MONASH University

MONASH BIOMEDICAL IMAGING AND LINKED LABORATORIES

ANNUAL REPORT 2020

Partners

MEMBERS

National Imaging Facility

Australian Research Council Centre of Excellence for Integrative Brain Function

VBIC

Monash MedTech

SUPPORTERS

Australian Government Department of Industry, Innovation and Science

VICTORIA State Government

NCRIS National Research Infrastructure for Australia An Australian Government Initiative

ARMI Australian Regenerative Medicine Institute

SCIENCE AND INDUSTRY ENDOWMENT FUND

COLLABORATORS

Australian Synchrotron

JÜLICH FORSCHUNGSZENTRUM

CSIRO

MonashHealth

HZDR HELMHOLTZ ZENTRUM DRESDEN ROSSENDORF

AlfredHealth

PARTNERS

SIEMENS Healthineers

BRUKER

magnetic INSIGHT

Mediso

Contents

Cover image:
Description: Dynamic visualisation of Alzheimer's pathology.
Researcher: Jennifer Tinston
Scanner: Bruker BioSpec 94/20 MRI

Director's Report

The COVID-19 pandemic significantly reduced the volume of research work and services that MBI could provide in 2020. Clinical research services decreased by approximately 78% in Jan-Oct 2020 compared to the same time period in 2019. However, preclinical research services both at MBI (Clayton) and ARA-MBI (Prahran) were largely unaffected by COVID-19. MBI's administration team led the COVID-19 response and enabled essential research projects to safely continue during the peaks of the pandemic.

Infrastructure and Technology

The capabilities within the Monash Biomedical Imaging Facility (MBI) will be expanded with the housing of a medium-high energy cyclotron to enable the production of diagnostic and therapeutic radioisotopes for research. The facility will be unique in Australia by providing Good Manufacturing Practice (GMP) production of radiometal (copper-64, zirconium-89, gallium-68) labelled radiopharmaceuticals that are currently unavailable or have limited availability in Australia. The project will be located in close proximity to the Victorian Heart Hospital in the Monash Technology Precinct and has the potential for expansion with the addition of a commercial manufacturing facility.

Magnetic particle imaging (MPI) is a non-invasive imaging technique that detects superparamagnetic iron oxide nanoparticle tracers *in vivo*. MPI systems use changing magnetic fields to generate a signal from the nanoparticles, and since the particles do not occur naturally, a signal is only detected from the administered tracer. Monash and RMIT University made a successful grant application to the Australian Research Council in 2019 to establish an MPI capability at ARA-MBI. The world's first MPI-CT scanner was delivered in mid 2020 but unfortunately the installation has been delayed until early 2021, due to COVID-19.

BrainPark is a world leading neuroscience research clinic dedicated to improving the physical, mental and brain health of Australians co-located at MBI in Clayton. The BrainPark team has developed novel digital assessment tools and innovative lifestyle and technology-based therapies, optimised for their therapeutic potential and scalability. These include therapeutic virtual reality, non-invasive brain stimulation, physical exercise, meditation and yoga, and cognitive training. Co-location of BrainPark with MBI's facilities enables seamless integration of brain science and imaging to determine how these interventions change the brain, and for whom they are most effective. Studies that use neuroimaging tools pre- and post-intervention are being undertaken to ensure that advances in understanding of brain function and human behaviour are translated into effective tools for creating healthy habits, brains and lifestyles.

A new collaboration has been established with CSIRO to develop a focused ultrasound preclinical imaging capability. During 2020, a Focused Ultrasound (FUS) Instrument was received from CSIRO and installed in the MBI preclinical imaging laboratories. The collaboration objective is to develop more effective targeted therapies for high grade glioma using MR guided focused ultrasound technologies. Monash and CSIRO have made commitments to support a facility scientist to operate the FUS and investigate rodent brain tumour models and establish a new tissue culture laboratory to enhance the in-house capabilities to investigate the models.

In spite of the pandemic 2020 was still a highly productive year with 261 papers and 4 book chapters being published by staff and research users from MBI, and a number of MBI staff receiving research awards and grants. Dr Zhaolin Chen, head of the MRI Imaging Analysis Team received an ARC Discovery Project grant to develop a biophysics informed deep learning framework for MRI. This project involves a paradigm shift from conventional non-quantitative MRI to ultra-fast, quantitative, and artefact free imaging by integrating biophysics and artificial intelligence.

A Monash Network of Excellence grant to extend collaboration in radiochemistry and biomaterials between Monash and the Helmholtz Zentrum Dresden Rossendorf (HZDR) research facility was awarded in 2019-20. Building on this success, the German Helmholtz Association recently announced the award of $6 million to HZDR to establish a Joint International Laboratory in collaboration with Monash University entitled, MHELTHERA: The Monash Helmholtz Joint International Laboratory for Radio-Immuno-Theranostics". The overall objective of the MHELTHERA collaboration is to develop next generation of radio-immuno-theranostic agents.

I would like to thank Professor Ian Smith for his continued inspiring leadership of the Monash Technology Research Platforms and for his guidance and advice during the first half of 2020, and for Professor Rebekah Brown's leadership as Vice-Provost of Research and Research Infrastructure during the second half of the year. I look forward to working closely with the new Monash research leadership team to ensure that MBI continues to play a major role in the Monash University strategic plan throughout the next decade.

My sincere thanks to all staff at MBI for their dedicated and excellent work during 2020. I would particularly like to thank Ms Kyle Reid who commenced her new appointment as General Manager in early 2020, immediately prior to the onset of the COVID-19 lockdowns. Despite only meeting her new work colleagues in person for the first couple of weeks, Kylie has done an outstanding job managing MBI throughout such a difficult period. All of the MBI staff including from the Management and Administration, Clinical Research Imaging, Imaging Methods and Analysis, and the Preclinical Imaging teams at MBI, Clayton and the ARA-MBI Preclinical Imaging team have performed extraordinarily well throughout the year under difficult circumstances. My particular thanks to Dr Robert Brkljača for his excellent management of the ARA-MBI Facility and his support of MR projects at ARA-MBI.

I would like to sincerely thank all MBI staff for their invaluable contributions throughout 2020 and for their continued commitment to excellence in supporting biomedical imaging research at Monash University.

Professor Gary Egan

Director MBI and CIBF; Distinguished Professorial Fellow, School of Psychological Sciences

Personnel

MBI AND ARA-MBI PERSONNEL

Director

Professor Gary Egan
Director MBI and CIBF; Distinguished Professorial Fellow, School of Psychological Sciences

Professor Michael Farrell
Associate Director MBI

Management and Administration

Ms Kylie Reid
General Manager, MBI

Ms Janelle Redding
Senior Administrative Officer

Ms Louise Mitchell
Senior Research Coordinator

Ms Gabi Di Camillo
Receptionist

Ms Nichola Thompson
Resources Coordinator

Ms Merrin Morrison
Communications Officer

Ms Louisa Detez
Administrative Officer

Preclinical (ARA-MBI)

Associate Professor David Wright
Director of Preclinical Imaging

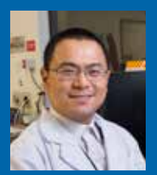
Dr Robert Brkljača
ARA-MBI Facility Manager and Support Scientist

Dr Bianca Jupp
ARA-MBI Lead PET/CT Scientist

Preclinical (Clayton)

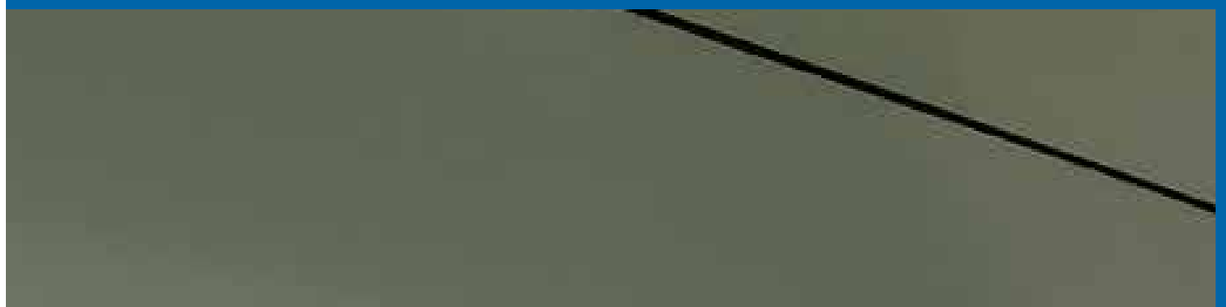
Dr Michael de Veer
Head of Preclinical Imaging

Dr Ekaterina Salimova
Research Fellow



Dr Gang Zheng
MRI Physicist

Ms Tara Sepehrizadeh
MR Imaging Scientist



Clinical Research Imaging

Mr Richard McIntyre
Clinical Head and Supervising Radiographer

Ms Alexandra Carey
Supervising Nuclear Medicine Technologist

- Ms Arlene Hobson
  MRI Radiographer, Monash Health and MBI
- Ms Paticia Heidmann
  MRI Radiographer, Monash Health and MBI
- Ms Fiona Gould
  MRI Radiographer, Monash Health and MBI
- Mr Van Vu
  MRI Radiographer, Monash Health and MBI
- Mr Cuong Tran
  MRI Radiographer, Monash Health and MBI
- Mr Scott Stewart
  MRI Radiographer, Monash Health and MBI
- Ms Lauren Hudswell
  Nuclear Medicine Technologist
- Mr Nemat Nadir
  Nuclear Medicine Technologist

Clinical Research Support

Ms Parisa Zakavi
Technical Assistant

Ms Christina Van Heer
Technical Assistant

Imaging analysis

Dr Zhaolin Chen
Head of Imaging Analysis

Dr Kamlesh Pawar
Research Fellow (Imaging Scientist)

Dr Shenjun Zhong
Research Fellow and Informatics Officer

Students
- Mr Viswanath P Sudarshan
- Mr Anjan Bhattarai
- Ms Himashi Peiris
- Mr Cameron Pain
- Mr Mevan Ekanayake

Radiochemistry

Dr Brett Paterson
Head of Radiochemistry

PhD Students
- Mr Cormac Kelderman
- Mr Patrick Davey
- Ms Melyssa Grieve
- Ms Sanjeevini Babu Reddiar

Honours Students
- Ms Rachel MacLean

BRAINPARK PERSONNEL

Prof Murat Yucel
Director

Dr Rebecca Segrave
Dep Director, David W Turner Senior Res Fellow and Head of Behaviour Group

Prof Leonardo Fontenelle
Head of Clinical Group

Dr Rico Lee
Head of Decision Making Group

Dr Chao Suo
Head of Technology Group

Dr Lucy Albertella
Research Fellow

Edouard Kayayan
Wilson Foundation-BrainPark Exercise Physiologist

Dr Karyn Richardson
Wilson Foundation-BrainPark Research Fellow

Dr Yann Chye
Research Fellow

Ms Amy Allen
Senior Operations Coordinator

Mr James Morrow
Implementation Coordinator

Ms Amelia Lowe
Wilson Foundation-BrainPark Research and Administrative Officer

Mr Sam Hughes
Exercise Physiologist

Research Assistants
- Rebecca Kirkham
- Nathan Dowling
- Joseph Pitt
- Leonie Duehlmeyer
- Chris Andara Olivia Chung
- Leonie Duehlmeyer
- Chris Andara
- Erynn Christensen
- Nathan Dowling

DPsych/Clinical PhD Students
- Alison Cullen
- Lauren den Ouden
- Olivia Chung
- Sakshi Dhir
- Louise Destree
- Mary-Ellen Brierley
- Emma Thompson
- Cassie Thompson

PhD Candidates
- Joshua Hendrikse
- Xiaoliu Zhang
- Daniel Myles
- Eugene McTavish
- Kavya Raj
- Suzan Maleki
- Craig Harper
- Catherine Brown

Honours Students
- Rachel Petukhova
- Alexandria Anthony
- David Luong
- Zoe Bettess
- Sandhiya Nathakumar
- James McLauchla
- Ruben Benakovic
- Campbell Ince
- Rebecca Kirkham
- Lena Wilkinson
- Rachel Ham
- Erin Crowe
- Prerika Sharma
- Joe Pitt

Facilities and Services

MBI provides imaging expertise and technological capabilities to support various fields of preclinical and clinical research, including radiochemistry and image analysis services. It is a node of the Australian National Imaging Facility (NIF) and offers researchers internal and external to the University (including government and industry) a full suite of multimodal and simultaneous imaging equipment alongside human testing facilities.

The Monash Clayton campus houses the most extensive range of imaging equipment, and is located within the Monash Technology Precinct, opposite the Victorian Heart Hospital and adjacent to the Australian Synchrotron. MBI also operates preclinical facilities at the Alfred Research Alliance – Monash Biomedical Imaging (ARA-MBI) site in Prahran and at the Monash Institute of Pharmaceutical Sciences (MIPS) in Parkville.

MBI offers access to the following instrumentation, including on-site technical support and training, and consultation on research projects.

HUMAN IMAGING FACILITIES

Human research studies can be performed with the following MBI human imaging and testing facilities at our main site in Clayton:

» 3T Magnetic Resonance Imaging (MRI)
» Simultaneous MR-PET
» Electroencephalography (EEG)
» Oculomotor/eye tracking
» Transcranial magnetic stimulation (TMS)
» Neurocognitive testing and interview rooms

PRECLINICAL IMAGING FACILITIES

Preclinical research can be undertaken using the following equipment:

Clayton site (Monash Biomedical Imaging)
» 9.4T MRI small animal scanner
» 3T MRI large animal scanner
» Simultaneous MR-PET scanner
» PET-SPECT-CT small animal scanner
» Vevo 2100 Ultrasound
» MRI guided focussed ultrasound
» Cardiovascular profiling
» CT large animal and human scanner

Prahran site (Alfred Research Alliance - Monash Biomedical Imaging)
» Magnetic Particle Imaging system
» 9.4T small animal imaging system
» PET-CT small animal imaging system

Parkville site (Monash Institute of Pharmaceutical Sciences)
» FLECT-CT small animal imaging system

BRAINPARK

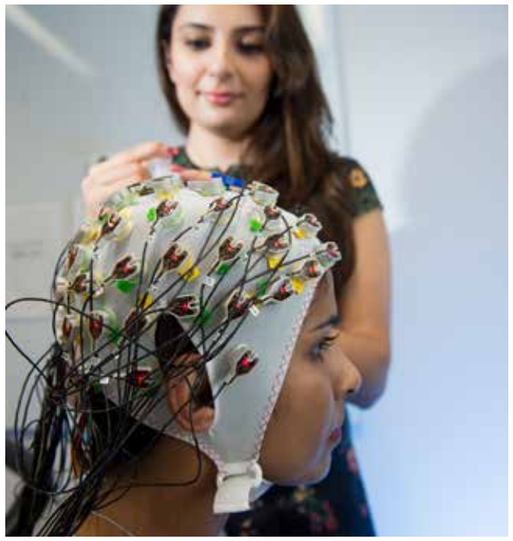
BrainPark houses the following equipment at MBI in Clayton:
- Gym
- Spin (cycle) room
- Exercise physiology
- Virtual reality studio
- Meditation/Yoga studio
- Meditation garden
- Brain training pods and clinical assessment rooms

We look forward to further expansion of MBI's capabilities, with the establishment of a GMP compliant cyclotron facility to enable the production of diagnostic and therapeutic radioisotopes for research.

TECHNICAL SUPPORT

The MBI Technical Support Team based at Clayton provides MBI users with highly specialised technical support to neuroimaging, physiological, and behavioural experiments. This type of hands-on support ranging from day to day hardware or software failures to more complex equipment setups, testing and coding of neurobehavioural tasks is a great asset to MBI.

In 2020, the Technical Support Team resolved approximately 500 support requests, developed 60 quality management and occupational health and safety documentation, set-up new stimulus computers for imaging and testing labs, and programmed new TMS-fMRI protocols. Furthermore, the team played a critical role in MBI's COVID-19 response by liaising with government bodies and equipment manufacturers regarding COVID-19 safety guidelines, and developing numerous risk assessments and COVID-19 equipment cleaning protocols.



ALFRED RESEARCH ALLIANCE - MONASH BIOMEDICAL IMAGING

The Alfred Research Alliance-Monash Biomedical Imaging (ARA-MBI) Facility is a node of MBI that is located at 75 Commercial Road, within the Baker Heart and Diabetes Institute. The facility is managed by Alliance partners, Monash University and the Baker Heart and Diabetes Institute, and is supported by the National Imaging Facility and the Victorian Biomedical Imaging Capability. ARA-MBI primarily supports preclinical imaging research and houses the latest imaging technologies, including a Magnetic Particle Imaging (MPI) system that was delivered in 2020.

The ARA-MBI team provides imaging support, technical guidance, and training for new and existing users, and advises on the most appropriate technologies for each preclinical imaging project.

Although the COVID-19 situation in 2020 was challenging, we saw increased commencement of new projects, along with increased utilisation across both the MRI and PET/CT scanners. The biggest growth was seen on our 9.4T MRI scanner, which reached almost 2000 hours of utilisation for the year.

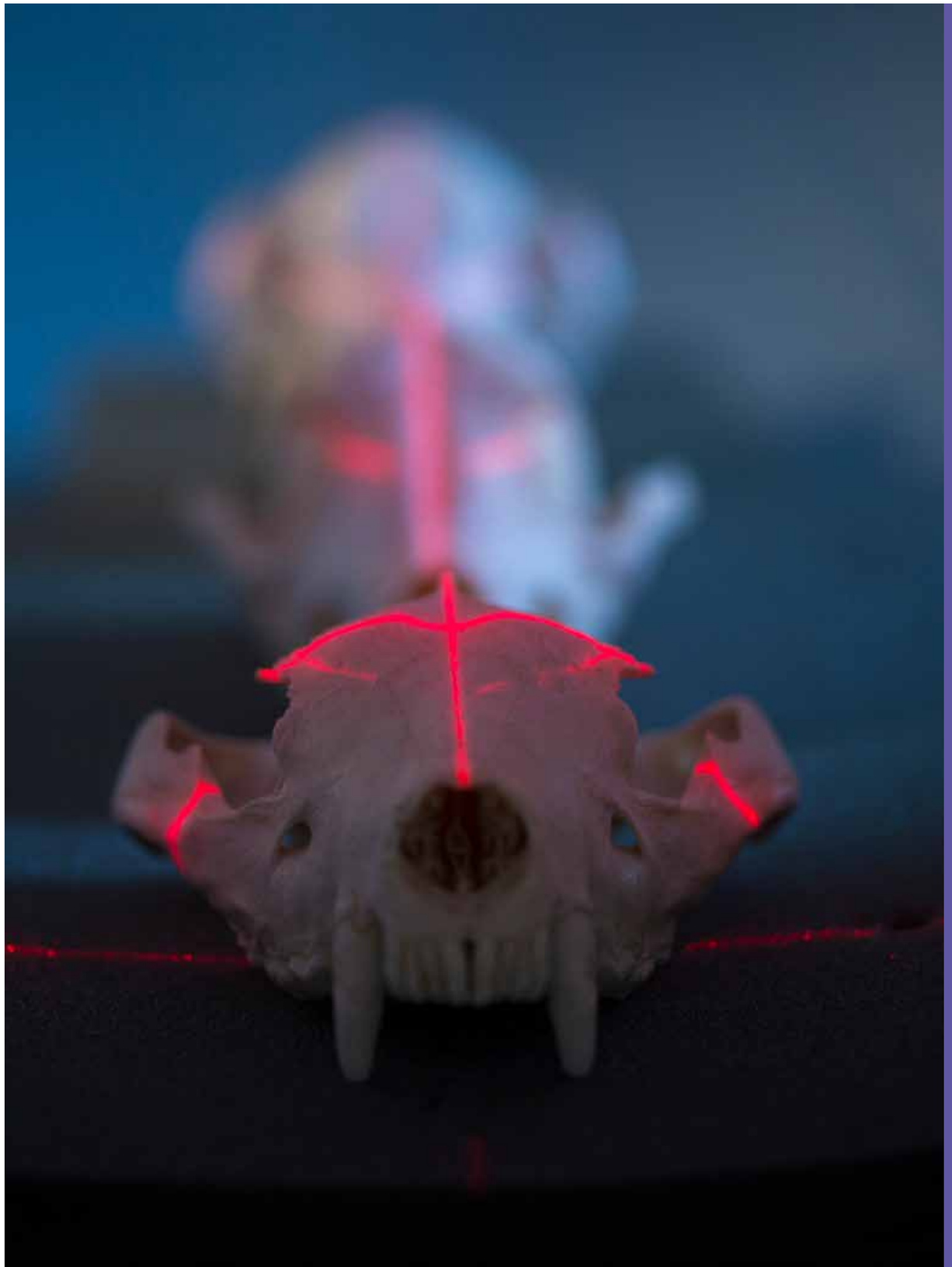
The facility houses a 9.4T Bruker MRI scanner which is equipped with a suite of coils, including mouse and rat surface cryoprobes. Our Mediso NanoPET-CT Imaging System is ideal for bench-to-bedside and back again translational applications, and is supported by a radio-HPLC and gamma counter. A new addition to the facility for 2020 was the delivery of a state-of-the-art Magnetic Particle Imaging (MPI) system. The MPI system was delivered just prior to the COVID-19 pandemic, however due to border closures the installation team returned to the U.S. and installation was not possible. Installation of the MPI system is expected for 2021.

BRAIN PARK

MBI is home to BrainPark - a world-first neuroscience research facility dedicated to improving the physical, mental and brain health of Australians. BrainPark provides research intervention programs with access to indoor/outdoor gym, exercise physiology lab, spin studio, virtual reality studios, brain training pods, clinical assessment rooms, and a meditation / yoga studio. Co-location of BrainPark with MBI facilities enables seamless integration of brain science and imaging to determine how these interventions change the brain, and for whom they are most effective.

Whilst BrainPark's utilisation was significantly impacted by the COVID-19 pandemic in 2020, we were able to further our research capacity with a successful NHMRC equipment grant facilitating the purchase and delivery of a state-of-the-art, medical grade HP Cosmos quasar med 3p with PDM2i treadmill. The system enables complete control, accuracy and safety of the gold standard physical and physiological assessments, and can expand our research capacity through its ability to measure gait analysis, critical for clinical and biomechanical research as well as rehabilitation. This is a critical piece of infrastructure for not only our current research projects, but to also enable future collaborations such as with the Victorian Heart Hospital.

Facility and research statistics

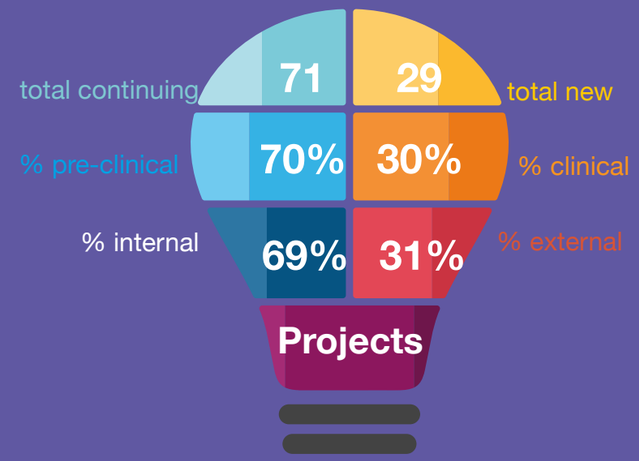


FACILITY STATISTICS

EQUIPMENT USAGE

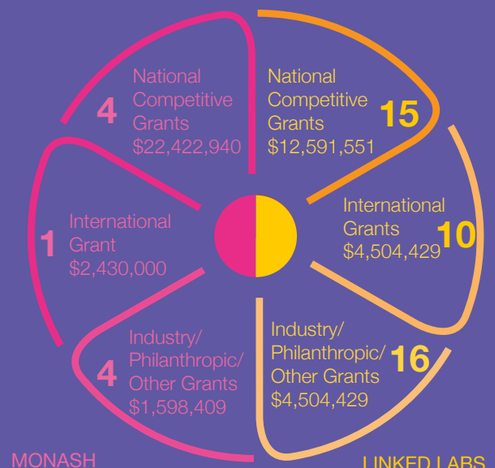
4909 hours

1588 reservations



RESEARCH STATISTICS

Grants



Publications

Book chapters

MBI 1

LINKED LABS 3

Journal articles

MBI 30

LINKED LABS 98

MBI-ARA-MBI User Community 133

Future Capability

AUSTRALIAN PRECISION RADIOPHARMACEUTICAL FACILITY

Accelerating precision medicine research

The capabilities within the Monash Biomedical Imaging Facility (MBI) will be expanded with the housing of a 16-30 MeV cyclotron to enable the production of diagnostic and therapeutic radioisotopes for research to advance diagnoses and treatments for cancer, cardiovascular, and neurological diseases.

The facility will be unique in Australia by providing Good Manufacturing Practice (GMP) production of radiometal labelled radiopharmaceuticals that are currently unavailable in Australia and for being located in the Monash Technology Precinct in close proximity to the Victorian Heart Hospital.

The Australian Precision Radiopharmaceutical Facility (APRF) will enable the rapid translation of phase I clinical trials using novel radiopharmaceuticals into phase II/III trials, and ultimately into routine clinical use.

Due for completion in 2024, the APRF has already received funding from the National Collaborative Research Infrastructure Strategy and Monash University.

Locally produced radiopharmaceuticals

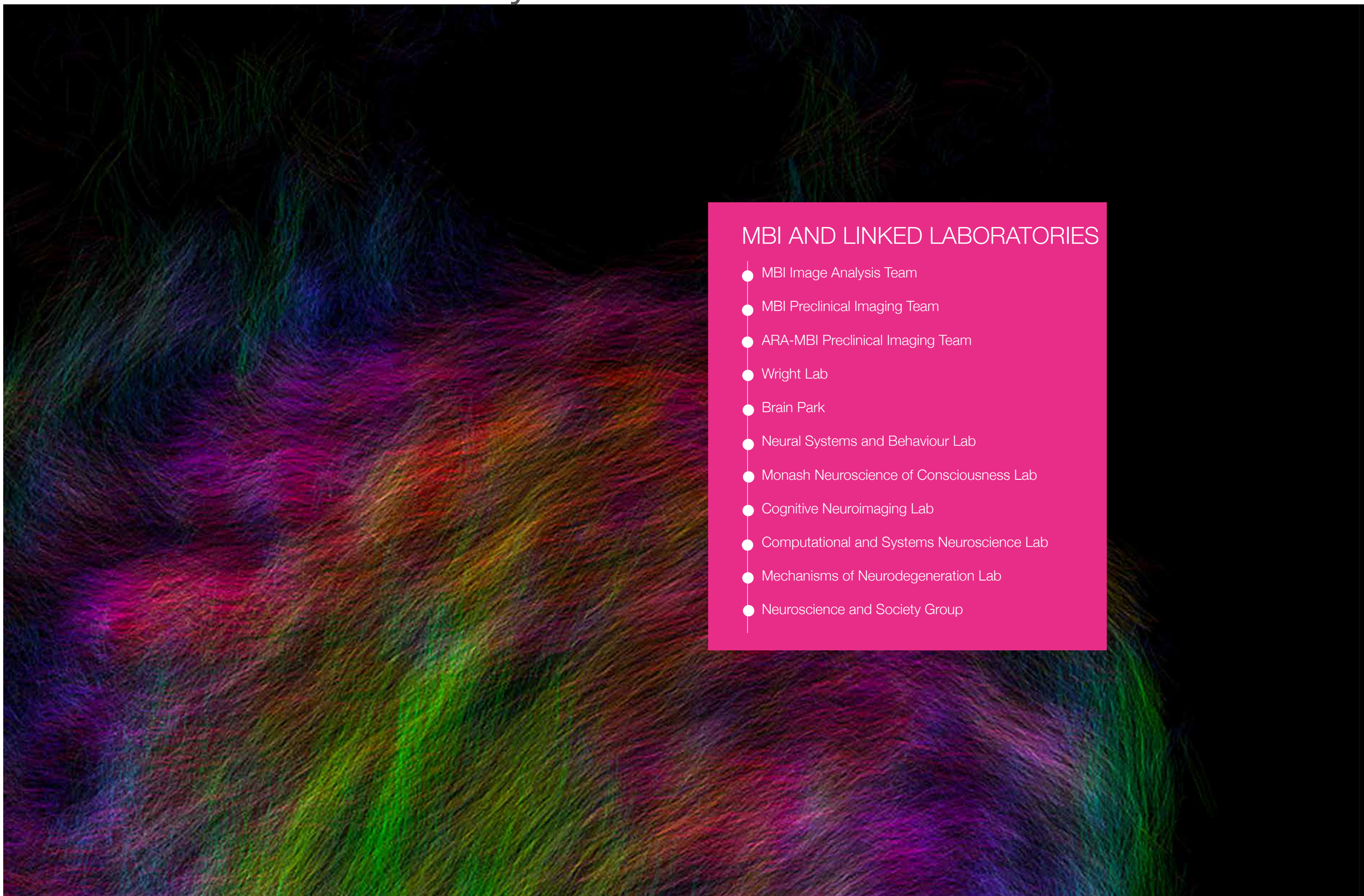
Initially, the APRF will produce radiometal labelled radiopharmaceuticals (copper-64, zirconium-89, gallium-68) using Good Manufacturing Practice (GMP) standards. Currently, there is no domestic GMP production capability for these radiopharmaceuticals for late stage clinical research studies.

The local supply of GMP compliant radiopharmaceuticals will establish a sovereign capability for researchers, pharmaceutical companies, and the healthcare sector to accelerate the development, translation and availability of novel nuclear medicines for the diagnosis and eventual treatment of cancer, cardiovascular, neurological and other diseases in Australia.

Potential for industry partners

Located in the heart of the Monash Technology Precinct, the APRF is opposite the Victorian Heart Hospital and has the potential for expansion. Future plans for the facility include the addition of industry partners to operate a commercial manufacturing facility to expand the facility into an integrated research and manufacturing enterprise for precision medicine.

Research and Discovery

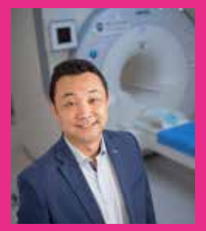


MBI AND LINKED LABORATORIES

- MBI Image Analysis Team
- MBI Preclinical Imaging Team
- ARA-MBI Preclinical Imaging Team
- Wright Lab
- Brain Park
- Neural Systems and Behaviour Lab
- Monash Neuroscience of Consciousness Lab
- Cognitive Neuroimaging Lab
- Computational and Systems Neuroscience Lab
- Mechanisms of Neurodegeneration Lab
- Neuroscience and Society Group

MBI IMAGE ANALYSIS

TEAM



Dr Zhaolin Chen
Head of Imaging Analysis

Dr Kamlesh Pawar
Research Fellow

Dr Shenjun Zhong
Research Fellow

Students

Mr Viswanath P Sudarshan

Mr Anjan Bhattarai

Ms Himashi Peiris

Mr Cameron Pain

Mr Mevan Ekanayake

In 2020, the Imaging Analysis team made significant advancement in the development and application of artificial intelligence in MRI and MR-PET imaging. The team collaborated with Alfred radiology for validation of deep learning-based MRI motion correction algorithms in clinics. The collaboration with Monash Health on artificial intelligence guided prostate cancer MR-PET imaging has resulted in publications at top tier nuclear medicine journals and conferences. The team is closely collaborating with industry for the development and application of low dose PET imaging and low field MR imaging.

The Imaging Analysis team continues to develop novel imaging methods. The image reconstruction methods have been published in renowned journals Medical Image Analysis and NeuroImage, with early results receiving oral presentation opportunities at ISMRM.

The imaging analysis team is leading a new national capability of mobile MR network, funded by the National Imaging Facility (NIF). This proposal is in collaboration with University of Queensland, South Australian Health and Medical Research Institute, Alfred Hospital, Royal Perth Hospital, Nvidia and Hyperfine. Internationally, the team continues collaboration with the Juelich research centre in Germany for the development of next generation MRI-PET technology.

The XNAT-based informatics framework at MBI has been successfully upgraded, which improved reliability and flexibility for our users supporting many research projects.

For more details, please contact:
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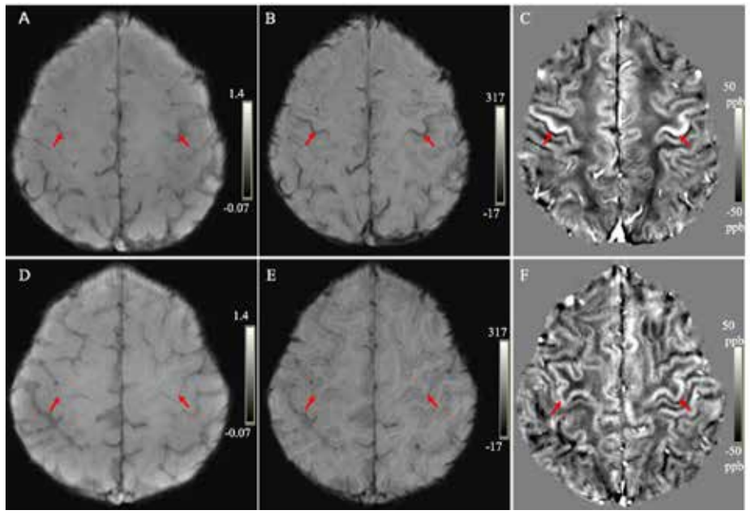
HIGHLIGHTS AND ACHIEVEMENTS

- Successful ARC discovery project grant # DP210101863, Biophysics-informed deep learning framework for magnetic resonance imaging, led by Zhaolin Chen
- Two oral presentations at the international society of magnetic resonance in medicine (ISMRM)
- Viswanath Sudarshan and Zhaolin Chen received Magna Cum Laude at ISMRM
- Viswanath received the prestigious award at IITB, “Naik and Rastogi” for best PhD thesis.

CASE STUDY

Iron dysregulation is a prominent hallmark of neuroinflammation. Histological evidence of iron dysregulation in the motor cortex of individuals with Amyotrophic Lateral Sclerosis (ALS) has been demonstrated. Its role in ALS pathogenesis warrants further investigation. Magnetic resonance imaging (MRI), with its unique capability to generate a variety of soft tissue contrasts, provides opportunities to image iron distribution in the human brain with millimeter to sub-millimeter anatomical resolution. Magnetic resonance based Quantitative Susceptibility Mapping (QSM) is a relatively new approach that provides a surrogate measurement of bio-metals, predominantly iron, in the human brain and provides quantification of magnetic susceptibility *in vivo*. QSM has demonstrated its superiority to detect paramagnetic iron in a range of neurodegenerative diseases, including ALS, compared to earlier techniques such as T1-weighted, T2-weighted, T2*-weighted and susceptibility weighted imaging (SWI). In this project, we used QSM to investigate motor cortex iron dysregulation in limb-onset ALS, both longitudinally and cross-sectionally. Our results suggest that iron level is increased in the motor cortex in limb-onset ALS relative to healthy controls and may not change significantly over the period of six-months. This study highlights the efficacy of QSM as a potential diagnostic and prognostic tool in limb-onset ALS.



*Visualization of differences in susceptibility contrasts using different MRI techniques in ALS. First row: ALS patient; Second row: Control. A,D: T2*WI; B,E: SWI; C,F: QSM. This figure is adopted from Bhattarai et al. (2021). https://doi.org/10.1002/jmri.27530*

MBI PRECLINICAL IMAGING

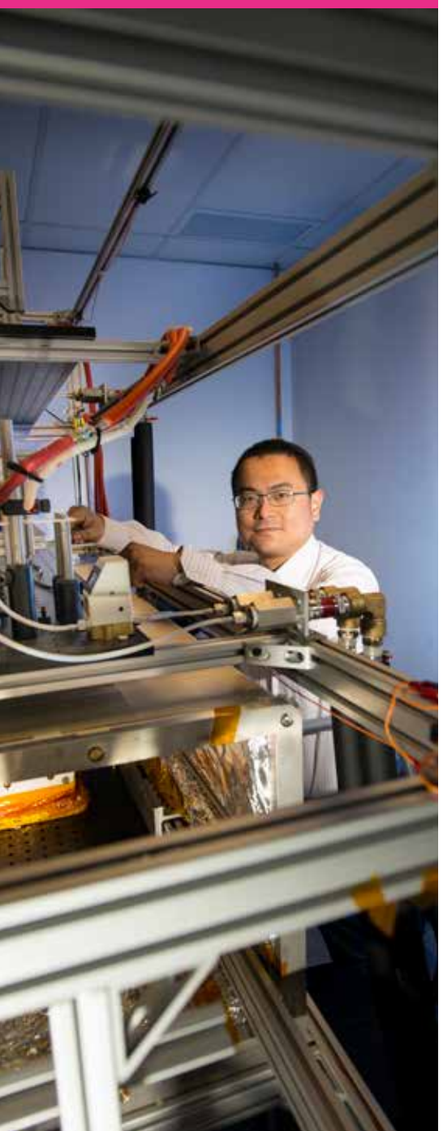
TEAM

Dr Michael de Veer
Head of Preclinical Imaging

Dr Ekaterina Salimova
Research Fellow

Ms Tara Sepehrizadeh
MR Imaging Scientist

Dr Gang Zheng
Research Fellow



In 2020, the MBI Preclinical Imaging Team remained onsite during the COVID-19 pandemic and supported and/or conducted a vast range of essential research utilising preclinical instrumentation and animal services.

Using the 9.4T MRI, the team supported longitudinal studies that investigated novel therapies for stroke (led by Dr Peter Crack, University of Melbourne), developed MRI protocols for kidney imaging (for studies led by Professor John Bertram), and investigated 19F-isoflurane MR imaging to better understand obesity (Dr Gang Zheng).

The CT scanners (Siemens Somatom and Inveon) provided Associate Professor Alistair Evans from the School of Biological Sciences together with Dr Justin Adams from the School of Biomedical Sciences capability to image bones, horns and teeth from a large array of museum specimens. This work is creating a database of 3-dimensional structures to determine the mathematical underpinnings of horn and tooth morphology.

The Vevo2100 (FUJIFILM/VisualSonics) ultrasound built capacity throughout 2020. Visulsonics provided a photoacoustic system under a loan agreement with MBI, this addition to the Vevo allows researchers to measure oxygenation of tissues and infrared contrast agents. PhD student, Mark Viddalon and his supervisor Dr Boon Mian Teo utilized the ultrasound to test new and highly novel contrast agents and MBI pre-clinical team member Dr Ekaterina Salimova continues to support a range of studies on the instrument.

The MBI radiochemistry facility enables researchers to label molecules with radioisotopes. The facility consists of a hot cell, analytical equipment (HPLC and TLC) and a gamma counter. Researchers can utilise the facility to synthesise and characterise radiotracers for use in PET and SPECT imaging in the pre-clinical facility. Dr Brett Paterson and his team continued to provide and expand its services in 2020 and worked closely with the MBI preclinical imaging team to undertake a number of PET and SPECT studies using the Inveon.

Dr Paterson's PhD student, Cormac Kelderman, developed new 99mTc radiotracers for SPECT imaging using thiosemicarbazone molecules. The radiotracers were shown to exhibit a range of hydrophilicities and demonstrated that subtle modifications to the structure of a 99mTc radiotracer can be used to control the biodistribution in mice with implications for new radiopharmaceutical design. Professor John Bertram, Dr Brett Paterson and Prof Katherine Denton of Monash University received interdisciplinary research seed funding from the Faculty of Science and Faculty of MNHS to develop PET radiotracers that can provide indirect measures of kidney glomerular numbers. PhD student Patrick Davey synthesised radiotracers using 68Ga and utilised the Inveon-PET-SPECT-CT under the supervision of Tara Sepehrizadeh.

Project contributors

Mr Mark Unger and Dr Harry Unger (MuPharma), Professor Nicolas Voelcker, Dr Ashley Dyer, Mr Eduardo Antunez Ceron (Melbourne Centre for Nanofabrication). Mr Patrick Davey and Dr Brett Patterson (MBI Radiochemistry Team), Ms Tara Sepehrizadeh, Dr Gang Zheng, Dr Michael de Veer (MBI Preclinical Imaging Team)

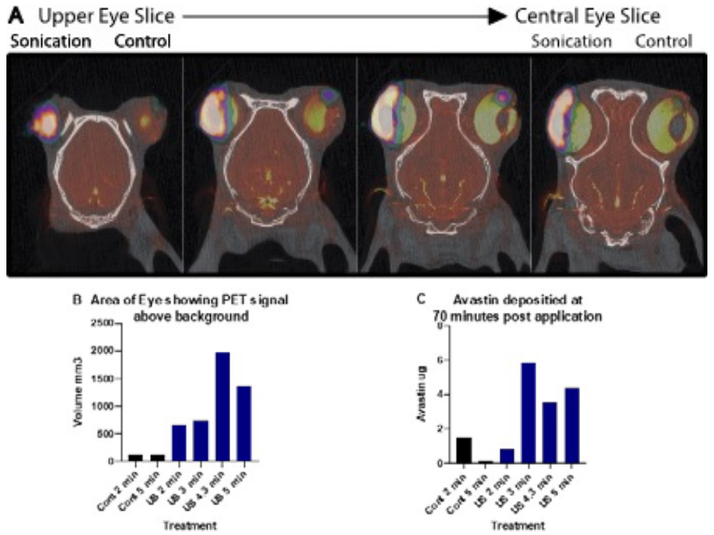
HIGHLIGHTS AND ACHIEVEMENTS

- Integrated radiochemistry capabilities with preclinical imaging services
- Supported industry project with muPharma and Melbourne Centre for Nanofabrication (case study next page)
- Installation of a Focussed Ultrasound (FUS) Instrument from CSIRO with co-committed support for a post-doctoral researcher to operate the FUS and develop neural tumour models.
- Acquisition of first scans on live mice using the FUS and production of first images showing the blood brain barrier opening
- Fit-out of new tissue culture laboratory to enhance our in-house capabilities to set up rodent tumour models.

CASE STUDY

Sonophoretic mediated, non-invasive delivery of Avastin

The monoclonal antibody bevacizumab, sold under the brand name AvastinTM, is a medication used to treat several types of cancers and the eye disease age-related macular degeneration. Avastin is conventionally delivered to the eye for the treatment of retinal diseases by clinicians using an intra-vitreal injection into the fluid within the centre of the affected eye. There is a clear need for less invasive and safer methods of delivery that deliver therapeutic amounts of Avastin to the choroid and retina where the disease manifests. A local company, muPharma lead by Mr Mark Unger and Dr Harry Unger a prominent ophthalmologist, have worked with Professor Nicolas Voelcker at the Melbourne Centre for Nanofabrication to produce a sonophoretic device to non-invasively deliver Avastin into the eye without injection or any damage to the sclera of the eye where the device is briefly applied. This was recently tested at MBI by delivering radiolabelled Avastin from the device into live rabbit eyes. Avastin was conjugated with NOTA-NCS, and free chelator removed with a 30kDa centrifugation filter (Amicon). The purified Avastin-NOTA was mixed with Gallium-68 and purified with a 30 kDa centrifugation filter. The labelled Avastin was loaded into the muPharma device and low power ~50kHz ultrasound was used throughout the studies involving applying the device to eyes for between 2 to 5 minutes. Over the 70 minute observation time, the sonophoretic device dramatically improved the delivery of 68-Ga-Avastin to the scleral surface of the eye where there was minimal uptake into the tear ducts.



(A) A composite of overlaid CT, MRI and PET slices from the top of the eye to the central region showing Avastin deposition in the left (Sonophoresis) and right (control) eyes. The PET signal is a heat map from low signal green-purple-bright yellow, high signal. (B and C) Graphs showing the effect of sonophoresis (US) time on the area of PET signal above background (B) and the quantitation of PET signal converted to the amount of Avastin (C) at 70minutes post application, Cont had the filled device applied with no power for the indicated time, US had the device applying ~50kHz to ocular tissue for the indicated time

ARA-MBI PRECLINICAL IMAGING

TEAM

Preclinical (ARA-MBI)

Dr Robert Brkljača
ARA-MBI Facility Manager and Support Scientist

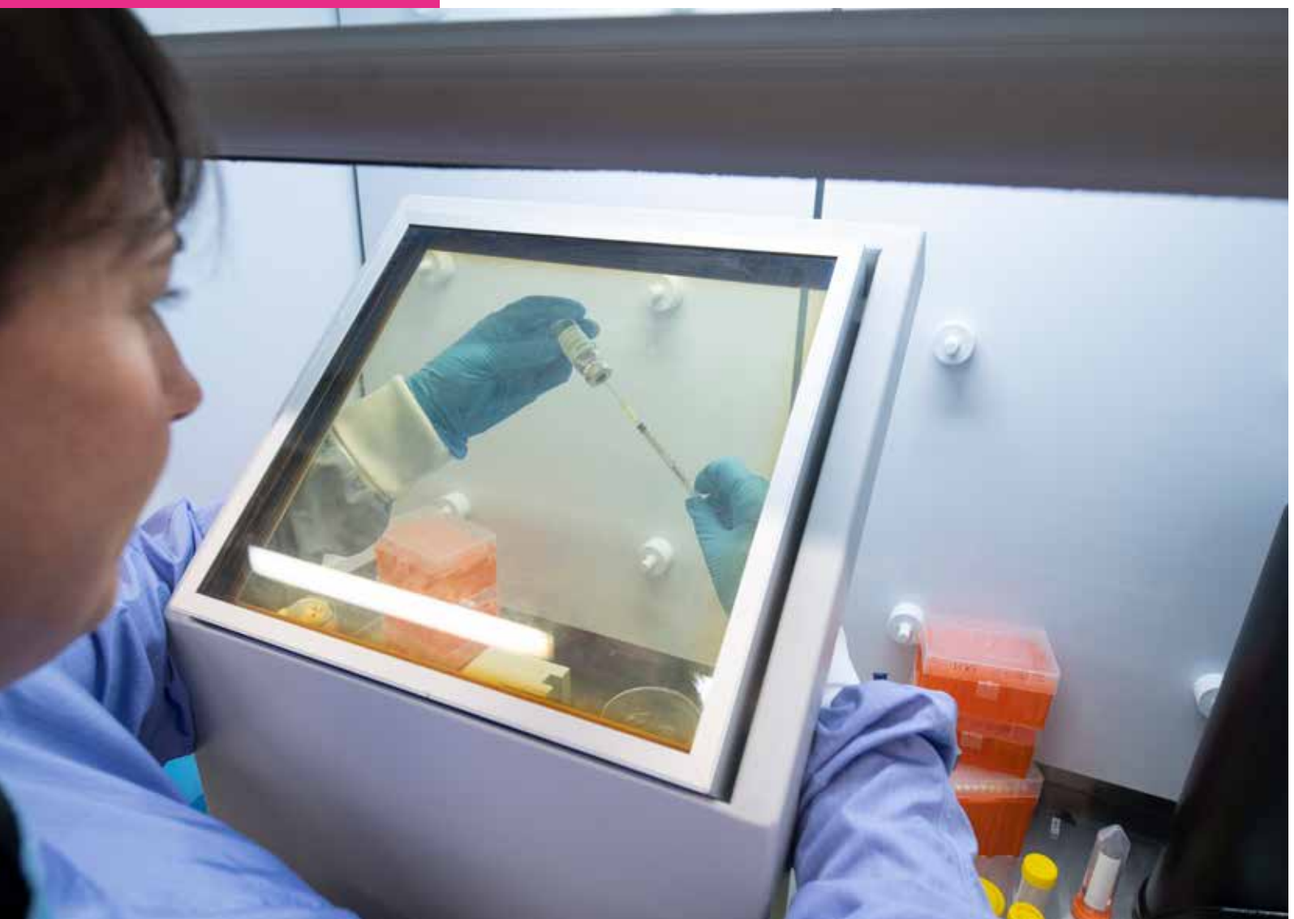
Dr Bianca Jupp
ARA-MBI Lead PET/CT Scientist

In 2020, the Preclinical Imaging Team at ARA-MBI was able to continue the growth of new projects being undertaken in the facility.

New projects using the 9.4T MRI included a study led by Dr Steven Petratos that investigated a multiple sclerosis model in mice using diffusion tensor tractography to visualize changes, along with a study led by Professor Julie McMullen which developed a new cardiac imaging protocol which can be applied to arrange of projects.

The CT scanner allowed Dr Karen Alt, Dr Bianca Jupp, and Lisa Hung to develop a novel methodology for iodine-based mouse lung tissue staining. This methodology enables the precise analysis of developmental changes, tissue damage and recovery with a focus on fine morphology alterations. The iodine-based staining shows no interference with post-processing histology staining.

The PET scanner was used by Dr Bianca Jupp, Dr Pablo Casillas-Espinosa, and Dr Lucy Vivash to examine the capacity of the new tau selective radiotracer [18F]-PI2620, to visualise this protein in a rodent model of ischemic stroke. PET scans using [18F]-PI2620 showed increased uptake within the striatum and adjacent cortical regions 24 hours following middle cerebral artery occlusion (MCAO) in rats, areas typically associated with neurodegeneration in this model. This work provides important proof of concept for the utility of this new radiotracer to study the role of tau in rodent models of neurodegenerative disease.



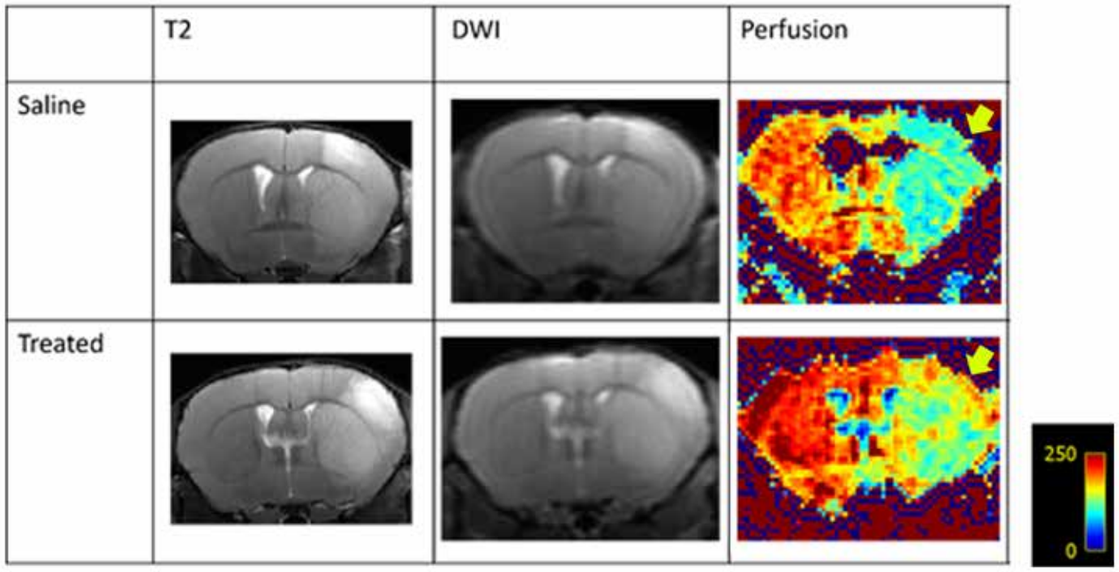
HIGHLIGHTS AND ACHIEVEMENTS

- Delivery of Magnetic particle imaging system
- New cardiac imaging protocol developed
- New CT protocol for lung imaging
- Radiation sharing agreement put in place between ARA-MBI and MBI

CASE STUDY

MRI Study

Two models of stroke in mice have been established; a focal ischaemia model – Middle Cerebral Artery Occlusion (MCAO), and a global hypoxia model – Double carotid artery ligation (DCAL). A therapeutic agent targeted to vascular cell adhesion molecule (VCAM)-1 has been tested, which is upregulated upon endothelial activation. The construct is expected to improve microvascular perfusion, so it was tested whether it could potentially improve stroke outcome in these models. MRI was utilised to determine infarct sizes as well as perfusion/diffusion mismatch to assess the ischaemic penumbra. Two cohorts (saline and treated) were completed of both MCAO and DCAL models (n=6). As seen in the above image, infarct sizes as well as overall area of perfusion was significantly improved after therapeutic treatment in both models, suggesting the treatment was effective in improving stroke outcome.



MRI images of in-vivo mice brains. Top row – untreated saline brain. Bottom row – drug treated brain. Red areas in perfusion image indicate overall area of perfusion that was improved after treatment.

Project contributors

Natasha Lee, Carly Selan, Joanne Chia, Sharelle Sturgeon, David Wright, Akram Zamani, Melrine Pereira, Harshal Nandurkar, and Maithili Sashindranath

WRIGHT LAB

TEAM

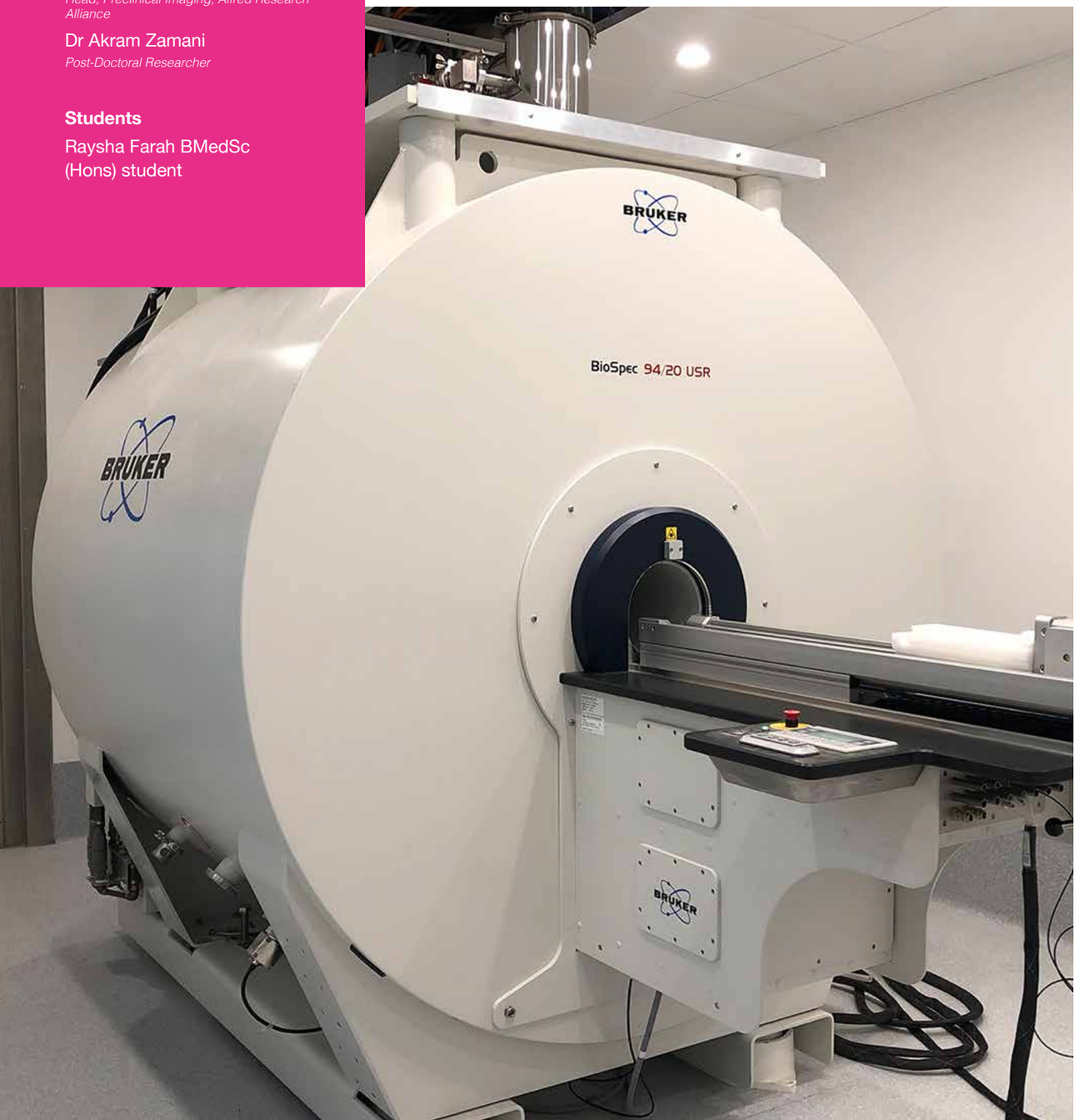
A/Prof David Wright
Head, Preclinical Imaging, Alfred Research Alliance

Dr Akram Zamani
Post-Doctoral Researcher

Students

Raysha Farah BMedSc (Hons) student

Led by Associate Professor David Wright, our lab uses cutting-edge anatomical and molecular MR methods to improve our understanding of disease pathophysiology. With a strong focus on neurodegeneration, we work with experimental models of motor neuron disease, traumatic brain injury (TBI), stroke, Alzheimer's disease and epilepsy, and validate our imaging results with a wide array of physiological and histological measures. Employing a bench-to-bedside-to-bench approach, once validated these biomarkers are translated to the clinical setting to improve patient outcomes.



HIGHLIGHTS AND ACHIEVEMENTS

- Associate Professor David Wright, won the Victorian Biomedical Imaging Capability (VBIC) Emerging Leader Award for 2020
- Received an international philanthropic grant of $1.1M, for the project "Testing of the effect of E2730 treatment on multimodality in-vivo biomarkers of GABAergic function in healthy rats and preclinical chronic epilepsy models"
- Awarded a $46K grant from the Bethlehem Griffiths Research Foundation to study "Glymphatic clearance as a novel therapeutic target for motor neurone disease"

CASE STUDY

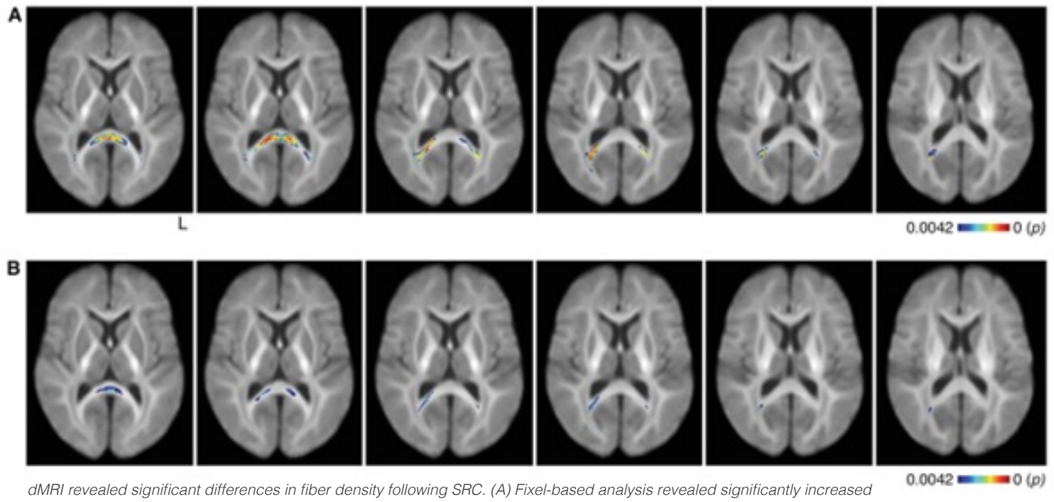
Diffusion Imaging Reveals Sex Differences in the White Matter Following Sports-Related Concussion

Sports-related concussion (SRC) is a serious health concern however, the biological sex differences in pathological profile is poorly understood. Evidence suggests that despite research bias focusing on male SRC, females are more likely to suffer from poorer outcomes than their male counterparts. With acute brain changes persisting beyond the resolution of self-reported symptoms, it is important to fully understand the temporal and spatial patterns of white matter disruption so expert advice can be considered when determining it is safe to return-to-play.

A cohort of recently concussed athletes (n = 14) underwent MRI scans 24–48-h after injury, and again at 2-week postinjury (when cleared to return-to-play), alongside age- and education-matched nonconcussed control athletes. Diffusion-weighted MRI was used to analyse white matter pathways in the brain, which revealed acute and persisting white matter changes in athletes with SRC at both 48-h postinjury and 2-weeks postinjury, compared with their nonconcussed counterparts, and despite SRC athletes being cleared to return to play. This may suggest increased cerebral vulnerability beyond the resolution of self-reported symptoms.

Additionally, sex differences in this study showed greater white matter disruption in male concussed athletes when compared with female SRC athletes, consistent with the males in this cohort reporting more symptoms and increased symptom severity, following SRC when compared with the female cohort. Although these findings contradict prior studies, it clearly justifies the need for additional research to provide a greater understanding of biological sex differences in SRC outcomes.

These findings have important implications for the clinical management of concussion, including guiding return-to-play decisions.



dMRI revealed significant differences in fiber density following SRC. (A) Fixel-based analysis revealed significantly increased fiber density in the splenium of SRC athletes compared with CTL 48 h after SRC. (B) Although these differences had largely resolved by 2-week postinjury, SRC athletes still exhibited a narrow focus of increased fiber density in the same location. Changes in fiber density are shown overlaid on the study template image. Color bar indicates FWE-corrected P value. Left hemisphere indicated by "L" beneath first panel.

BRAIN PARK

TEAM

Prof Murat Yücel, *Director*

Dr Rebecca Segrave, *Deputy Director, David W Turner Senior Research Fellow and Head of Behaviour Group*

Prof Leonardo Fontenelle, *Head of Clinical Group*

Dr Chao Suo, *Head of Technology Group*

Dr Rico Lee, *Head of Decision Making Group*

Dr Lucy Albertella, *Research Fellow*

Dr Karyn Richardson, *Wilson Foundation-BrainPark Research Fellow*

Dr Yann Chye, *Research Fellow*

Ms Amy Allen, *Senior Operations Coordinator*

Mr James Morrow, *Implementation Coordinator*

Me Sam Hughes, *Exercise Physiologist*

Mr Edouard Kayayan, *Wilson Foundation-BrainPark Exercise Physiologist*

Ms Amelia Lowe, *Wilson Foundation-BrainPark Research and Administrative Officer*

Research Assistants

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Xiaoliu Zhang
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Eugene McTavish
Kavya Raj
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Craig Harper
Catherine Brown

DPsych/Clinical PhD Students

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Lauren den Ouden
Olivia Chung
Sakshi Dhir
Louise Destree
Mary-Ellen Brierley
Emma Thompson
Cassie Thompson

Honours Students

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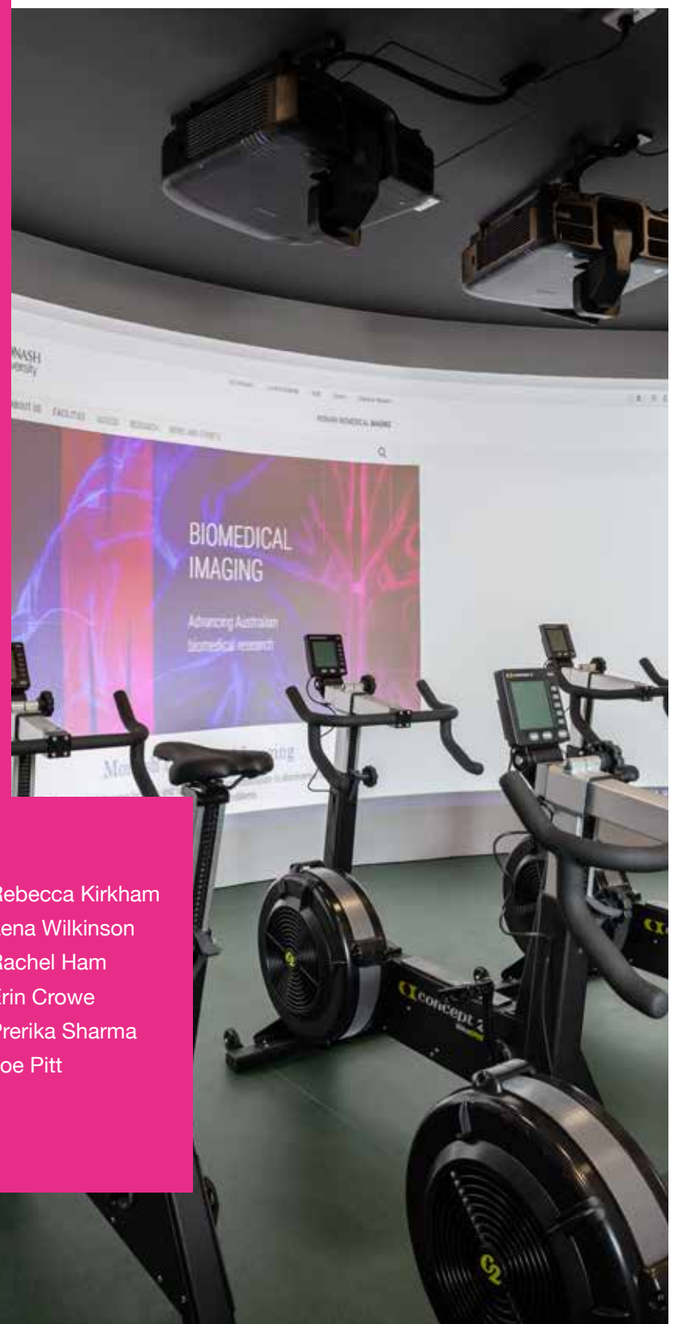
Alexandria Anthony
David Luong
Zoe Bettess
Sandhiya Nathakumar
James McLauchla
Ruben Benakovic
Campbell Ince
Rebecca Kirkham
Lena Wilkinson
Rachel Ham
Erin Crowe
Prerika Sharma
Joe Pitt

USING NEUROSCIENCE TO CREATE HEALTHY HABITS, BRAINS AND COMMUNITIES

As experts in the science of brain plasticity, behaviour, cognition, and mental health, the BrainPark team investigate how everyday lifestyle activities and digital tools can be used to both track and to improve brain and mental health.

To see other aspects of our work please view our website: www.brainpark.com



HIGHLIGHTS AND ACHIEVEMENTS

- Dr Rico Lee was awarded a 5-year NHMRC Investigator grant (through the Medical Research Future Fund scheme) of $645,205 to apply the BrainPAC digital assessment tool to study neurocognitive mechanisms in individuals experiencing various addictions.
- A $110,000 grant for 18 months was awarded to Prof Murat Yücel, Dr Lucy Albertella and Dr Rico Lee by the Department of Defence (Science and Technology) to develop a neuropsychological assessment for cognitive fitness and tools to guide peak performance under challenging conditions.
- Dr Karyn Richardson (Wilson Foundation-BrainPark Research Fellow) was accepted with a full scholarship to train with the renowned International Behavioural Trials Network
- PhD candidate Dan Myles received a $44,000 scholarship and project grant from NSW Office of Responsible Gambling. His is combining BrainPark's Virtual Reality with methodologies from experimental psychology and cognitive neuroscience, under a public health and community perspective.
- Dr Rebecca Segrave and Dr Karyn Richardson were awarded a $40,000 Health Smart Grant from the nib Foundation, as one of just 6 projects funded from over 200 applicants. The funding will support "PEAK" (i.e. peak-performance), a fun and empowering behaviour change program that seeks to embed regular neuroscience-informed physical exercise into the lifestyles of Australian university students to improve their mental, cognitive and brain health. They will partner with world leaders in human behaviour change; the UCL Centre for Behaviour Change; to design and implement PEAK.

CASE STUDY

Our everyday behaviours, such as sleep, physical activity, and social connections, have a potent impact on our mental health and the health of our brain. Behavioural interventions harness that power by identifying which behaviours have the most positive effects, and what behaviour change strategies best help people embed them into their lifestyles for the long-term. While behavioural interventions have enormous potential for enhancing community wellbeing, making sustained lifestyle change is challenging. In research settings it's common for over 50% of people to drop out of behavioural intervention trials, and for those that do remain many don't engage in a third or more of the intervention activities. This is a major challenge for the field of lifestyle medicine, and one that has been turned on its head at BrainPark. A key study is the Brain Exercise and Addiction Trial (BEAT). When people use cannabis regularly for many years it can have a negative impact on the health of their brain. The hippocampus (a key brain region for memory, learning, and emotional processing) is particularly vulnerable to the effects of heavy cannabis use. The good news is that the brain harm caused by long-term cannabis use can be reversed and the BrainPark team are researching strategies that speed up the process of brain health recovery. One such strategy may be exercise. Regular exercise has a positive effect on physical and mental health and can increase the size of the hippocampus. This study is comparing the effects of two different exercise programs to investigate whether the programs have a positive impact on brain health and, if they do, whether one is more effective than the other.

NEURAL SYSTEMS AND BEHAVIOUR LAB

TEAM

Prof Alex Fornito
Head, Neural Systems and Behaviour Lab

Lab Manager
Chao Suo

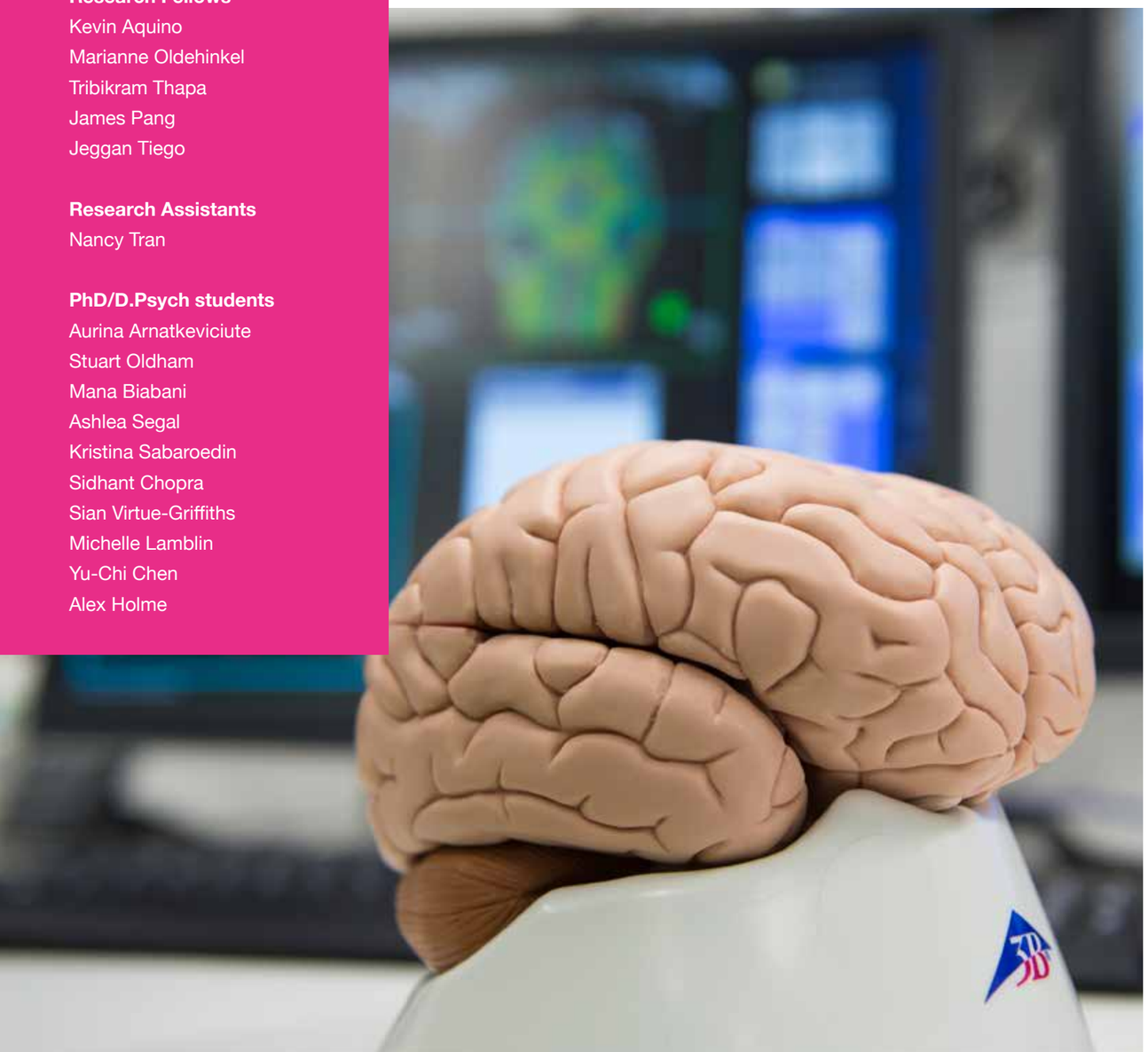
Research Fellows
Kevin Aquino
Marianne Oldehinkel
Tribikram Thapa
James Pang
Jeggan Tiego

Research Assistants
Nancy Tran

PhD/D.Psych students
Aurina Arnatkeviciute
Stuart Oldham
Mana Biabani
Ashlea Segal
Kristina Sabaroedin
Sidhant Chopra
Sian Virtue-Griffiths
Michelle Lamblin
Yu-Chi Chen
Alex Holme

The Neural Systems and Behaviour Lab (NSB) aims to understand how the brain works in health and disease. Headed by Professor Alex Fornito, researchers at NSB view the brain as complex, intricately connected network and use an interdisciplinary approach to develop a multiscale understanding of brain function from molecules to mind. Questions that we tackle include:

- How do genes sculpt the complex network organization of the brain?
- How do individual differences in brain network connectivity relate to behaviour?
- How are brain networks disrupted by mental illness?
- How does brain structure constrain brain function?
- Can we develop mathematical models of how brain networks develop and function?



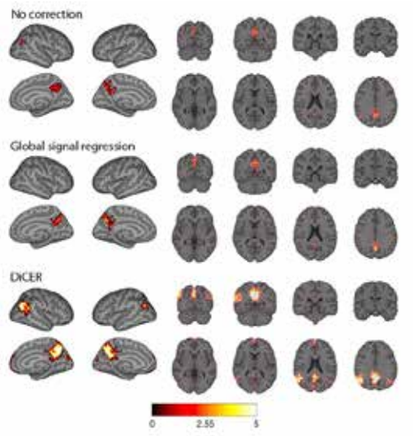
HIGHLIGHTS AND ACHIEVEMENTS

- Awarded a $2M+ NHMRC Investigator Grant for ”A network approach to mapping and modifying brain changes in psychosis”, with funding to begin in 2021.
- Published a Nature Paper - Brosnan, M.B., Sabaroedin, K., Silk, T. et al. Evidence accumulation during perceptual decisions in humans varies as a function of dorsal frontoparietal organization. Nat Hum Behav 4, 844–855 (2020). https://doi.org/10.1038/s41562-020-0863-4
- Was invited as a Keynote presenter for the 2020 international meeting of the Organization for Human Brain Mapping (OHBM, held virtually)
- Aurina Arnatkeviciute won Australasian Cognitive Neuroscience Society Emerging Research Award
- Aurina Arnatkeviciute won Dean’s Award for Doctoral Thesis Excellence
- Alex Fornito named a Clarivate Analytics Highly-Cited Researcher

CASE STUDY

Methods for improved connectome mapping with MRI

MRI data are noisy and are often subject to a series of complicated processing steps to minimize noise contributions to the signal. Many different processing options are available, raising questions about which are most effective. In 2020, NSB published two key papers comprehensively analysing the impact that data processing choices have on analysis results. One study, focused on maps of anatomical brain connectivity constructed with diffusion Magnetic Resonance Imaging (MRI), evaluated how 240 different data processing pipelines, generated from plausible combinations of 16 different processing options, mitigate the contamination of connectivity estimates by in-scanner head motion (Oldham et al. *NeuroImage*, 2020). The work showed that different processing options vary considerably in their denoising efficacy and identified specific steps that are particularly beneficial for minimizing motion-related contamination. A second study focused on the identification and removal of widespread signal deflections in functional MRI data (Aquino et al. *NeuroImage*, 2020). These deflections represent coherent signal changes affecting the entire brain, are often attributable to changes in respiration or head motion, and have a major influence on connectivity estimates. Our study showed that a commonly used procedure called global signal regression does not work as effectively as previously thought and proposed a new method, called Diffuse Cluster Estimation and Removal (DiCER), that is more successful at denoising and which improves statistical power in subsequent connectivity analyses (Aquino et al. *NeuroImage*, 2020). These studies provide clear recommendations for best practices in data processing and analysis, supporting the generation of more robust and reproducible results.



DiCER improves statistical sensitivity for mapping brain functional networks. Figure shows the results of an independent component analysis obtained following no correction for widespread signal deflections (top), the popular approach of global signal regression (middle), and our new approach, called DiCER (bottom). DiCER increases statistical estimates of within-network functional connectivity while also being more effective at minimizing motion-related contamination of the data.

MONASH NEUROSCIENCE OF CONSCIOUSNESS LAB

TEAM

Prof Naotsugu Tsuchiya
Head, Monash Neuroscience of Consciousness Lab

Thomas Andrillon
Sub-Head (NHMRC ECF 2019-2024)

Regan Gallagher
Postdoctoral Fellow

Ariel Zeleznikow-Johnston
Postdoctoral Fellow

Research Assistants
Yota Kawashima
Qianchen Liang

PhD Students
William Wong
Elise Rowe
Angus Leung
Sharon Daniel
Roberto Munoz
Jasmine Walter

Honours students
Maria Borsaru
Elain Pinggal
Alicia Yokoyama

The Monash Neuroscience of Consciousness (MoNoC) Research Laboratory primarily aims to understand the neural basis of consciousness. Since October 2020, we are driving a research project which we call Qualia Structure. Funded by the Japan Society for Promotion of Science, our project aims 1) to reveal the structure of conscious experience through novel psychological experiments, utilizing online massive samples and other technologies, combined with big data analysis, 2) to study the structures of information that are extracted from the brain, and 3) to understand the relationships between the structures of qualia and information. Our goals include better understanding of the neural substrates of consciousness, improving the accuracy of measures of consciousness (funded by NHMRC), and improving the quality of human-machine interaction through understanding of the principle of conscious experience in humans and its implications in AI research.

HIGHLIGHTS AND ACHIEVEMENTS

- Three projects were funded and started (NHMRC Ideas grant, FQXi Consciousness in the Physical World, and Qualia Structure)
- Media coverage of our unique interdisciplinary research on consciousness with physicists in Dr Kavan Modi's group (funded by Monash's Network of Excellence grant)
- The lab head (Tsuchiya) was promoted to Professor (January)

CASE STUDY

Measuring changes in attention, not perception

Neuroscience has long grappled with the relationship between attention and conscious awareness, or perception. Recent research has demonstrated that the two processes are separate and use different pathways in the brain. This is illustrated by studies showing that we can be conscious of things we're not paying attention to, and not conscious of things we are paying attention to.

Most research into conscious awareness has shown that becoming aware of an object leads to an increase in brain activity. This activity is commonly measured using steady-state visually evoked potentials (SSVEPs) from electroencephalography (EEG) recordings, recorded at MBI. SSVEPs are the brain's response to visual stimulation at particular frequencies.

But our new research questions whether SSVEPs are the right tool to use when studying awareness. The research team was led by our PhD student Matthew Davidson.

We used EEG to record brain activity in people who viewed an optical illusion based on the concept of 'perceptual filling-in'. This natural phenomenon occurs when objects in peripheral vision disappear and are replaced, or filled in, by features from the surrounding visual area.

In the experiment, the participants focused on a point in the centre of a computer screen. Four coloured circles also appeared on the screen in their visual periphery, and the participants were asked to note when the circles seemed to vanish. The researchers identified the brain activity corresponding to each circle by flickering the circle images at different frequencies and measuring the SSVEPs at those frequencies.

If SSVEPs tracked consciousness, then they should decrease when the participants believed that a circle had vanished. Instead, the researchers found that SSVEPs increased when a circle disappeared from consciousness.

Previous work showed that paying attention to visual targets in perceptual filling-in experiments increases the probability that they will disappear. Thus, the researchers concluded that what they and others have actually been recording using SSVEPs are changes in attention, not in consciousness.

This finding challenges long-held assumptions about the link between SSVEPs and visual consciousness. It is also further evidence that attention and consciousness are distinct brain processes.

Next steps:

We are planning to investigate which areas of the brain are linked to attention and consciousness. They will do this by combining their experimental approach with techniques such as magnetoencephalography (MEG) and functional magnetic resonance imaging (fMRI).

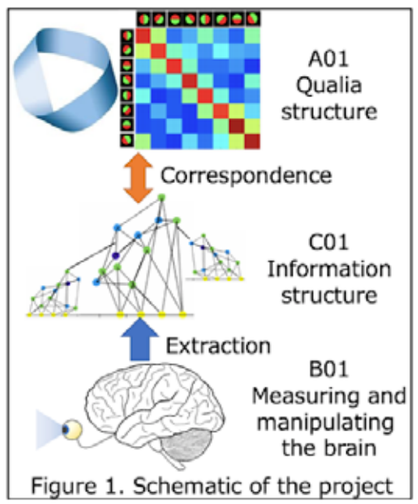


Figure 1. Schematic of the project

Davidson, M. J., Mithen, W., Hogendoorn, H., van Boxtel, J. J., Tsuchiya, N, (2020) The SSVEP tracks attention, not consciousness, during perceptual filling-in eLife 2020;9:e60031 DOI: 10.7554/eLife.60031 https://www.cibf.edu.au/attention-not-perception

COGNITIVE NEUROIMAGING LAB

TEAM

Dr Sharna Jamadar
Head, Cognitive Neuroimaging Lab

Dr Phillip Ward
Research Fellow

Students
Ms Winnie Orchard
Ms Emma Liang
Ms Ashlea Segal
Mr Eric Xu
Ms Disha Sasan

USING NEUROSCIENCE TO CREATE HEALTHY HABITS, BRAINS AND COMMUNITIES

The Cognitive Neuroimaging Lab investigates how our life experiences change our brains. The group brings together experts in cognitive neuroscience, physiology and neuroimaging methods to understand brain function in health and disease. We have core interests in examining resilience to the ageing process, and the neuroscience of parenthood across the lifespan.

In 2020, we made significant progress in the development of simultaneous MRI-PET as a tool to study human brain function. We published the first study of 'metabolic connectivity' in the human brain. While functional connectivity measures coherence of the fMRI blood oxygenation signal across the brain, metabolic connectivity measures coherence of glucose metabolism across the brain. Simultaneous MR-PET allows the simultaneous measurement of both types of connectivity, thereby measuring the spatiotemporal dynamics of the two primary sources of energy in the brain, oxygen and glucose. Supported by our ARC Linkage Project with Siemens, we – together with the Image Analysis team – made our simultaneous MR-PET data publicly available.

In 2020, we also made significant progress in the study of human parenthood. We published the first scientific description of 'phantom kicks' – phantom foetal kicks that up to 2 in 5 mothers experience long after the birth of their child. We also published the first fMRI study of the effects of parenthood in the late life brain. Winnie Orchard found that the patterns of functional connectivity in older adults indicates that motherhood may be beneficial for brain function in late life.

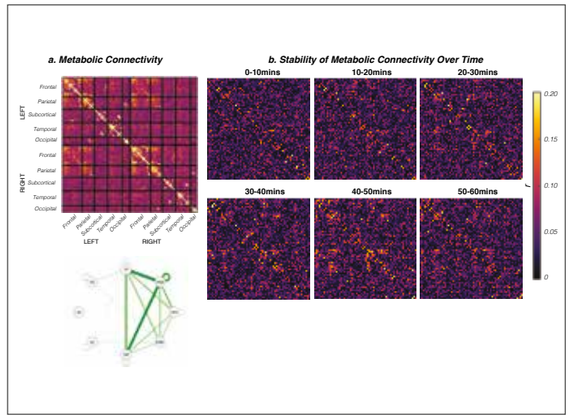
HIGHLIGHTS AND ACHIEVEMENTS

- Continued development of simultaneous MRI-PET as a tool to study human brain function
- Release of two simultaneous MRI-PET datasets on the OpenNeuro platform. The Monash rsPET-MR and Monash vis-fPET-fMRI datasets represent the only publicly-available simultaneous MRI-PET datasets. The Monash rsPET-MR dataset quickly became the most downloaded PET dataset on the platform
- We discovered that individual levels of haemoglobin in the blood significantly affect fMRI measures of functional connectivity. This finding has significant implications for people using fMRI as a tool to study brain function, and a number of scientists now measure and control for haemoglobin levels in their studies
- In a surprising result, we found that the leading quantitative model of cognitive compensation in older adults could not account for age-related fMRI changes during visuospatial working memory. Moreover, a statistical test of publication bias revealed only 4 published studies had ever statistically demonstrated the effect, indicating that much more work is required to validate and test the reproducibility of models of compensation
- We discovered that around 2 in 5 women experience 'phantom' foetal kicks after pregnancy – up to 24 years after the end of pregnancy. This work was highlighted as having significant implications for obstetric care in a commentary published in response to our article
- We discovered that parenthood has a protective effect in late life, with the number of children a woman has parented associated with cortical structural and functional measures more similar to younger than older brains
- Our parental brain research garnered significant media attention. Winnie Orchard made numerous media appearances, including Channel 7 Sunrise, Channel 10 Studio 10 and the ABC Health Report with Normal Swan. Collectively, Winnie's media appearances reached over 1.6million people in 2020

CASE STUDY

Simultaneous MR-PET of Resting Brain Connectivity

In this ARC Linkage Project with Siemens Healthineers and Forschungszentrum Jülich, we have pioneered the first simultaneous MR-PET study of functional and metabolic brain connectivity in humans, using the MBI 3T Siemens Biograph mMR. Functional connectivity is most commonly measured using functional MRI (fMRI) in humans. fMRI functional connectivity measures the coherence of blood oxygenation level dependent signals across the brain, and has been hugely significant for understanding network connectivity in the brain. However, fMRI-based measures of functional connectivity provide insight into only one aspect of brain connectivity, that based on the coherence of oxygenated signals. Positron emission tomography (PET) measures using the glucose analogue [18F]fluorodeoxyglucose (FDG) provide insight into the metabolic basis of brain connectivity. Drawing upon significant technical development work that we and others have made in high temporal resolution FDG-PET imaging, we measured the coherence of glucose uptake across the brain in young healthy individuals. We found that metabolic connectivity is most prominent in the frontoparietal cortices, and is related to individual differences in executive function. We released this dataset publicly on the OpenNeuro platform (ds002898) and it quickly became the most-downloaded PET dataset on the platform, with over 170 downloads to date. Our technical validation of the dataset published in Nature Scientific Data illustrated core technical features of the metabolic connectome: defining the effects of spatiotemporal filtering, and the stability of the connectome across time. This important work provides the framework for future studies of the metabolic aspects of brain connectivity.



The metabolic connectome. (a) the metabolic connectome primarily shows frontoparietal connectivity (top). The network graph reflects this connectivity pattern, with networks within the frontoparietal cortices showing the strongest connectivity, including the frontoparietal network, dorsal and ventral attention networks, sensorimotor network, and default mode network. (b) Across a 60min scan, the structure of the metabolic connectome emerges only later in the scan, at the time when plasma radioactivity measures are the most stable.

COMPUTATIONAL AND SYSTEMS NEUROSCIENCE LAB

TEAM

A/Prof Adeel Razi
Head

Dr Leonardo Novelli
Research Fellow

A/Prof. Sadia Shakil
Adjunct Research Associate

Ms Garance Delagneau
Research Assistant

Mr Sid Chopra
Research Assistant

PhD Students

Mr Devon Stoliker

Mr Lingbin Bian

Mr. Aswin Paul

Honours Student

M. Hannah Cummins

Our lab's research vision is to perform cross-disciplinary research combining engineering, physics, and machine-learning approaches to answer questions that are motivated by and grounded in neurobiology. This will enable us to go beyond the traditional boundaries in order to understand how the brain implements cognition.

Our research program's priority areas include:

- development of multi-modal (e.g., functional MRI, diffusion MRI, EEG) and multi-scale Bayesian methods to characterise brain network dynamics and how these dynamics reorganise with different brain pathologies;
- development of neuroscience-inspired artificial intelligence schemes to understand how brain performs reasoning, learning and planning;
- use of classical psychedelics (e.g. LSD and Psilocybin) in combination with computational modelling to understand neural mechanisms underlying altered states of consciousness.

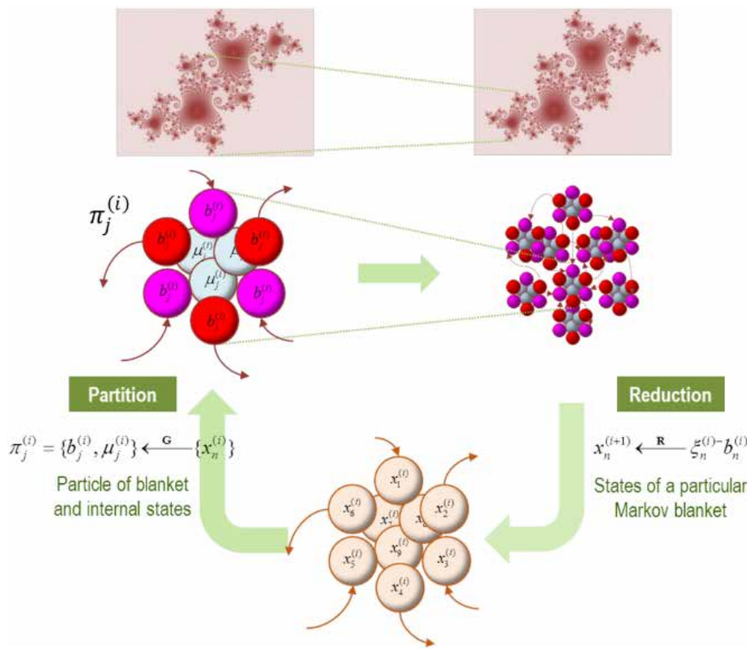
HIGHLIGHTS AND ACHIEVEMENTS

- Dr Razi was awarded a 5 year NHMRC Investigator Fellowship (Emerging Leadership). He will start his Fellowship in January 2021.
- Dr Razi was awarded an Australian Research Council's 'Discovery Project' grant "Multiscale and multimodal modelling of brain dynamics" together with Andrew Zalesky and Karl Friston, which commenced in October 2020.
- Dr Razi was selected as the CIFAR Azrieli Global Scholar in the Brain, Mind and Consciousness program, which will be effective from 2021 -2023.

CASE STUDY

Multi-scale analysis of human brain networks

At the inception of human brain mapping, two principles of functional anatomy underwrote most conceptions—and analyses—of distributed brain responses: namely, functional segregation and integration. There are currently two main approaches to characterizing functional integration. The first is a mechanistic modelling of connectomics in terms of directed effective connectivity that mediates neuronal message passing and dynamics on neuronal circuits. The second phenomenological approach usually characterizes undirected functional connectivity (i.e., measurable correlations), in terms of intrinsic brain networks, self-organized criticality, dynamical instability, and so on. This project investigates a treatment of effective connectivity that speaks to the emergence of intrinsic brain networks and critical dynamics. It is predicated on the notion of Markov blankets that play a fundamental role in the self-organization of far from equilibrium systems. Using the apparatus of the renormalization group, we show that much of the phenomenology found in network neuroscience is an emergent property of a particular partition of neuronal states, over progressively coarser scales. As such, it offers a way of linking dynamics on directed graphs to the phenomenology of intrinsic brain networks. This work is in collaboration with the Wellcome Centre for Human Neuroimaging at University College London.



Blankets of blankets. This schematic illustrates the recursive procedure by which successively coarser scale (and slower) dynamics arise from subordinate levels in a complex system of interacting elements. Here we use renormalisation group theory for scale-invariant transitions between multiple scales or levels.

MECHANISMS OF NEURODEGENERATION LAB

TEAM

Dr Ian Harding
Head, Mechanisms on Neurodegeneration Lab

Dr Rebecca Kerestes
Research Fellow

Dr Louisa Selvadurai
Research Manager

Dr Will Khan
Research Scientist

Students

Ms Jo Wrigglesworth

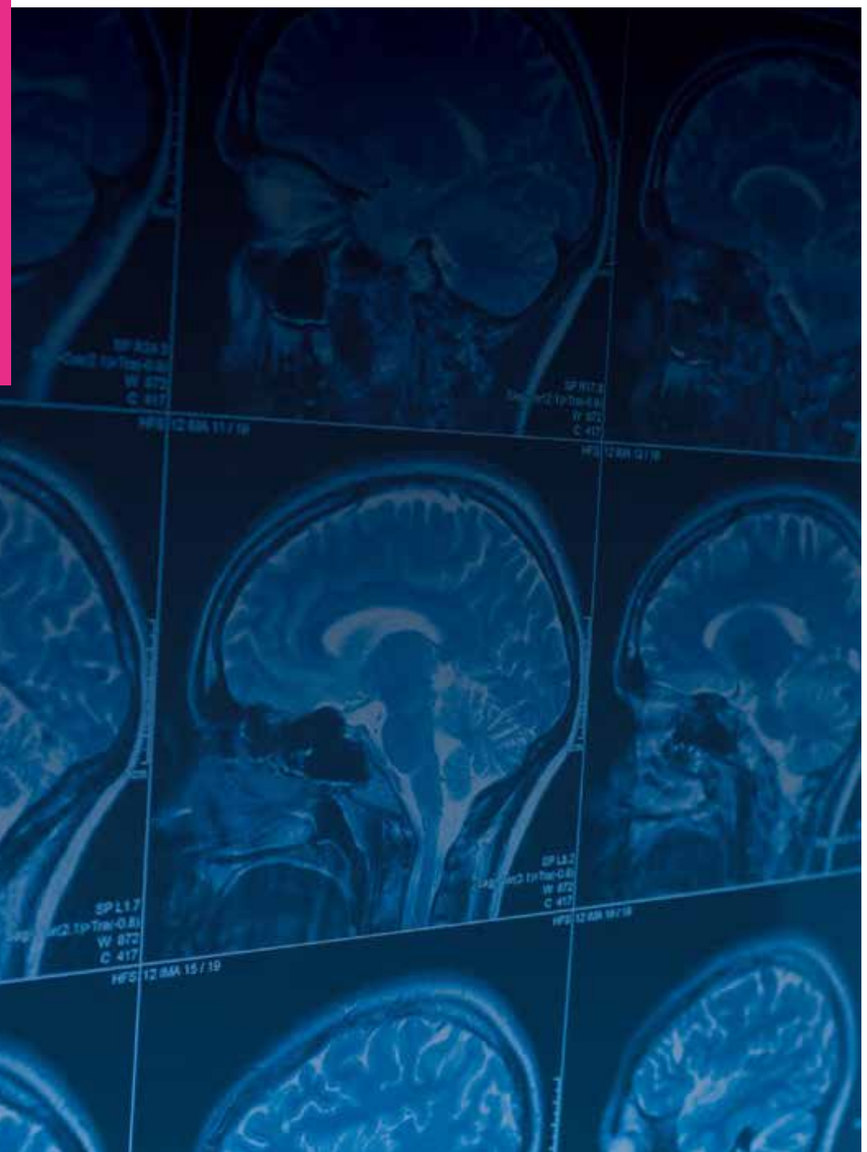
Ms Hiba Bilal

Mr Ikhsan Nur Karim

Mr Tom Biczok

The Mechanisms of Neurodegeneration research group uses magnetic resonance imaging (MRI) and positron emission tomography (PET) to investigate and track brain changes in people with neurodegenerative diseases. This work principally focuses on individuals with inherited subcortical diseases, including Friedreich ataxia, Spinocerebellar ataxias, and Huntington's disease. Additional work in other neurodegenerative disorders and in preclinical animal models is also being undertaken with our collaborators.

The broad aims of our research include biological phenotyping, such as describing changes in brain structure and function, and mechanistic inferences, including cellular/molecular-level measurements of inflammation, oxidative stress, and metabolic dysfunction. Our studies seek to provide more comprehensive disease descriptions and to identify measures relevant to tracking disease progression or treatment efficacy.



HIGHLIGHTS AND ACHIEVEMENTS

- First-in-disease PET scans targeting neuroinflammation and oxidative stress in people with inherited movement disorders (including Friedreich ataxia and Huntington's disease)
- Launched a pioneering approach for remote assessment of motor, cognitive, and speech function in people with inherited movement disorders
- First outputs generated from an international collaboration to aggregate MRI data in rare diseases (ENIGMA-Ataxia)
- Awarded >$5M in new funding for imaging projects in ataxias and COVID19

CASE STUDY

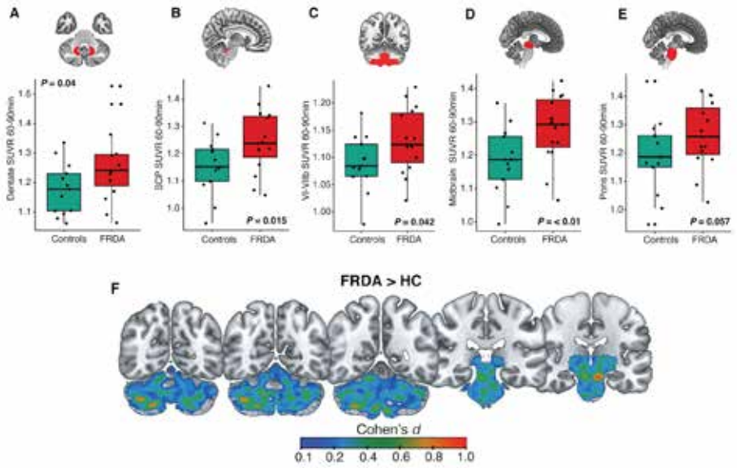
Neuroinflammation in Inherited Movement Disorders

Our flagship research program uses hybrid MR/PET technology, investigational PET radiotracers, and blood markers to investigate pathological processes and sub-cellular measures of disease expression and progression.

Increased immune activity in the brain is proposed to accompany, or even contribute to, neuropathology in many neurodegenerative diseases, with implications for disease treatment and tracking. In 2020 we completed a study of neuroinflammation in Friedreich ataxia (FRDA), an inherited neurodegenerative movement disorder that targets the cerebellum of the brain. This study was conducted with funding support from the Friedreich Ataxia Research Alliance, an international philanthropic organisation. Using the MBI PET/MR scanner and the radiotracer [18F]-FEMPA, which binds to activated immune cells in the brain, we undertook a first-in-disease study of immune activity in the brain.

In 15 individuals with FRDA relative to 13 healthy controls, we found evidence for increased neuroinflammation in areas of known pathology. These changes correlated with disease progression. In parallel, we also found evidence of increased levels of the cytokine IL-6 in blood plasma. These findings indicate that altered immune activity is evident in both the brain and body of people with FRDA.

Further work to determine how immune activity is related to neurodegeneration in FRDA is necessary to determine its potential viability as a treatment or treatment monitoring target.



Boxplots showing increased [18F]-FEMPA uptake in individuals with FRDA compared to controls in (A) the dentate nuclei, (B) superior cerebellar peduncles, (C) inferior-posterior cerebellar (VI-VIIb) lobe, (D) midbrain, and (E) pons. Voxel-level coronal views of the Cohen's d effect size map (F) provides a complementary depiction. FRDA = Friedreich ataxia, HC = healthy controls.

Citation: Khan W, Corben LA, Bilal H, Vivash L, Delatycki MB, Egan GF, Harding IH. (In Press). Neuroinflammation in the cerebellum and brain-stem in Friedreich ataxia: an [18F]-FEMPA PET study. Movement Disorders.

NEUROSCIENCE AND SOCIETY GROUP

TEAM

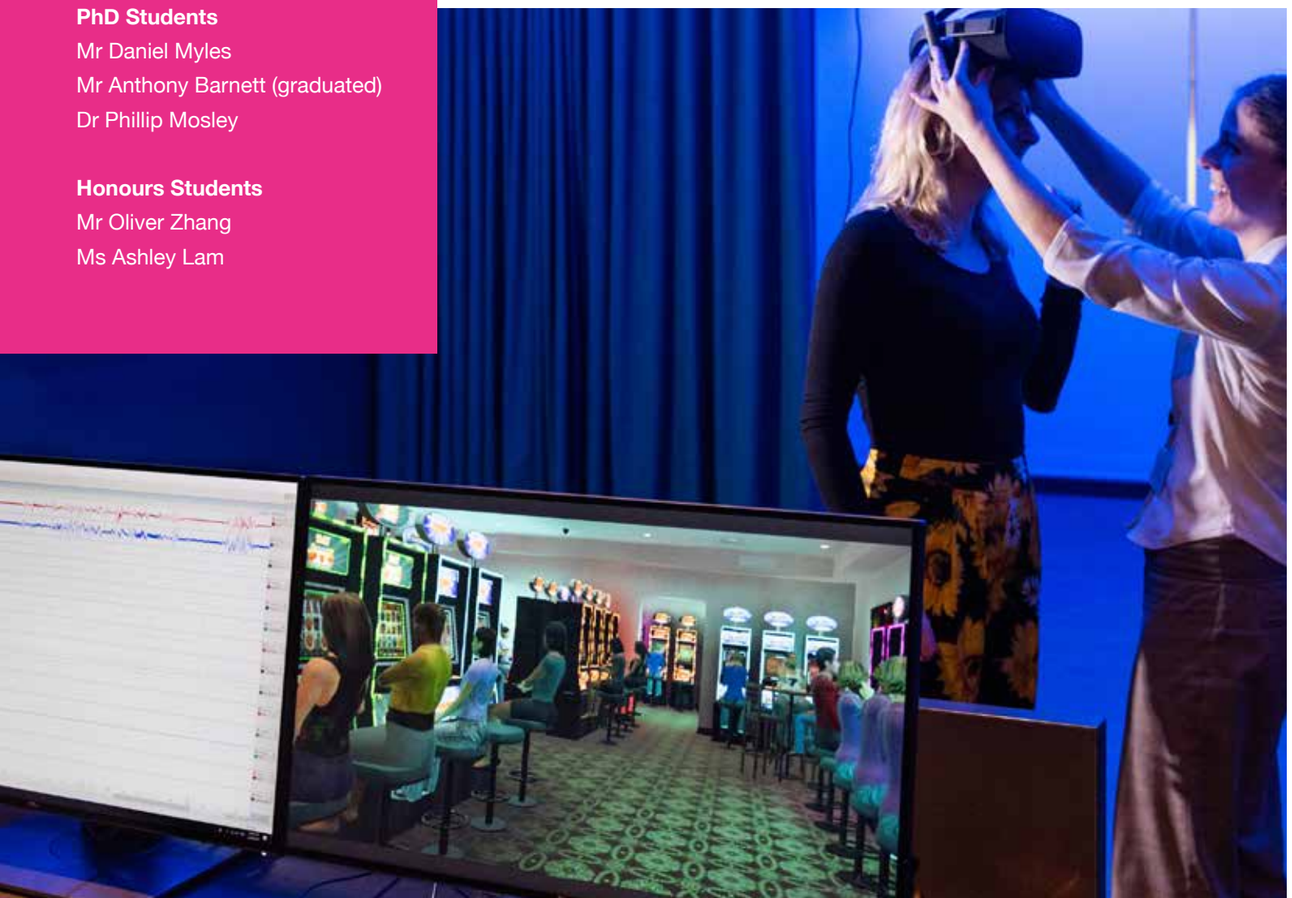
A/Prof Adrian Carter
Head, Neuroscience and Society Group
Dr Andrew Dawson
Postdoctoral Research Fellow

Clinical PhD Students
Mr Patrick Haylock
Ms Michaela Barber
Ms Sarah Haines
Ms Victoria Gentile
Ms Theoni Whyman
Ms Cassandra Thomson (graduated)
Ms Alison Cullen (graduated)

PhD Students
Mr Daniel Myles
Mr Anthony Barnett (graduated)
Dr Phillip Mosley

Honours Students
Mr Oliver Zhang
Ms Ashley Lam

The Neuroscience and Society Group is a collection of interdisciplinary researchers and practitioners examining the impact of neuroscience research and technology on society. The group includes expertise from neuroscience, psychology, social science, philosophy, ethics and public health. Our principle aim is to ensure the responsible research, innovation and use of emerging neurotechnologies, including brain computer interfaces, deep brain stimulation, direct-to-consumer brain recording and stimulating devices, psychedelic drugs, and remote sensors. Neuroscience research and the new technologies that it produces can have unexpected and harmful effects on end-users that slows the effective translation of these technologies into society. Our researchers engage with a range of communities and stakeholders involved in the development and use of neurotechnologies to ensure that they meet the needs of all end-users, yielding optimal benefit, while meeting societal norms and values. Community engagement is also key to foster public support for the use of technologies that can raise ethical concerns, including privacy, discrimination, impacts on agency, autonomy and identity, coercion, surveillance and fairness. We also work with stakeholders to ensure the effective governance and regulation of emerging technologies in a way that supports and guides innovation while reflecting public values. The Neuroscience and Society Group has productive collaborations with scientists, engineers and developers, and clinical and legal practitioners across Monash, including those at Monash Biomedical Imaging, BrainPark, Monash Institute for Medical Engineering, Monash Vision Group, Monash Data Futures Institute, the National Centre for Healthy Ageing, as well as leading groups across the country and globally.



HIGHLIGHTS AND ACHIEVEMENTS

- Associate Professor Adrian Carter was an elected member of the Board of the Directors for the International Neuroethics Society
- Associate Professor Adrian Carter chaired the Program Committee for the INS Annual Meeting. The meeting was the largest in the history of the Society. We doubled the number of registrations (>350) and the number of countries from which people attended (>30), whilst running the first virtual meeting during a global pandemic. We also held an INS and IEEE-Brain joint international public event 'I am Human' about the impact of brain computer interfaces on society, initiating an enduring partnership between these two organisations. This event received >650 registrants, including >200 from industry
- Associate Professor Adrian Carter was invited to be Editor-in-Chief of the journal Neuroethics (Springer)
- Graduated 3 PhD students
- Mr Daniel Myles was awarded a prestigious PhD top-up scholarship and project funds from the NSW Office of Responsible Gambling ($44k) to investigate losses disguised as wins; a controversial feature of electronic gambling machine design

CASE STUDY

Misleading, Illusory and Deceptive: An Analysis of Losses Disguised as Wins in Electronic Gambling Machines

This project explores a contentious design feature of electronic gambling machines (EGMs) known as "losses disguised as wins" (LDWs). LDWs occur when a gambling product pays out less than an initial wager and yet celebrates the outcome as though it were a genuine win—despite it being a loss. These deceptive features of EGMs keep gamblers gambling for longer and are thought to contribute to the addictive nature of the machines.

Our aim is to provide additional evidence that LDWs are often mistaken for genuine gains and increase the rate or intensity of reinforcement during EGM gambling. If this is the case LDWs likely contribute to gambling addiction or harm, and further, would suggest that current designs are inconsistent with Australian Consumer Law and the Australian Gaming Machine National Standard, which states that an EGM design must "not be misleading, illusory or deceptive".

We are employing a number of methodologies in pursuit of these aims, including an event-related EEG study (electroencephalography) in partnership with the Decision Neuroscience Laboratory at the University of Melbourne, online behavioural studies, and a collaboration with researchers at BrainPark developing a VR gambling program for use as a clinical tool and to assess the impact of proposed changes in EGM regulation and policy. We are also collaborating with colleagues at the Monash School of Social Sciences on a study to determine whether explaining the LDW design feature to a representative community sample increases interest or support for regulatory change or shifts attitudes towards EGM gambling. When completed, these studies will provide new evidence supporting changes in policy and regulation of EGMs that will reduce gambling harm.

PUBLICATIONS

Description: Magnetic Particle Imaging of Xenograft Mouse

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Monash Neuroscience of Consciousness Lab Journal Articles

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Haun, A., Tsuchiya, N. (2020). Reasonable criteria for functionalists; scarce criteria from phenomenological perspective. *Cogn Neurosci*, 12(2): 95-96. doi:10.1080/17588928.2020.1838473.

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Schauer, G., Ogawa, C.Y., Tsuchiya, N., et al. (2020). Conscious perception of flickering stimuli in binocular rivalry and continuous flash suppression is not affected by tACS-induced SSR modulation. *Conscious Cogn*, 82: 102953. doi:10.1016/j.concog.2020.102953.

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Tsuchiya, N., Saigo, H. (2020). What does it mean to enrich the definition of consciousness in consciousness research using (enriched) category theory? OSF Preprint. doi:10.31219/osf.io/87e96.

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COGNITIVE NEUROIMAGING LAB JOURNAL ARTICLES

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Orchard, E.R., Ward, P., Sforazzini, F., et al. (2020). Relationship between parenthood and cortical thickness in late adulthood. *PloS one*, 15(7): e0236031. doi:10.1371/journal.pone.0236031.

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Soloveva, M.V., Jamadar, S.D., Hughes, M., et al. (2020). Brain compensation during response inhibition in premanifest Huntington's disease. *Brain Cogn*, 141: 105560.doi:10.1016/j.bandc.2020.105560.

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COMPUTATIONAL AND SYSTEMS NEUROSCIENCE LAB JOURNAL ARTICLES

Adamson, M.M., Shakil, S., Sultana, T., et al. (2020). Brain Injury and Dementia in Pakistan: Current Perspectives. *Front Neurol*, 11: 299. doi:10.3389/fneur.2020.00299.

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Palacios, E.R., Razi, A., Parr, T., et al. (2020). On Markov blankets and hierarchical self-organisation. *J Theor Biol,* 486: 110089. doi:10.1016/j.jtbi.2019.110089.

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MECHANISMS ON NEURODEGENERATION LAB JOURNAL ARTICLES

Harding, I.H., Lynch, D.R., Koeppen, A.H., et al. (2020). Central Nervous System Therapeutic Targets in Friedreich Ataxia. *Hum Gene Ther*, 31(23-24): 1226-1236. doi:10.1089/hum.2020.264.

Öz, G., Harding, I.H., Krahe, J., et al. (2020). MR imaging and spectroscopy in degenerative ataxias: toward multimodal, multisite, multistage monitoring of neurodegeneration. *Curr Opin Neurol*, 33(4): 451-461. doi:10.1097/WCO.0000000000000834.

Thompson, P.M., Jahanshad, N., Ching, C., et al. (2020). ENIGMA and global neuroscience: A decade of large-scale studies of the brain in health and disease across more than 40 countries. *Transl Psychiatry*, 10(1): 100. doi:10.1038/s41398-020-0705-1.

Wang, Y., Harding, I.H., Testa, R., et al. (2020). Structural and functional brain abnormalities in children with schizotypal disorder: a pilot study. *NPJ Schizophr*, 6(1): 6. doi:10.1038/s41537-020-0095-7.

NEUROSCIENCE AND SOCIETY GROUP BOOK CHAPTERS

Barnett, A., Hall, W., Carter, A. (2020). Disease, wellness, and addiction: A global perspective, in *Global Mental Health and Neuroethics*, D. Stein, I. Singh (Ed). Amsterdam: Elsevier. p. 211-224.

Dawson, A., Hall, W., Carter, A. (2020). Cognitive research on addiction in a changing policy landscape, in *Cognition and Addiction*, A. Verdejo-Garcia (Ed). Amsterdam: Elsevier. p. 321-329.

NEUROSCIENCE AND SOCIETY GROUP JOURNAL ARTICLES

Barber, M., Gardner, J., Savic, M., et al. (2020). Ibogaine therapy for addiction: Consumer views from online fora. *Int J Drug Policy*, 83: 102857. doi:10.1016/j.drugpo.2020.102857.

Barnett, A., O'Brien, K., Hall, W., et al. (2020). Support for the psychosocial, disease and brain disease models of addiction: A survey of treatment providers' attitudes in Australia, the UK, and U.S. *J Subst Abuse Treat*, 115: 108033. doi:10.1016/j.jsat.2020.108033.

Barnett, A., Savic, M., Pienaar, K., et al. (2020). Enacting 'more-than-human' care: Clients' and counsellors' views on the multiple affordances of chatbots in alcohol and other drug counselling. *Int J Drug Policy*, 94: 102910. doi:10.1016/j.drugpo.2020.102910.

Barnett, A.I., Pickersgill, M., Dilkes-Frayne, E., et al. (2020). Neural imaginaries at work: Exploring Australian addiction treatment providers' selective representations of the brain in clinical practice. *Soc Sci Med*, 255: 112977. doi:10.1016/j.socscimed.2020.112977.

Bouguettaya, A., Lynott, D., Carter, A., et al. (2020). The relationship between gambling advertising and gambling attitudes, intentions and behaviours: a critical and meta-analytic review. *Curr Opin Behav Sci*, 31: 89-101. doi:10.1016/j.cobeha.2020.02.010.

Burrows, T., Verdejo-Garcia, A., Carter, A., et al. (2020). Health Professionals' and Health Professional Trainees' Views on Addictive Eating Behaviours: A Cross-Sectional Survey. *Nutrients*, 12(9): 2860. doi:10.3390/nu12092860.

Carter, A., Hardman, C.A., Burrows, T. (2020). Food Addiction and Eating Addiction: Scientific Advances and Their Clinical, Social and Policy Implications. *Nutrients*, 12(5): 1485. doi:10.3390/nu12051485.

Haines, S., Savic, M., Picco, L., et al. (2020). Unintended consequences of using real time prescription monitoring systems. *Med J Aust*, 213(3): 142.e1. doi:10.5694/mja2.50616.

Maltman, K., Savic, M., Manning, V., et al. (2020). 'Holding on' and 'letting go': a thematic analysis of Australian parent's styles of coping with their adult child's methamphetamine use. *Addict Res Behav*, 28(4): 345-353. doi:10.1080/16066359.2019.1655547.

O'Brien, K.S., Puhl, R.M., Latner, J.D., et al. (2020). The Effect of a Food Addiction Explanation Model for Weight Control and Obesity on Weight Stigma. *Nutrients*, 12(2): 294. doi:10.3390/nu12020294.

Thomson, C., Carter, A. (2020). Ethical issues in experimental treatments for psychiatric disorders: Lessons from deep brain stimulation. *Transl Issues Psychol Sci*, 6(3): 240-246. doi:10.1037/tps0000267.

Thomson, C.J., Segrave, R.A., Racine, E., et al. (2020). "He's Back so I'm Not Alone": The Impact of Deep Brain Stimulation on Personality, Self, and Relationships in Parkinson's Disease. *Qual Health Res*, 30(14): 2217-2233. doi:10.1177/1049732320951144.

WRIGHT LAB JOURNAL ARTICLES

Christensen, J., Wright, D.K., Yamakawa, G.R., et al. (2020). Repetitive Mild Traumatic Brain Injury Alters Glymphatic Clearance Rates in Limbic Structures of Adolescent Female Rats. *Sci Rep*, 10(1): 6254. doi:10.1038/s41598-020-63022-7.

Eyolfson, E., Carr, T., Khan, A., et al. (2020). Repetitive Mild Traumatic Brain Injuries in Mice during Adolescence Cause Sexually Dimorphic Behavioral Deficits and Neuroinflammatory Dynamics. *J Neurotrauma*, 37(24): 2718-2732. doi:10.1089/neu.2020.7195.

Lee, N.T., Selan, C., Chia, J., et al. (2020). Characterization of a novel model of global forebrain ischaemia-reperfusion injury in mice and comparison with focal ischaemic and haemorrhagic stroke. *Sci Rep*, 10(1): 18170. doi:10.1038/s41598-020-75034-4.

Pham, L., Wright, D.K., O'Brien, W.T., et al. (2020). Behavioral, axonal, and proteomic alterations following repeated mild traumatic brain injury: Novel insights using a clinically relevant rat model. *Neurobiol Dis*, 148: 105151. doi:10.1016/j.nbd.2020.105151.

Symons, G.F., Clough, M., Fielding, J., et al. (2020). The Neurological Consequences of Engaging in Australian Collision Sports. *J Neurotrauma*, 37(5): 792-809. doi:10.1089/neu.2019.6884.

Symons, G.F., Clough, M., O'Brien, W.T., et al. (2020). Shortened telomeres and serum protein biomarker abnormalities in collision sport athletes regardless of concussion history and sex. *J Concussion*, 4: 1-11. doi:10.1177/2059700220975609.

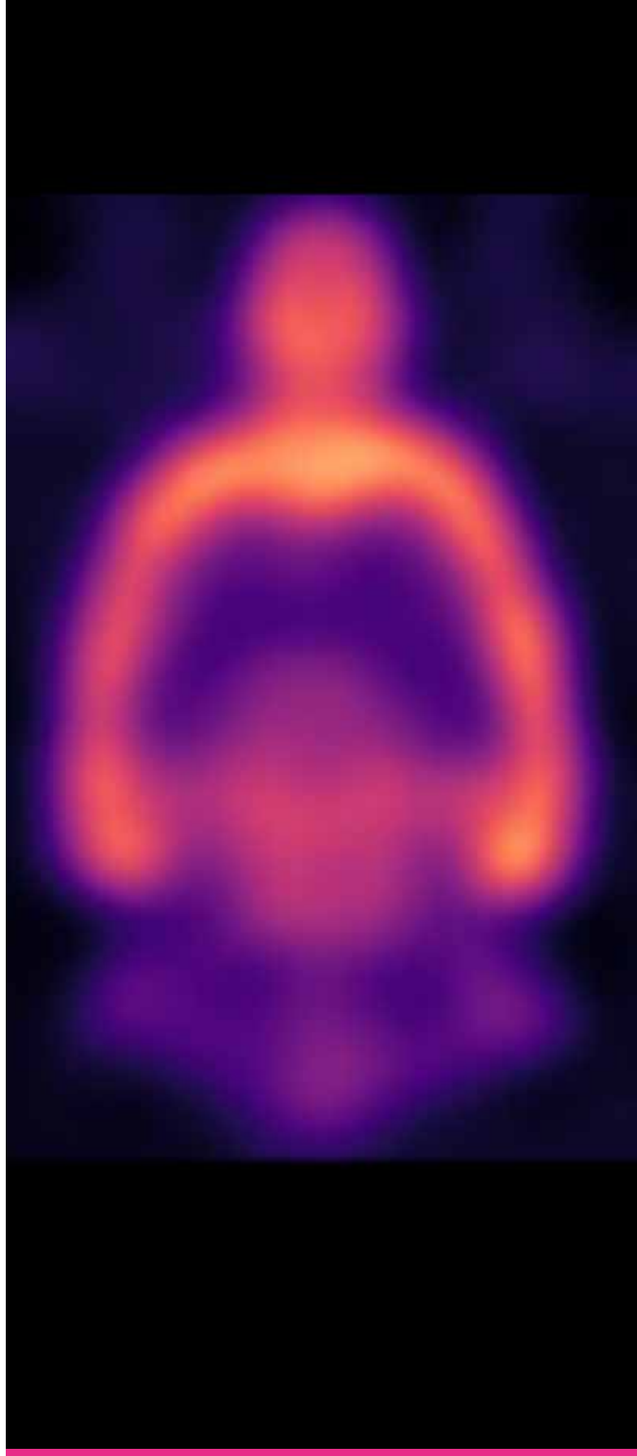
Tabor, J., Wright, D.K., Christensen, J., et al. (2020). Examining the Effects of Anabolic-Androgenic Steroids on Repetitive Mild Traumatic Brain Injury (RmTBI) Outcomes in Adolescent Rats. *Brain Sci*, 10(5): 258. doi:10.3390/brainsci10050258.

Wright, D.K., Mayo, J.N., Sun, M., et al. (2020). Contrast enhanced magnetic resonance imaging highlights neurovasculature changes following experimental traumatic brain injury in the rat. *Sci Rep*, 10(1): 21252. doi:10.1038/s41598-020-77975-2.

Yaghmaie, N., Syeda, W.T., Wu, C., et al. (2020). QSMART: Quantitative susceptibility mapping artifact reduction technique. *NeuroImage*, In press. doi:10.1016/j.neuroimage.2020.117701.

Zamani, A., O'Brien, T.J., Kershaw, J., et al. (2020). White matter changes following experimental pediatric traumatic brain injury: an advanced diffusion-weighted imaging investigation. *Brain Imaging Behav*, In press. doi:10.1007/s11682-020-00433-0.

Zamani, A., Ryan, N.P., Wright, D.K., et al. (2020). The Impact of Traumatic Injury to the Immature Human Brain: A Scoping Review with Insights from Advanced Structural Neuroimaging. *J Neurotrauma*, 37(5): 724-738. doi:10.1089/neu.2019.6895.



Description: [18F]-flumazenil uptake in the rat brain (2021)
Researcher: Bianca Jupp
Sanner: Mediso nanoScan PET/CT

GRANTS

MBI

Bachmann, M., Egan, G.F., Kopka, K., et al. (2021-2025). MHELTHERA - Monash Helmholtz Theranostics Joint International Laboratory. *Helmholtz Association (Germany)*, $2,430,000.

Bourne, J., Leopold, D., Egan, G.F. (2018-2021). The pulvinar drives visual cortical development and plasticity in early life. *NHMRC Project Grant*, $1,230,780.

Chen, Z., Egan, G.E., Law, M., et al. (2021-2023). Biophysics-informed deep learning framework for magnetic resonance imaging. *ARC Discovery Project*, $518,700.

Chen, Z., Pawar, K., Egan, G.E. (2018-2020). Development of motion correction strategy for quantitative MR-PET imaging. *Siemens*, $195,000.

Egan, G., Rosa, M., Lowery, A., et al. (2014-2020). Centre of Excellence for Integrative Brain Function. *ARC Centre of Excellence*, $20,000,000.

Egan, G.E., Jamadar, S.D., Chen, Z., et al. (2018-2022). Simultaneous to synergistic MR-PET: integrative brain imaging technologies. *ARC Linkage Project*, $673,460.

Egan, G.F., de Veer, M., Puttick, S., et al. (2020-2022). Developing more effective targeted therapy for high grade glioma with MR guided focussed ultrasound. *CSRIO,* $254,550.

Egan, G.F., Porter, C., Andrews, P., et al. (2019-2020). Network of Excellence in Molecular Imaging and Radiopharmaceuticals. *Monash University*, $191,000.

Holloway, L., Chen, Z. (2021-2023). Australian Cancer Data Network: distributed learning from clinical data. *Australian Research Data Commons*, $957,859.

BRAINPARK

Lee, R. (2021-2025). To utilise a purpose-built mhealth tool to understand drivers of addiction and to improve treatment engagement and outcomes. *Medical Research Future Fund*, $645,205.

Myles, D. (2020). Combining BrainPark's Virtual Reality with methodologies from experimental psychology and cognitive neuroscience, under a public health and community perspective. *NSW Office of Responsible Gambling, Gambling Research Capacity Grant*, $44,000.
Richardson, K. (2020). Training Scholarship. *International Behavioural Trials Network.*

Segrave, R., Richardson, K. (2020). PEAK: Enabling peak mental wellbeing, cognitive performance and brain health. *NIB Health Smart Grant*, $40,000.

Yucel, M., Albertella, L., Lee, R. (2020). To develop a neuropsychological assessment for cognitive fitness and tools to guide peak performance under challenging conditions. *Department of Defence (Science and Technology)*, $110,000.

NEURAL SYSTEMS AND BEHAVIOUR LAB

Fornito, A. (2020-2025). A network approach to mapping and modifying brain changes in psychosis. *NHMRC Investigator Grant,* $2,163,244.

MONASH NEUROSCIENCE Of CONSCIOUSNESS LAB

Andrillon, T. (2018-2020). The origin of thoughts: neural mechanisms of spontaneous thought generation in wakefulness and sleep. *HFSP Long-Term Fellowship*

Andrillon, T. (2020-2024). Fathoming sleep depth: a novel approach to the understanding and assessing of sleep-state misperception in insomnia. *NHMRC Early Career Fellowship*, $327,000.

Andrillon, T., Windt, J., Bei, B. (2018-2020). Are wake and sleep intertwined phenomena? Insights from EEG experiments in humans. *Monash University Platform Access Grant*, $14,700.

Garrido, M., Tsuchiya, N., Rustishauser, U., et al. (2018-2020). Multimodal testing for a fast subcortical route for salient visual stimuli. *ARC Discovery Project*, $414,792.

Koizumi, A., Tsuchiya, N. (2018-2021). Discovery of the neuronal mechanisms within sensory cortical areas that supports fear memory. *Japan Society for the Promotion of Science*, 3,510,000 JPY.

Tsuchiya, N. (2020). 250,000 CPU-core hours. *National Computational Merit Allocation Scheme*, $30,000 In kind.

Tsuchiya, N., Arabzadeh, E., Kheradpezouh, E., et al. (2019-2020). Computing integrated information across behavioural states with single-neuron activity recorded by 2-photon calcium imaging from rodent somatosensory cortex. *ARC Centre for Integrative Brain Function Strategic Initiative Project*, $5,000.
Tsuchiya, N., Fulcher, B., Carter, A., et al. (2020-2024). Integrating theory-guided and data-driven approaches for measuring consciousness. *NHMRC Ideas Grant*, $1,042,607.

Tsuchiya, N., Modi, K., Pollock, F., et al. (2020). Intelligence and consciousness in the physical world. *FQXi Foundational Questions Institute mini grant*, $8,050 USD.

Tsuchiya, N., Oizumi, M., Kawasaki, H., et al. (2018-2020). Neural origins of conscious perception in no-report paradigms. *ARC Discovery Project*, $314,286.

Tsuchiya, N., Phillips, Saigo, H. (2020-2022). Consciousness in the physical world. *FQXi Foundational Questions Institute*, $75,900 USD

Tsuchiya, N., Yamada, Oizumi, M. (2020-2023). Understanding the relationship between the structure of qualia and information. *Japan Society for the Promotion of Science*, 69,440,000 JPY.

COGNITIVE NEUROIMAGING LAB

Jamadar, S.D. (2020-2024). Neural metabolic connectivity in ageing and neurodegeneration. *NHMRC Emerging Leader Fellowship*, $625,480.

Karayanidis, F., Fabiani, M., Gratton, G., et al. (2020-2022). Linking arterial, brain and cognitive integrity in healthy older adults. *ARC Discovery Project,* $539,000.

Ward, P. (2020-2024). A connectomic approach to understanding cerebrovascular disease in the elderly. *NHMRC Emerging Leader Fellowship*, $639,750.

COMPUTATIONAL AND SYSTEMS NEUROSCIENCE LAB

Razi, A. (2021-2025). Understanding early stage neurodegeneration using computational modelling. *NHMRC Investigator Grant*, $624,000.

Razi, A., Foldi, C., Howhy, J. (2020). Insights into the therapeutic potential of psychedelic medicine for anorexia nervosa: from reinforcement learning and adaptive behaviour to consciousness and self. *Monash University Arts/MNHS Interdisciplinary Research Scheme* $23,163.

Razi, A., Verdejo-Garcia, A. (2020-2021). Treating obesity with brain stimulation. *Monash University Strategic Support Funds*, $40,000.
Razi, A., Zalesky, A., Friston, K. (2020-2023). Multiscale and multimodal modelling of brain dynamics. *ARC Discovery Project*, $525,000.

MECHANISMS ON NEURODEGENERATION LAB

Anderson, C., Zoungas, S., Naismith, S., et al. (2021-2023). Statin Treatment for COVID-19 to Optimise Neurological Recovery (STRONGER) Trial. *Medical Research Future Fund COVID19* $2,375,779.

Diciotti, S., Mascalchi, M., Harding, I.H. (2020-2021). Artificial Intelligence for individual profiling and prediction: probing the FractaL dimension of brain MRI in FriEdreich ataXia and SCAs using the ENIGMA-Ataxia international meta-dataset (FLEX-AI). *Italian Association for Ataxia,* $82,000.

Georgiou-Karistianis, N., Corben, L., Harding, I.H., et al. (2021-2025). A natural history study to TRACK brain and spinal changes in individuals with Friedreich ataxia (TRACK-FA). *Friedreich Ataxia Research Alliance and Pharmaceutical Partners* $1,972,898.

Harding, I.H. (2020-2021). Investigator-Initiated Collaborative Research, ENIGMA-Ataxia Research Consortium. *Takeda Pharmaceuticals (USA)*, $85,000.

Harding, I.H. (2021). *Senior Postdoctoral Fellowship. Monash University*, $70,000.

Harding, I.H., Corben, L.A., Delatycki, M.B., et al. (2019-2021). Neuroinflammation in Friedreich Ataxia: Mechanism, Biomarker, and Therapeutic Target. *Friedreich Ataxia Research Alliance (USA)*, $283,665.

Harding, I.H., Storey, E., Klockgether, T., et al. (2020-2023). Neurodegeneration in Spinocerebellar Ataxias: Biomarkers, Mechanisms, and Variability. *NHMRC Ideas Grant,* $1,165,360.

Verdejo-Garcia, A., Andrews, Z., Lockie, S., et al. (2019-2022). The Neurocircuitry of Food Choice in Obesity. *NHMRC Project Grant*, $765,000.

Zoungas, S., McNeil, J., Storey, E., et al. (2019-2023). Prevention of Stroke in Older Australians. *The Heart Foundation*, $2,768,702.

NEUROSCIENCE AND SOCIETY GROUP

Carter, A. (2017-2021). Translating neuroscience into treatments and public health policies for addictive behaviours. *NHMRC Career Development Fellowship in Public Health*, $425,048.

Carter, A. (2020). Understanding the impact of Real-Time Prescription Monitoring on the Victorian community: Insights from the Pharmaceutical Helpline. *Turner Institute for Brain and Mental Health Community Engagement Grant,* $15,000.

Carter, A. (2020). Brain training games in Minecraft: Education edition – a proof-of-concept study. *Turner Institute for Brain and Mental Health Industry Grant,* $14,958.

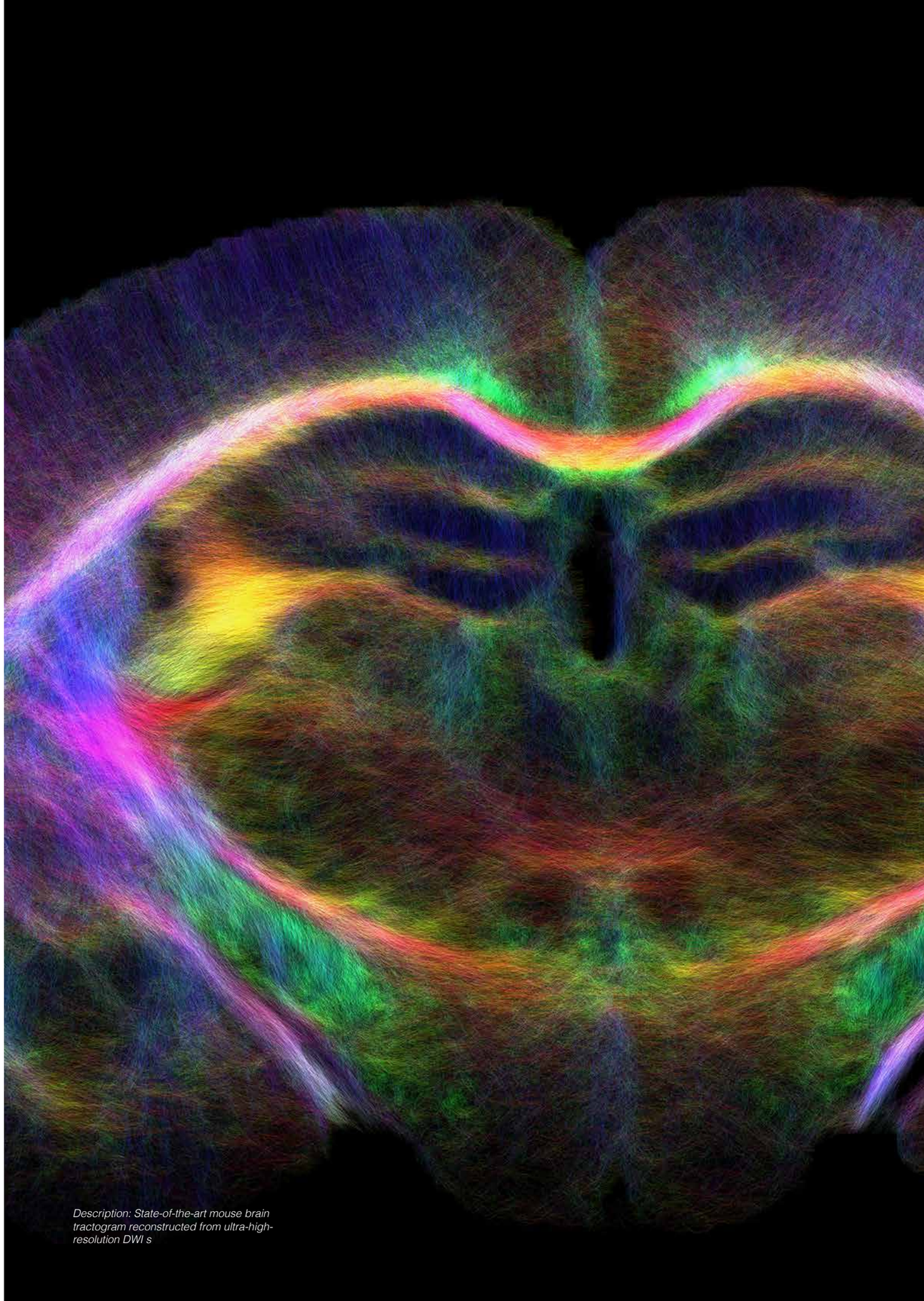
Carter, A. (2020). AI for older Australians in aged-care facilities: challenges and opportunities. *Monash University Interdisciplinary Research Grant* $44,913.

Carter, A. (2020-2021). Do “losses disguised as wins” in Australian pokies cause harm? *New South Wales Office of Responsible Gambling, Gambling Capacity Grant and PhD Scholarship*, $44,000.

WRIGHT LAB

O’Brien, T., Kwan, P., Ali, I., et al. (2020-2021). Testing of the effect of E2730 treatment on multimodality in-vivo biomarkers of GABAergic function in healthy rats and preclinical chronic epilepsy models. *Eisai Inc (United States)*, $1,100,000.

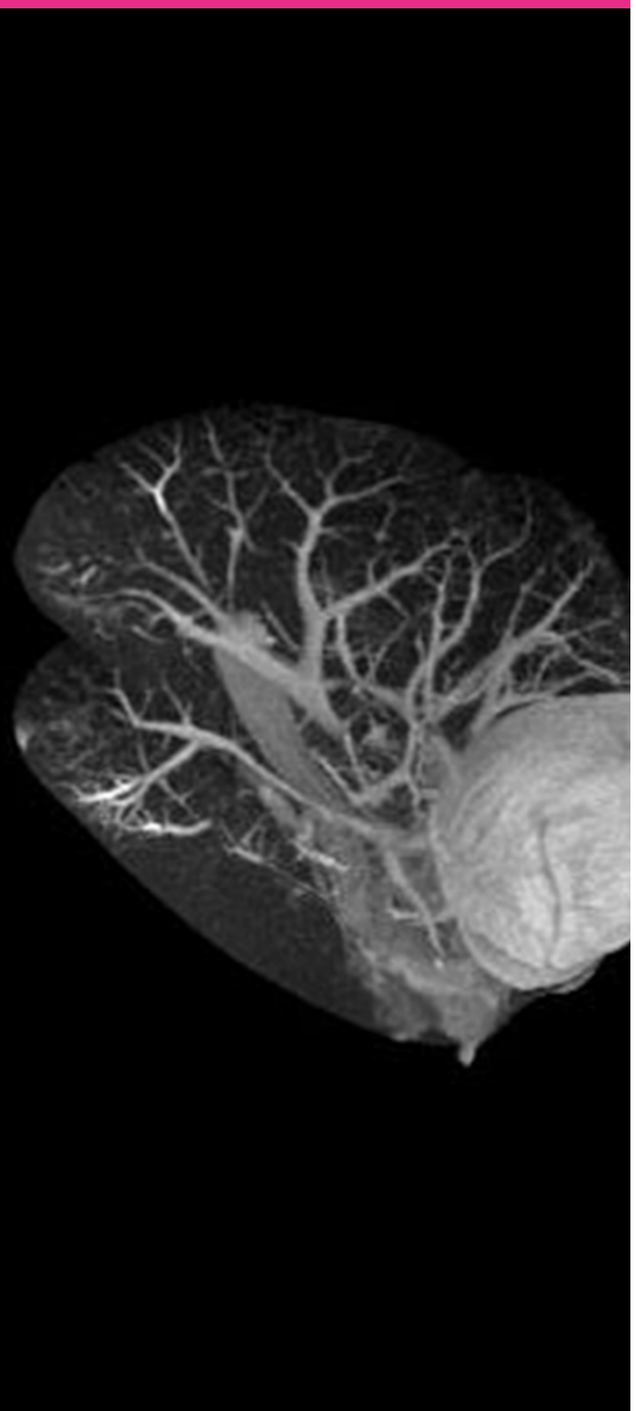
Wright, D. (2020). Glymphatic clearance as a novel therapeutic target for motor neurone disease. *Bethlehem Griffiths Research Foundation*, $46,000.



Description: State-of-the-art mouse brain tractogram reconstructed from ultra-high-resolution DWI s

COLLABORATIONS AND PARTNERSHIPS

Description: Computed Tomography of a Mouse Lung



COLLABORATIONS

Victorian Biomedical Imaging Capability

The Victorian Biomedical Imaging Capability (VBIC) is the peak body for the biomedical research imaging community in Victoria. Current VBIC members include Monash University, The Florey Institute of Neuroscience and Mental Health, the University of Melbourne, Swinburne University, and the Olivia Newton John Cancer Wellness and Research Centre. The business development and management activities of VBIC are undertaken by Neurosciences Victoria. During 2020 VBIC was prominent in the promotion of biomedical imaging research within Victoria with the VBIC Annual Network meeting held virtually. in November. The meeting focused on major research programs, innovation in imaging research, and imaging in drug development. The program included presentations by industry panel members to promote greater collaboration between industry partners and biomedical imaging researchers, as well as presentations of major national imaging research programs led by researchers from VBIC member organisations.

Monash Health

Clinical imaging staffing arrangements at MBI are undertaken in partnership with Monash Health. In 2020 Monash Health provided radiographers and nuclear medicine technologists to operate the clinical MRI and MR-PET scanners at MBI. Monash Health staff also provide research support to users from industry in addition to users from tertiary and research institutions.

National Imaging Facility

The National Imaging Facility (NIF) was established in 2007 with funding from the National Collaborative Research Infrastructure Scheme (NCRIS) and is now the peak imaging research infrastructure network across Australia. Monash University is one of the 13 nodes of the Facility and as a member of NIF provides access to the MBI and ARA-MBI biomedical imaging facilities to researchers across Australia. The National Imaging Facility received additional NCRIS funding for the period 2018-23 to expand and strengthen the national infrastructure.

Jülich Forschungszentrum, Germany

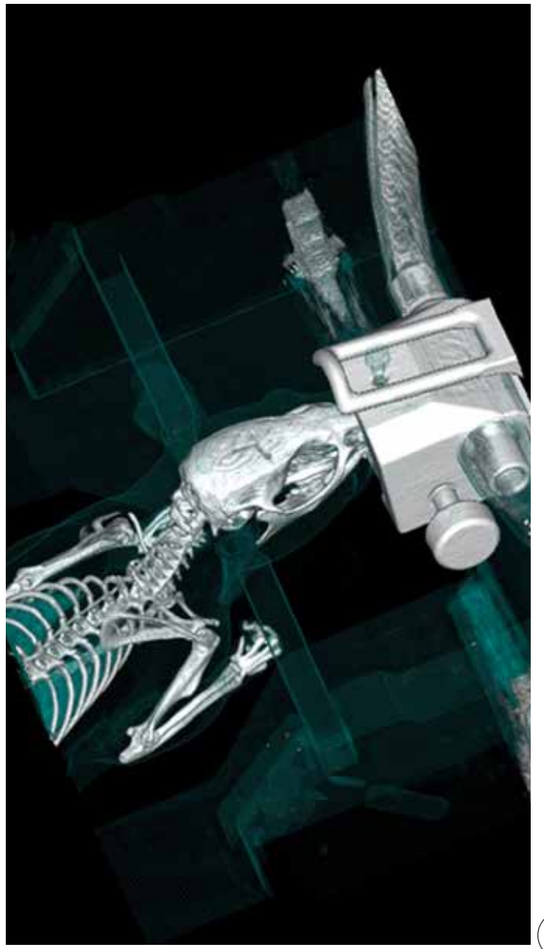
MBI has a long-standing collaboration with Jülich Forschungszentrum (FZJ), Germany in the field of hybrid MR-PET imaging. FZJ leads a Helmholtz innovation Fund project to develop a next generation BrainPET scanner for ultrahigh field 7 Tesla MR-PET imaging of the human brain. Under the Helmholtz Validation Fund project, MBI and FZJ have an agreement to exchange staff and students between the facilities in Melbourne and Germany in order to promote knowledge transfer and exchange, and to develop new simultaneous MR-PET applications to enhance and expand the capabilities and offerings at MBI. The project has progressed through the design and assembly stages with simulation results indicating that the scanner will achieve sub-2mm spatial resolution PET images. Completion of the assembly is scheduled for late 2020 with the first human brain scans planned for 2021. Members of the MBI Image Analysis team have responsibility for the PET attenuation and motion correction algorithms required for the integrated system.

Helmholtz Zentrum Dresden Rosendorff (HZDR)

Monash University and the Helmholtz Zentrum Dresden Rosendorff (HZDR) have built upon their 16 year collaboration in chemistry by securing funding from the German Government and HZDR to establish a new multidisciplinary Joint International Laboratory. The international laboratory involves more than 20 researchers to enhance research cooperation between Australia and Germany in the field of precision medicine towards improvement of treatments for patients with cancer, heart disease and infectious diseases. The two institutions have a long standing and successful collaborative research in the development of radiopharmaceuticals, including ultrasmall nanomaterials for imaging, immunotherapeutics based on antibodies, recombinant derivatives thereof, and cellular therapies based on immune effector cells. The partners have complementary expertise in imaging and treatment in the fields of cancer and heart disease, and both institutions are equipped with world-class biomedical imaging platforms. The current research focus includes the development and clinical translation of switchable cellular radio-immuno-theranostics for imaging and treatment of tumours.

CSIRO

The collaboration between MBI and CSIRO strengthened substantially during 2020. In mid-2020 ethics approval to optimise the parameters of focussed ultrasound (FUS) to safely and precisely open the blood brain barrier (BBB) in a reproducible manner was granted. The LP100 FUS instrument was successfully integrated with the 9.4T MRI, and by late 2020 a number of settings, including different acoustic pressures and microbubble concentrations were tested with the system. A number of successful instances of the targetted opening of the BBB were achieved and the team is very close to a robust set of methods and parameters that reliably and safely open the BBB in mice. Work has also commenced on developing the tumour models essential to testing the effects of FUS on brain tumours. This technology has the potential in rodent models and humans to open the blood brain barrier for the targeted delivery of blood borne therapeutics into the brain. The state of the art MR imaging and guided focused ultrasound capability will be available to all researchers on request.



ARC Centre of Excellence for Integrative Brain Function

Led by Monash University, the Australian Research Council Centre of Excellence for Integrative Brain Function (Brain Function CoE) aims to understand how the brain interacts with the world. By focusing on the complex brain functions that underlie attention, prediction and decision-making, Centre researchers are undertaking fundamental investigations into the principles of brain structure and function. The Centre is a collaboration between Monash University, the University of Queensland, the University of Sydney, the University of New South Wales, the Australian National University, the University of Melbourne and international partner institutions from Europe, North America and Asia. A number of Centre Chief and Associate Investigators, postdoctoral Fellows and PhD student Scholars are based at MBI and extensively use MBI's world class research imaging facilities. The Centre provides the opportunity for MBI-based researchers to collaborate with researchers in a unique program addressing one of the greatest scientific challenges of our time - understanding the link between brain activity and human behavior.

Alfred Health

MBI and the Departments of Medical Imaging and Clinical Neurosciences at the Alfred Hospital have established a clinical neurosciences research imaging collaboration. The partnership includes the University of Southern California, Los Angeles and the ARC Centre of Excellence for Integrative Brain Function. The objectives of the partnership are to facilitate the exchange for research utilisation of medical images between campuses of Monash University, to advance the use of artificial intelligence technologies for the reconstruction and analysis of biomedical images, and to establish a platform for the integration of medical imaging across the University.

PARTNERSHIPS

Siemens

Monash University and Siemens Healthcare established a collaboration agreement in 2010 to support the establishment of biomedical imaging research infrastructure at Monash. The agreement enables Monash scientists to access pre-commercial MR, PET and CT imaging technologies that provide opportunities for Monash researchers to undertake innovative studies using novel advanced techniques. The collaboration has resulted in a major ARC Linkage Project grant to build software technologies for joint MR-PET image reconstruction and modelling. Siemens Healthcare and Monash University are working towards building upon the successes of the existing collaboration and focusing our activities in areas of mutual strategic interest and strength, being 'Cardiovascular' and 'Digital Health/AI'.

Bruker

The new Bruker 9.4T MRI scanner at the Alfred Research Alliance – Monash Biomedical Imaging node at the Alfred Hospital became fully operational in 2019. The facility has generated significant interest amongst preclinical users as the use of cryocoil technology provides a major signal to noise improvement for ultrahigh high contrast imaging applications. In conjunction with the acceptance of the new 9.4 T scanner at ARA-MBI and the upgrade of the scanner at the Clayton node, Bruker reaffirmed their commitment to the provision of comprehensive local and international support to ensure optimal utilisation of the advanced preclinical MR imaging technologies.

Mediso

The preclinical PET-CT scanner at the ARA-MBI node became operational in early 2019 and provides high-sensitivity, high-resolution PET-CT imaging to support applications in neuroscience, cardiovascular, oncology and infectious disease research applications. The PET-CT scanner was supplied by Mediso Medical Imaging Systems, Hungary and installed with a universal animal handling platform for large axial fieldof-view imaging to allow rapid scanning and reconstruction of up to four mice concurrently.

Magnetic Insight

Monash University received an equipment grant from the Australian Research Council in 2019 to establish the first Magnetic Particle Imaging (MPI) facility in Victoria. MPI is a breakthrough technology with applications in the fields of cell tracking, material science and biotechnology. A novel alternating magnetic field technology is used to detect the magnetic properties of iron-oxide nanoparticles that is able to produce images faster than Position Emission Tomography and with higher sensitivity than Magnetic Resonance Imaging. The MPI Facility will be provided by Magnetic Insight, USA and located at the Alfred Research Alliance – Monash Biomedical Imaging node. The Facility promises to contribute to the generation of new knowledge in the nanotechnology, molecular imaging and industrial biosciences research sector.

MONASH University

MONASH BIOMEDICAL IMAGING

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