visual Science	MDHS	Michael Ibbotson (OVS), Paul Martin (Clinical Opthal. & Eye Health), Michael Wibral (JW Goethe University, Frankfurt), Joseph Lizier (CSIRO)	Tracking the dynamics of information processing in cortical circuits.
Prof Barry Hughes	Mathematics and Statistics	Science	Tobias Merson (FINMH), Kerry Landman (Mathematics & Statistics)	Modelling the generation of oligodendrocyte cell topography in white matter.
Dr Karim Seghouane	Electrical and Electronic Engineering	Engineering	Colette McKay, Natalie Rickard & Adnan Shah (Bionics Institute)	A new prognostic tool for cochlear implantation using function near-infrared spectroscopy.
Dr Simon Murray	Anatomy and Neuroscience	MDHS	Malcolm McConville (Biochemistry & Molecular Biology)	The influence the neurotrophins exert on the lipid profile of peripheral myelin.

Melbourne Neuroscience Institute (MNI) Fellowships

The MNI awarded 2014 Fellowships to Dr Michael Hildebrand, a Postdoctoral Fellow in the Department of Medicine, Austin Health,and Dr Christine Nguyen, a Research Fellow in the Department of Optometry and Vision Sciences to promote the University's interdisciplinary research projects in the neurosciences.

Dr Christine Nguyen

Summary of project: The ability to non-invasively visualise neurons and blood vessels is an attribute unique to the eye. This window provides unparalleled insight into general health, as many cardiovascular and central nervous system disorders have distinct manifestations in the eye. These attributes render the eye, and in particular the neurovascular retina, an ideal biomarker for disease. Alzheimer's disease is in desperate need of a viable biomarker. At present the only definitive diagnosis of Alzheimer's disease is via post-mortem confirmation of plaques in the brain and a viable biomarker has been identified as a key to the development of effective treatments. Recent advances in brain PET imaging show promise as a biomarker for Alzheimer's however the technology is expensive. Thus an inexpensive, early and quantitative marker of disease is essential for correctly targeting patients and developing effective treatments to combat this devastating illness. While changes in the brain are well recognised in AD, growing evidence shows that the disease also affects the eye, opening the possibility of optically imaging amyloid-beta in the eye as a biomarker for Alzheimer's disease

Outcomes: This fellowship has resulted in data which shows that amyloid beta in a test-tube exhibits a particular light reflectance signature. When this is injected into the eye it can be seen that this reflectance signature is preserved through the transmission properties of the front of the eye thus making assessment of amyloid beta in the living retina a viable option.

Dr Michael Hildebrand

Summary of project: Epilepsy is a common disorder estimated to affect 3% of Australians. Speech disorders are one of the most common reasons for paediatric referral with an annual cost of > $3,000 per patient. For both diseases 70% of cases are likely to have a genetic component. I have completed pilot experiments to determine the feasibility of a new gene testing method for epilepsy genes. In initial experiments ten known and three candidate epilepsy genes were sequenced in 314 patients with epilepsy, including 8 twin pairs, with different types of seizures, to identify epilepsy-causing mutations.

Outcomes: I included four patients previously shown to have specific gene mutations causing their epilepsy and was able to detect these mutations, validating the method. In 16 other patients with epilepsy I have identified new variants that are likely to contribute to their seizures. This represents genetic diagnosis of epilepsy in up to 5% of cases. For example, in one patient we

identified a mutation in a potassium channel gene and showed in human cells that this genetic change increases activity of the channel, causing his seizures. This study provides proof of principle for development of a comprehensive gene screening panel for epilepsy in a large number of patients including twins.

I now apply this approach to patients with speech disorders to develop a similar gene screening platform for this disease. This represents the first step towards direct translation of primary genetic discoveries to the clinical neurology setting.

I was successfully funded as CIA for an NHMRC R.D. Wright Career Development Fellowship Level 1 in February 2014. I received an internal University of Melbourne FMDHS Fellowship Establishment Grant ($35,000 in research support) in May 2014 as a consequence of the external fellowship funding.

I was also funded as CIA for an NHMRC Project Grant entitled 'Exploring somatic mutation in focal epilepsies' in November 2014. These funds are to investigate genes using the techniques described above in our cohort of twins and surgical patients with focal epilepsy.

2015 Fellowship Recipients

Dr Alexandra Grubman (Department of Pathology)

Regulation of inflammation and amyloid clearance by neuroprotective copper complexes.

Dr Andrew Watt (FINMH)

Mechanisms modulating B-amyloid propagation in Alzheimer's disease.

Above: 2014 MNI Fellows Dr Michael Hildebrand and Dr Christine Nguyen.

Strategic Research Australian Postgraduate Awards

In 2014, the Melbourne Neuroscience Institute 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.

Melbourne Neuroscience Institute 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 2015 commencement are:

- Damien Crone (Melbourne School of Psychological Sciences) – *The neural basis of moral decision making.*
- Michael Erlichster (Medicine, Royal Melbourne Hospital) – *Development of point-of-care molecular diagnostic devices for application in precision medicine.*
- Danielle Lee (Anatomy and Neuroscience) – *Effects of chronic BACE inhibition on the development & function of excitatory synapses.*

6

GOVERNANCE

Advisory Board

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

The MNI would like to extend thanks to our retiring MNI Advisory Board Chair, Professor Liz Sonenberg for her superb leadership and guidance throughout her four year term in this position. We welcome the appointment of Professor Mark Hargreaves, Pro Vice-Chancellor (Research Partnerships & External Relations) as the new Chair in 2015.

2014 Membership:

NAME	TITLE
Professor Liz Sonenberg (Chair)	Pro Vice-Chancellor (Research Collaboration) Melbourne Research, UoM
Professor Trevor Kilpatrick	Director, MNI, UoM
Professor Stephen Smith	Dean, Faculty of Medicine, Dentistry and Health Sciences, UoM
Professor Greg Qiao	Assistant Dean (Research), Melbourne School of Engineering, UoM
Professor Karen Day	Dean, Faculty of Science, UoM
Dr Andrew Milner	Chief Executive Officer and Managing Director, Neurosciences Victoria
Professor Richard Head	Deputy Vice Chancellor & Vice President: Research & Innovation, University of South Australia

Associate Professor Andrew Metha	Deputy Director, MNI
Professor Glenn Bowes	Associate Dean (External Relations), Faculty of Medicine, Dentistry and Health Sciences, UoM
Professor Bob Williamson	Ex-Secretary for Science Policy, Australian Academy of Science, Faculty of Medicine, Dentistry and Health Sciences, University of Melbourne
Dr Keith McLean	Theme Leader: Biomedical Materials and Devices, CSIRO

Scientific Consultative Forum

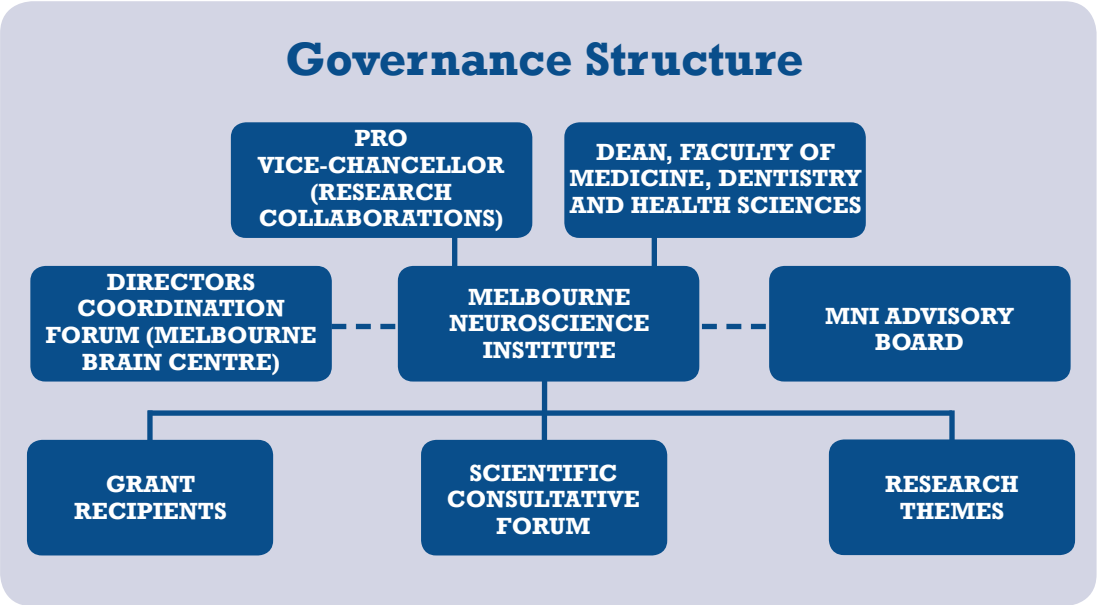
The Scientific Consultative Forum comprises Heads or delegates from Departments involved in neuroscience-related research. Members of the forum assist the MNI by providing a coordinated vision for the award of core research support funds provided by MNI and by providing key strategic advice, ancillary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

Community Consultative Forum

The Community Consultative forum has provided affiliates, members of the public, school teachers, research representatives and University advancement and alumni representatives with a forum to promote dialogue, consultation and input concerning the public outreach program of the MNI.

The MNI recognises the value of engaging with the community and also places considerable emphasis on the need to work closely with other members of the Parkville Precinct. Part of our organisational focus includes embedding the fundamentals of collaboration, consultation and co-design of initiatives into all of our interactions with the community. This involves fostering partnerships with representatives of the community to develop and implement public programs that meet the expectations of both the community and internal stakeholders.

In 2015 the Community Consultative Forum will move to an e-communication model to ensure year-long consultation and dialogue.


Governance Structure
PRO VICE-CHANCELLOR (RESEARCH COLLABORATIONS)
DEAN, FACULTY OF MEDICINE, DENTISTRY AND HEALTH SCIENCES
DIRECTORS COORDINATION FORUM (MELBOURNE BRAIN CENTRE)
MELBOURNE NEUROSCIENCE INSTITUTE
MNI ADVISORY BOARD
GRANT RECIPIENTS
SCIENTIFIC CONSULTATIVE FORUM
RESEARCH THEMES

Melbourne Neuroscience Institute

Address | Melbourne Brain Centre, 30 Royal Parade
The University of Melbourne Vic 3010

Twitter | twitter.com/UoMNeuroscience

Phone | +61 3 8344 1819 | *Email* info-mni@unimelb.edu.au

www.neuroscience.unimelb.edu.au

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