

Brain and Mind Centre

Annual Report 2017-18



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Overview

Key research themes

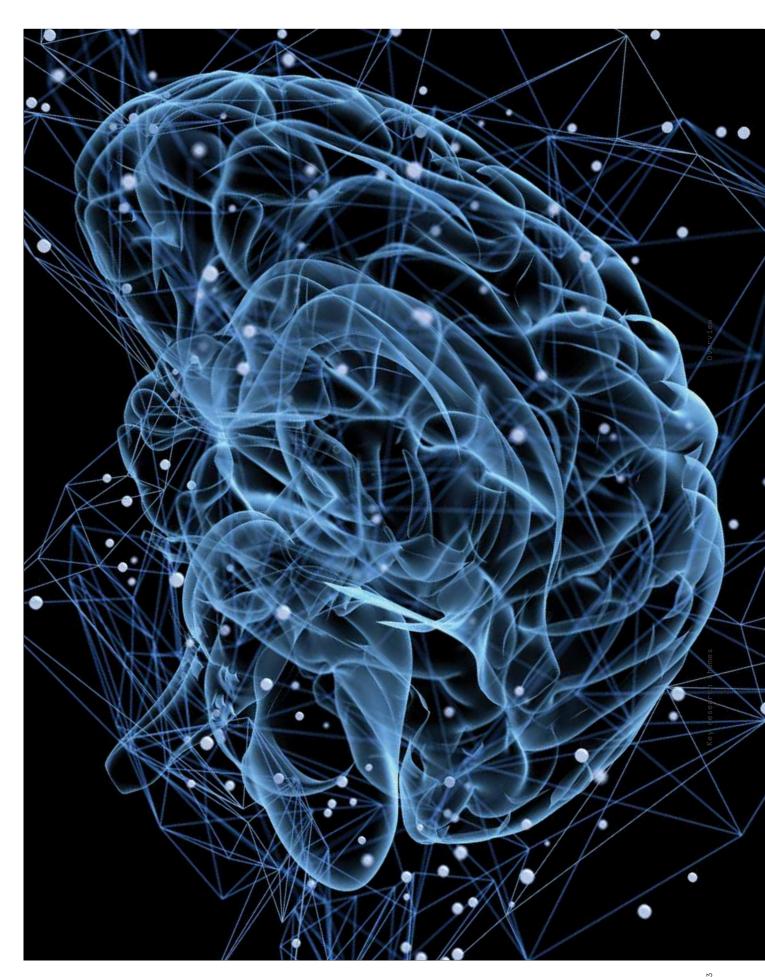
At the University of Sydney's Brain and Mind Centre, our teams partner across borders and disciplines in pursuit of a common goal: to develop better treatments for conditions of the brain and mind, and improve health outcomes now and for future generations.

Our multidisciplinary research teams are at the forefront of brain and mind sciences. We work to find answers to some of the world's most pressing health concerns, including:

- childhood development and behaviour disorders
- youth mental health and addiction
- ageing and neurodegeneration.

Our visionary research teams span preclinical, clinical and translational research. Our work extends beyond laboratories and clinics to our strong partnerships with industry, government, the community, other healthcare providers and diverse branches of academia to make a real difference to people's lives.





The

Welcome

Co-Directors' message

Welcome to the Brain and Mind Centre Annual Report, which celebrates our many achievements over the past two years.



Professor Matthew Kiernan AM Co-Director, Discovery and Translation



Professor Ian Hickie AM Co-Director, Health and Policy



Rod Gilrov. Chief Operating Officer Brain and Mind Centre

2017-18 has been a period of growth and exploration of new potential for the Brain and Mind Centre. Our collaborations, both across University of Sydney campuses, and with external partners such as Local Health Districts, government, industry and community bodies, have led to the establishment of exciting new multidisciplinary research teams. The unique perspective of these teams means we can combine cutting-edge research with safe and effective clinical approaches, this enables us to pioneer new systems of care for those affected by disorders of the brain and mind.

The last two years have seen a focus on further developing our strategic partnerships with industry. By working closely with a range of industry partners, the Brain and Mind Centre has been able to translate new technologies and research discoveries into innovations that benefit society and the economy. One such success has come from our Computational Neuroscience team. Itself a unique collaboration between the Faculty of Medicine and Health and the Faculty of Engineering and Information Technology, the team has partnered with the Sydney Neuroimaging Analysis Centre and I-MED Radiology Network on a \$2.36 million Cooperative Research Centre-Project to develop and commercialise algorithms to improve diagnostic neuroimaging.

The partnership will benefit people with a range of neurological illnesses, including multiple sclerosis and dementia.

Our transformative work would not be possible without philanthropy. In a climate where it has never been more difficult to secure competitive grant funding, philanthropy has allowed our innovative research to continue to thrive. In particular, private donations have supported the appointment of a number of leading researchers within the Brain and Mind Centre. Following a \$1.5 million commitment from a private family, the Brain and Mind Centre has been able to establish a new Chair in translational research. 2018 saw the appointment of Professor Cindy (Shin-Yi) Lin to this position, the Kam Ling Barbara Lo Chair in Neurodegenerative Disorders. Professor Lin's academic leadership will enable the Centre to leverage its efforts to develop novel diagnostic biomarkers and lead clinical trials of new therapies for a range of neurodegenerative disorders.

Philanthropy has also been vital in the support of a future generation of leaders in the brain and mind sciences by funding early-career research fellowships. Thanks to a very generous donation from the Bluesand Foundation, Dr Eleanor Drummond has been appointed to a three-year fellowship as Bluesand Fellow in Alzheimer's Disease.

Dr Ramon Landin-Romero, the Appenzeller Neuroscience Fellow in Alzheimer's Disease, has been similarly supported by Otto and Judy Appenzeller, who generously donated funding to establish a three-year fellowship at the Brain and Mind Centre.

We also congratulate Professor
Adam Guastella on his recent
appointment to the role of Michael
Crouch Chair in Child and Youth
Mental Health. In this position,
Professor Guastella will further
build our partnerships with
Westmead Children's Hospital,
Kids Research, the Cerebral Palsy
Alliance Research Institute and
Nepean Blue Mountains Local
Health District, providing academic
leadership in the area of child and

youth mental health. Together with colleagues Professors Nadia Badawi, Russell Dale and Joshua Burns, Professor Guastella is leading the newly established Child Neurodevelopment and Mental Health team at the Brain and Mind Centre, which is committed to identifying novel interventions to address the significant health and societal issues associated with child neurodevelopmental disorders and mental health.

The vast number of achievements highlighted in this report, from peer-reviewed publications and grants to fellowships and awards, is a testament to the tireless work of our researchers over the last two years.

We hope you enjoy this publication and look forward to our continued successes.

Matthe Kielian

Professor Matthew Kiernan AMCo-Director, Discovery and Translation

Jan Hickie

Professor Ian Hickie AM
Co-Director, Health and Policy

R. Colley

Rod Gilroy, Chief Operating Officer



L-R Professor Ian Hickie, Professor Matthew Kiernan and Rod Gilroy

Welcome

Message from the University

The University of Sydney is home to a select number of pan-university multidisciplinary initiatives which bring together talented researchers across diverse disciplines to advance teaching and research objectives in a collaborative environment.



Professor Duncan Ivision Deputy Vice-Chancellor, Research University of Sydney



Professor Laurent Rivory Pro Vice-Chancellor, Strategic Collaborations and Partnerships University of Sydney

These initiatives create thought leadership, delivering research excellence and education opportunities in established and developing areas of strength, across all of our faculties. The initiatives have the remit of conducting transformative and translational research, ensuring a positive contribution to our society, while providing invigorating and inspiring opportunities for our academics and students.

The Brain and Mind Centre is an exemplar of these multidisciplinary initiatives. In the Australian government's 2018 and inaugural assessment of engagement and impact of Australian university research, the Brain and Mind Centre was recognised as having the highest possible level of societal impact for their interdisciplinary approach to mental health care:

"[The Brain and Mind Centre] ...
has focused on developing new
multidisciplinary models of mental
health care – concentrating on
children and young people – where
early intervention can have large
economic and social benefits over
the long term. The impacts of
these new models are personal and
collective; assisting individuals to
achieve their full potential, while
growing the 'mental wealth' of the
nation. The Brain and Mind Centre

leads national policy development through sustained engagement with Governments, those living with mental illness [and] the wider community, and it invests in new health system partnerships, emphasising innovative youth services and utilisation of information technologies."

This is just one of the Centre's accomplishments. We are thrilled to present a summary of the important and ongoing work that they conducted throughout 2017 and 2018.

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Professor Duncan Ivison
Deputy Vice-Chancellor, Research
University of Sydney



Professor Laurent Rivory Pro-Vice-Chancellor, Research University of Sydney

Welcome

Message from Teresa Anderson



Teresa Anderson Chief Executive Sydney Local Health District

Our district has a strong tradition of research excellence and we continue to be world leaders in translational research, thanks to our strong collaborations with the University of Sydney, our medical research institute partners as well as the Northern Sydney and Western Sydney Local Health Districts, and Sydney Children's Hospital Network, as part of Sydney Health Partners.

Following the recognition of Sydney Health Partners as a National Health and Medical Research Council Advanced Health Research and Translation Centre in 2015, we have been working closely with the Brain and Mind Centre on a number of key health priorities in mental health and neuroscience.

In particular, we continue to lead the development of Sydney Neuroimmunology, a team of internationally renowned clinicians and researchers from across the Sydney Health Partners network, who are at the forefront of research into diseases of the brain and mind that are associated with immune dysfunction. The partnership will enable improved access to specialist diagnostic immunology services for patients with suspected neuroimmune disorders, as well as provide unprecedented opportunities to develop novel diagnostic biomarkers of disease and develop new and innovative treatments for some of the most debilitating neurological disorders.

The development of novel clinical trials, particularly in the area of youth mental health, is another

major priority for this partnership. Sydney Local Health District, Sydney Health Partners and the Brain and Mind Centre are investing heavily in the people, information technology infrastructure and clinical platforms needed not only to test new treatments (such as cannabidiols, ketamine, immunotherapies and circadian-based behavioural and pharmacological treatments) in young people with complex depressive, bipolar or psychotic disorders, but also new ways of delivering highly personalised and measurement-based care. This utilises the new IT platforms developed by the Brain and Mind Centre and the unique youth health service partnerships that we have developed (such as headspace and other new Commonwealthsupported intensive services). Together, we have very significantly increased our capacity for further novel clinical trials and linked health services research that is critical to national mental-health policy developments.

We look forward to continuing our partnership with the Brain and Mind Centre into the future.

Teresa Anderson

Chief Executive Sydney Local Health District

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Enhancing children's wellbeing to prevent problems later in life.

Our core business

Our team brings together world leaders of child clinical research to improve child neurodevelopment and mental wellbeing.

Neurodevelopmental disorders affect approximately one in 10 Australian children and include Autism Spectrum Disorder, Attention Deficit Hyperactivity Disorders, Cerebral Palsy and Tourette's Syndrome. These disorders impact cognitive, social, and emotional development in the first years of life. Our clinical researchers specialise in developing innovative assessments and treatments that support child development and mental health. We also work to identify factors that contribute to vulnerability, resilience and well-being in children and their families.



A preventative, holistic and supportive approach to child mental health



The Child Neurodevelopment and Mental Health team are focused on childhood disorders of the brain and mind. Our research aim is to address the developmental and emotional needs of the child in collaboration with clinical services and industry. The team focuses their work on cross-cutting platforms across the University of Sydney campuses at Westmead, Nepean and Camperdown and in partnership with the Sydney Children's Hospital Network (Westmead and Randwick) and their

This network consists of the largest cohorts of children with neurodevelopmental and mental health needs nationally and provides a landmark platform for developing new knowledge and practices.

clinical services.

Our team works with the community (families, professionals across disciplines and children) to improve assessment and early interventions in child neurodevelopmental disorders and mental health broadly. This includes:

- developing optimal assessment approaches that address the needs of children and their families.
- using technology to improve client-centred care and communication between researchers, clinicians and families, as well as opportunities for larger research projects capitalising on data linkage.
- identifying clinical and biological markers (genomic, epigenomic, metabolomic, microbiomic, physiological and cognitive) to inform assessment and clinical decision making or as targets for new interventions.

- delivering high-quality clinical trials using large, selected child cohorts and targeting the neurodevelopmental and mental health needs of children and families in order to inform best-practice care.
- population health linkage studies to inform high-quality surveillance data to advise evidence-based policy.

Through this approach, the team aims to identify and treat each child at the earliest possible time with the best possible approaches, in order to address the significant health and societal issues associated with child neurodevelopmental disorders and mental health.

The team is focused on developing an evidence-base to reduce the impact of childhood adversity that diminishes life potential, as well as providing individuals and families with greater opportunities to lead healthy, productive and fulfilling lives.

Our team

Led by internationally regarded child psychologist and the Michael Crouch Chair in Child and Youth Mental Health, Professor Adam Guastella; Paediatric Neurologist and Head of Kids Neuroscience Centre at the Children's Hospital at Westmead, Professor Russell Dale; Chair of Cerebral Palsy - Cerebral Palsy Alliance, Professor Nadia Badawi; Paediatric epidemiologist and the Financial Markets Foundation for Children Chair in Translational Childhood Medicine at Children's Hospital at Westmead, Professor Natasha Nassar; and Associate Dean Research (Health Sciences) and NSW Director of the Paediatric Gait Analysis Service, Professor Joshua Burns, the team takes a novel, transdiagnostic approach to child neurodevelopment and mental health.

A multidisciplinary approach

The team integrates highperforming researchers across multiple disciplines, including imaging, neurochemistry, genomics, biomechanics, psychology, neurology, psychiatry, paediatrics, speech pathology, and occupational therapy. It brings together the University of Sydney's research leaders from multiple Local Health Districts to form partnerships that facilitate clinical trials of behavioural therapies, and neuropsychological, genomic, inflammatory and neurobiological interventions.

The University of Sydney

Child Neurodevelopment and Mental Health Highlights

Appointment of Professor Adam Guastella to the new Crouch Chair in Child and **Youth Mental Health**

At the end of 2018, the University of Sydney appointed Professor Adam Guastella as the Michael Crouch Chair in Child and Youth Mental Health. Leveraging generous philanthropic funding, the newly created position will provide academic leadership in the area of child and youth mental health, working collaboratively with leading researchers and the community across the Brain and Mind Centre, the Children's Hospital at Westmead Clinical School and the Sydney Children's Hospital Network.

Partnering with Cerebral Palsy Alliance

The Cerebral Palsy Alliance Research Institute aims to prevent and cure cerebral palsy as well as find innovative treatments and interventions. Their researchers work across disciplines to conduct cutting-edge research and translate research findings into practice. The Cerebral Palsy Alliance Research Institute are a key partner in the Child Neurodevelopment and Mental Health team.



Professor Adam Guastella

Patient spotlight

Hayden's story

Hayden was diagnosed with Autism Spectrum Disorder when he was two years old. His mother Christine spent years trying various therapies and medications, but nothing made a difference. Hayden was trapped in his own world, unable to communicate.

"He didn't want to be in a group or participate," Christine explains. "He wouldn't even sit down in a circle. A small transition or change in activity would result in a tantrum. He didn't trust me or anyone trying to help him."

After contacting multiple paediatricians, Christine was directed to the Brain and Mind Centre where she learned of a new trial for autistic children involving oxytocin. This was a turning point in Hayden's life.

"It was the first time he was really able to engage and become aware he was not the only person in the room," says Christine. "I had no idea Hayden was aware of his surroundings until he started saying things like, 'Oh, I like that car'."

The Brain and Mind Centre treatment enabled Hayden to make friends, sit quietly and learn new things at school. Recently, he even attended school camp for three nights. "The changes I saw from the trial completely changed the way Hayden engaged," says Christine. "He wanted to be part of a group, he didn't fight and his language and social skills improved."





Hayden

Youth Mental Health

Transforming the mental health care of young people.

Youth Mental Health

Our core business

The Youth Mental Health and Technology team puts young people at the centre of their own care. We partner with health services to develop innovative treatments for young people aged 12–30 with emerging mental health disorders.

A new way forward

There is a great need to transform the way in which clinical care is delivered to young people with emerging mental health disorders such as anxiety, depression, other mood disorders and psychosis. Specialised clinical assessment is required and treatment systems need to be much more customised to the individual's unique needs.

We aim to transform how clinical care is delivered to young people with mental health issues. Rather than rely on broad diagnostic generalisations, we want to see clinicians diagnose and treat young people in a way that caters to the individual needs of each person.

Our research focus

We focus on three main streams of research:

- Clinical service development: continuously improving health services for young people by systematically evaluating services.
- Technology: optimising online environments to deliver services, track progress and provide feedback to young people and their clinicians.
- Clinical research: ongoing longitudinal patient studies to develop and trial new interventions for complex mental health issues.

Collaboration for better outcomes

Our research program is heavily integrated with headspace Camperdown. headspace is the national youth mental health foundation, providing early intervention and mental health services to young people aged 12–25.

We are also collaborating with St. Vincent's Private Hospital – USpace, Australia's first private mental health service targeted to the needs of young adults aged 16–30, and Mind Plasticity, a private specialist practice consortium.

The integration of cutting-edge research with safe and effective clinical care enables us to quickly and effectively translate our research findings into different clinical services, facilitating continuous improvements to mental health services for the benefit of young people in Australia.



Youth Mental Health Key projects and clinical trials

Longitudinal cohort study

The Brain and Mind Youth Cohort Study began in 2008. More than 10 years later, we have assessed more than 8000 individuals with early phases of anxiety, mood or psychotic disorders. In partnership with St Vincent's Private Hospital – USpace, we are now also including inpatients.

From this cohort we have learned a lot about long-term functional outcomes and observed that young people in need of care are led to services that either over- or under-treat them; or, as their needs change, these young people find it difficult to transfer between services.

These data suggest that more sophisticated treatment strategies may be required to achieve significant and sustained functional improvements. In order to address this problem, we are currently establishing a new longitudinal tracking study linked to a new clinical trial network, which will allow for personalised care at scale for young people.

Self-managed healthcare through digital technology: Project Synergy

We are using new digital technologies to develop health systems that better meet the holistic needs of young people with mental health issues. Working with InnoWell Pty Ltd (a joint venture between the University of Sydney and PricewaterhouseCoopers), we are trialling the use of a digital platform that can be tailored to the unique needs of the young person, which is then collaboratively managed by the person seeking care and their clinician.

In time, this technology may be used as the first point of contact in clinical care. The Australian Government's Department of Health has provided funds to InnoWell for a series of research trials, known as Project Synergy, running from 2017–2020, to test this platform across different population groups, including young people.

Through the InnoWell Platform, specifically InnoWell Care, young people can:

- complete real-time questionnaires and view their results immediately
- monitor their ongoing progress
- choose, in collaboration with their clinician, treatment options tailored to their unique needs.

This seamless continuum of support from online services through to healthcare providers offered by the Platform aims to facilitate young people's access to the right care at the right time, thereby fundamentally improving the system of care in Australia's youth mental health services.

The InnoWell Platform is currently being implemented within 11 headspace locations across Australia, ensuring the platform is tested to meet the diverse needs, contexts and experiences of Australia's young people.



Personalised and responsive care

The current diagnostic approach in mental healthcare services can be ambiguous, particularly in the early stages of an illness. This is a major challenge for clinicians when trying to identify the most suitable and effective treatment strategies. To this end, we have developed a new clinical staging model to help clinicians accurately identify the severity of the illness a young person they are assisting may have.

With this knowledge, options for safer and more effective interventions can be discussed between the young person and their treating team, in line with the stage of illness the young person has. This approach will help healthcare providers deliver better quality services, especially to young people who have a clear need for mental health care but may not otherwise receive it. It can also help clinicians consider the potential trajectory or future pathway of an illness to better guide individual support, intervention and service design.

Clinical, cognitive, and circadian profiling of young inpatients with severe mental disorders

As a part of the clinical service at St. Vincent's Private Hospital – USpace, we are recruiting young patients aged between 16 and 30 (mean age of about 18), with varying and comorbid disorders (largely a primary diagnosis of depression), including psychotic symptoms. Clinical, cognitive, and circadian profiling of this patient cohort will increase our knowledge about different phenotypes within young people with severe mental disorders. This knowledge will be used to develop measured-based, highly personalised treatment strategies.

General mental health

Our broad program of research also includes:

- developing novel suicideprevention strategies
- the effects of cannabidiol on brain metabolism and inflammation using position emission tomography (PET)
- youth cyberbullying
- personalised approaches to education and employment participation
- mechanistic studies to understand the neurobiological basis of mental illnesses in young people, including assessment of neuropsychology, neuroimaging and sleep-wake and circadian rhythms
- digitally-supported care pathways for the delivery of better care for young people with emerging mood or psychotic disorders
- standardised screening, assessments and novel immune therapies in atypical mood and psychotic disorders.



headspace Day being celebrated at Camperdown

Youth Mental Health Highlights

Project Synergy begins implementation phase

We have begun supporting the implementation and evaluation of the InnoWell Platform across 11 different headspace locations around Australia, including:

- five centres within the North Coast Primary Health Network footprint; specifically, Port Macquarie, Grafton, Lismore, Tweed Heads and Coffs Harbour
- five centres within the Central and Eastern Sydney Primary Health network footprint; specifically, Camperdown, Bondi Junction, Ashfield, Hurstville and Miranda
- headspace Edinburgh North.

headspace Camperdown was the first of the sites to go live in November 2018, with the InnoWell Platform offered as part of care delivery within this service. Headspace Port Macquarie, Lismore and Edinburgh North have also gone live, with over 400 young people invited to use the platform across these centres to-date. It is anticipated that the platform will be live in the remaining centres by September 2019.

Collaborating to investigate the role of sleep patterns in mood disorders

Together with Monash University, the National Institute of Mental Health and international collaborators, the Brain and Mind Centre is leading key research into abnormalities in the body clock as an underlying cause of mood disorders. While abnormal sleep-wake patterns are commonly reported in mood disorders, it is currently unclear how disruption of the circadian body clock contributes to the development and persistence of these mental illnesses, and how correcting this can improve outcomes. With the latest international expertise, this research is at the forefront of the field and is conducted with the aim of providing important information to guide the improvement of treatment for young people with mood disorders.

Dagmar Koethe appointed as Associate Professor in Psychiatry

Associate Professor Dagmar Koethe will lead clinical trials researching emotionally unstable patients and support corresponding trials in a variety of psychiatric and neuropsychiatric conditions, such as affective disorders, early psychosis and autoimmune-related mental health disorders.



New database to track years of research

Over the last 10 years, youth mental health research at the Brain and Mind Centre has provided a wide variety of data across different measures and in differing formats. 2018 saw the development of a powerful integrated database specifically to access and analyse this data efficiently, expanding the potential for research that utilises this youth mental health data.

Fellowships awarded

Professor Ian Hickie has been awarded a National Health and Medical Research Council (NHMRC) Senior Principal Research Fellowship: Optimising personalised Care, at scale, for Young People with Emerging Mood Disorders

Grants and major projects

Crisis resolution team
Optimisation and Relapse
prevention (CORE) translational
research for the Australian and
digital environments

Led by: Milton, A.
Supported by: Hickie, I.
& Davenport. T.

Granting body: Brain and Mind Centre Research Development Grant Years: 2019–2020 Amount: \$20,000

Project Synergy: continuing the co-design, development, implementation and evaluation of the InnoWell Platform

Led by: Hickie, I., Davenport, T.

& Cross, S.

Granting body: Australian

Government Department of Health

Years: 2017-2020 Amount: \$30M



headspace Day collateral

Youth Mental Health

Key publications

- Merikangas, K.R., Swendsen, J., Hickie, I.B., Cui L., Shou, H., Merikangas, A.K., Zhang, J., Lamers, F., Crainiceanu, C., Volkow, N.D., & Zipunnikov, V. (2018). Real-time mobile monitoring of the dynamic associations among motor activity, energy, mood, and sleep in adults with bipolar disorder. *JAMA Psychiatry*. Advance online publication. doi 10.1001/ jamapsychiatry.2018.3546.
- 2. Chervonsky E., & Hunt, C. (2018). Emotion regulation, mental health, and social wellbeing in a young adolescent sample: A concurrent and longitudinal investigation. Emotion, 9(2), 270-282.
- Lee, R.S.C., Hermens, D.F., Naismith, S.L., Kaur, M., Guastella, A.J., Glozier, N., Scott, J., Scott, E.M., & Hickie, I.B. (2018). Clinical, neurocognitive and demographic factors associated with functional impairment in the Australian Brain and Mind Youth Cohort Study (2008–2016). BMJ Open, 8(12):e02265.

- Ospina-Pinillos, L., Davenport, T., Iorfino, F., Tickell, A., Cross, S., Scott, E.M., & Hickie, I.B. (2018). Using new and innovative technologies to assess clinical stage in early intervention youth mental health services: Evaluation study. *Journal of Medical Internet Research*, 20(9):e259.
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- Iorfino, F., Hermens, D.F., Cross, S.P.M., Zmicerevska, N., Nichles, A., Groot, J., Guastella, A.J., Scott, E.M., & Hickie, I.B. (2018). Prior suicide attempts predict worse clinical and functional outcomes in young people attending a mental health service. Journal of Affective Disorders, 238:563-69.

- 7. Crouse, J.J., Moustafa, A.A., Bogaty, S.E.R., Hickie, I.B., & Hermens, D.F. (2018) Parcellating cognitive heterogeneity in early psychosis-spectrum illnesses: A cluster analysis. Schizophrenia Research, 202:91-98.
- Cross, S.P., Scott, J.L., Hermens, D.F., & Hickie, I.B. (2018). Variability in clinical outcomes for youths treated for subthreshold severe mental disorders at an early intervention service. *Psychiatric Services*, 69(5):555-561.
- 9. Tickell AM, Lee RSC, Hickie IB, et al. The course of neuropsychological functioning in young people with attenuated vs discrete mental disorders. Early Interv Psychiatry 2017.
- Scott, J., Murray, G., Henry, C., Morken, G., Scott, E., Angst, J., Merikangas, K.R., & Hickie, I.B. (2017). Activation in bipolar disorders: A systematic review. *JAMA Psychiatry*, 74(2):189–196.

Researcher Spotlight

Dr Frank Iorfino

Dr Frank Iorfino's PhD, completed in 2018, focused on modelling social and occupational functioning, as well as studying suicidality outcomes, for young people attending youth mental health services. Titled 'Personalised mental health care for young people: Using past outcomes to build future solutions', this work contributed to our understanding of how to identify young people at risk for poor illness trajectories. It also explored the development of health-service solutions to some of these problems, by investigating the use of new technologies to help services identify and monitor young people's outcomes over time.

This work played a significant role in the development of a new technology platform that is being implemented and tested in mental health services across Australia through Project Synergy, a series of research trials conducted by the University of Sydney and InnoWell. As a post-doctoral research fellow for Project Synergy, Frank is continuing his work in this area with a focus on evaluating and improving the real-world applicability and integration of the platform.

"I enjoy working in a truly clinical research team, where researchers, clinicians, young people and their families are working together to solve real-world problems through research and development in a health service environment," Frank says. "I feel privileged to work within a multidisciplinary team that is so motivated and focused on having a real impact. It's special to be in a position where you can see the ways your work is changing the lives of the people your research aims to improve."

"I feel privileged to work within a multidisciplinary team that is so motivated and focused on having a real impact"

Dr Frank Iorfino, Youth Mental Health



Dr Frank Iorfino

University of Sydney

Patient spotlight

Jess's story

Mood disorders can affect every part of a person's life. For some, it makes working, studying and socialising impossible. This was certainly the case for Jess, who lived with depression for much of her life. "I was severely depressed and had constant battles with anxiety from a young age" Jess recalls. Simple daily tasks like eating, sleeping and showering became unbearable. Eventually, Jess was forced to leave high school. She couldn't be in public without experiencing severe anxiety and struggled with self-harm and suicidal thoughts.

It was a chance meeting between Jess's mother and a psychiatrist working with headspace and the Brain and Mind Centre that sparked change for Jess. She took part in one of its research programs involving cognitive studies, MRI scans and sleep research.

"The Brain and Mind Centre is pretty much the reason I am here today" Jess says. Jess is now in her final year of university. She works part-time and maintains strong, loving relationships with her family and partner. She's also become a mental health advocate and met the Prime Minister.

Today, Jess is able to see herself in a different light. "I started to break away from the constant years I had been referring to and believing myself to be a mental illness and nothing more", she says.

By getting treatment and support she needed, Jess defied her own expectations and can now live a life that is defined by her achievements, not her illness.



Jess got her driver's licence on her first attempt

"The Brain and Mind Centre is pretty much the reason I am here today"

Brain and Mind Centre patient

Psychology Clinic

Accredited postgraduate training in clinical psychology and affordable therapy for the general public.

Psychology Clinic

Our core business

The Psychology Clinic sits within the Clinical Psychology Unit (CPU) located at the Brain and Mind Centre. This unit is part of the School of Psychology within the Faculty of Science. The CPU provides the theoretical foundation of clinical psychology practice and the Psychology Clinic is devoted to the translation of this knowledge to clinical practice in a real-life, dynamic, clinical setting.

The Clinic enables the development of trainees with the competencies necessary to be a clinical psychologist, through direct clinical experience, supported by careful supervision of this practice. The Clinic provides a comprehensive clinical psychological assessment and treatment service to people within our University and broader community. There is a dual purpose then: to provide a service to our trainees and to the community of people seeking psychological assistance.

The Clinic provides affordable psychological assessment, early intervention and treatment services across the lifespan for a broad range of psychological and mental health difficulties, including anxiety, depression, life events, grief and loss, health and illness, relationships, parenting and family, behavioural difficulties, study and work, resilience, and learning difficulties for adults and children. Self-referrals as well as secondary and tertiary referrals are received from within the University community including the Counselling and Psychological Service (CAPS), headspace, Camperdown and the General Practice service in the Wentworth Building. Referrals are also received from the wider community, including General Practitioners, Psychiatrists, and Adult and Child Mental Health Services within the Sydney Metropolitan Area.

The CPU accepts a total of 20 post-graduate Master of Clinical Psychology and Master of Clinical Psychology and Doctor of Philosophy trainees each year. Trainees commence their clinical academic training in Semester 1 and begin their Psychology Clinic Internal Placement in Semester 2 for a period of 12-months.

In 2018, 2400 occasions of service were provided across 3 clinic days. In addition, some 171 appointments were related to the School of Psychology and the various research projects of the Masters of Clinical Psychology/PhD trainees (MCP/PhD). These research projects relate to investigations of Adult Autism Spectrum Disorder and Social Anxiety Disorder in adults and children.

Our broad aim is to continue to maintain our high level training through the provision of high quality evidence-based psychological interventions, as well as supporting the School of Psychology and Clinical Psychology Unit's MCP/PhD clinical research program. Longer term goals include systematising a database that allows for an investigation of the prevalence of mental health difficulties presenting to our Clinic, across the lifespan, and examining treatment outcomes following treatment with our service.

Psychology Clinic

Highlights

- Provision of over 2000 occasions of service for the early intervention and treatment of psychological and mental health difficulties utilising evidencebased practice for the University and wider community in 2018
- Over 20 post-graduate clinical psychology trainees successfully completing their training onto full registration as psychologists with over 80% achieving work in their field within a year of graduation
- Continuing to conduct clinical research leading to publications
- Establishing new networks for clinical training in diverse populations, most recently with the Health Services Division Central Australian Aboriginal Congress Aboriginal Corporation

Page

Psychology Clinic Key publications

- 1. Butow, P., Turner, J., Gilchrist, J., Sharpe, L., Smith, A., Fardell, J., Tesson, S., O'Connell, R., Girgis, A., Gebski, V., Asher, R., Bell, M., Beith, J., Grunewald Zola, K., Thewes, B., et al (2017). Randomized Trial of ConquerFear: A Novel, Theoretically Based Psychosocial Intervention for Fear of Cancer Recurrence. Journal of Clinical Oncology, 35(36), 4066-4077.
- 2. Dudeney, J., Sharpe, L., Jaffe, A., Jones, E., Hunt, C. (2017). Anxiety in youth with asthma: A metaanalysis. Pediatric Pulmonology, 52(9), 1121-1129.
- 3. Hadzic, R., Sharpe, L., Wood, B. (2017). The Relationship Between Pacing and Avoidance in Chronic 9. Mantz, S., Abbott, M. (2017). Pain: A Systematic Review and Meta-Analysis. The Journal of Pain, 18(10), 1165-1173.
- 4. Hay, P., Touyz, S., Arcelus, J., Pike, K., Attia, E., Crosby, R., Madden, S., Wales, J., La Puma, M., Heriseanu, A., et al (2018). A randomized controlled trial of the compuLsive Exercise Activity TheraPy (LEAP): A new approach to compulsive exercise in anorexia nervosa. International Journal of Eating Disorders, 51(8), 999-1004.
- 5. Heriseanu, A., Hay, P., Corbit, L., Touyz, S. (2017). Grazing in adults with obesity and eating disorders: A systematic review of associated clinical features and meta-analysis of prevalence. Clinical Psychology Review, 58, 16-32.

- 6. Jones, E., Sharpe, L. (2017). Cognitive bias modification: A review of meta-analyses. Journal of Affective Disorders, 223, 175-183.
- 7. Joplin, S., Stewart, E., Gascoigne, 13. Scott, A., Sharpe, L., Thayer, Z., M., Lah, S. (2018). Memory Rehabilitation in Patients with Epilepsy: a Systematic Review. Neuropsychology Review, 28(1), 88-110.
- 8. Mantz, S., Abbott, M. (2017). Obsessive-Compulsive Disorder in Paediatric and Adult Samples: Nature, Treatment and Cognitive Processes. A Review of the Theoretical and Empirical Literature. Behaviour Change, 34(1), 1-34.
- The relationship between responsibility beliefs and symptoms and processes in obsessive compulsive disorder: A systematic review. Journal of Obsessive-Compulsive and Related Disorders, 14, 13-26.
- 10. McAulay, C., Mond, J., Touyz, S. (2018). Early intervention for bipolar disorder in adolescents: A psychosocial perspective. Early Intervention in Psychiatry, 12(3), 286-291.
- 11. Menzies, R., Zuccala, M., Sharpe, L., Dar-Nimrod, I. (2018). The effects of psychosocial interventions on death anxiety: A meta-analysis and systematic review of randomised controlled trials. Journal of Anxiety Disorders, 59, 64-73.

- 12. Scott, A., Sharpe, L., Hunt, C., Gandy, M. (2017). Anxiety and depressive disorders in people with epilepsy: A meta-analysis. Epilepsia, 58(6), 973-982.
- Miller, L., Wong, T., Parratt, K., Nikpour (Mohamed), A. (2018). A qualitative examination and theoretical model of anxiety in adults with epilepsy. Epilepsy and Behavior, 85, 95-104.
- 14. Sesel, A., Sharpe, L., Naismith, S. (2018). Efficacy of Psychosocial Interventions for People with Multiple Sclerosis: A Meta-Analysis of Specific Treatment Effects. Psychotherapy and Psychosomatics, 87(2), 105-111.
- 15. Sharpe, L., Brookes, M., Jones, E., Gittins, C., Wufong, E., Nicholas, M. (2017). Threat and fear of pain induces attentional bias to pain words: An eye-tracking study. European Journal of Pain, 21(2), 385-396.
- 16. Smith, A., Sharpe, L., Thewes, B., Turner, J., Gilchrist, J., Fardell, J., Girgis, A., Tesson, S., Descallar, J., Bell, M., Butow, P., et al (2018). Medical, demographic and psychological correlates of fear of cancer recurrence (FCR) morbidity in breast, colorectal and melanoma cancer survivors with probable clinically significant FCR seeking psychological treatment through the ConquerFear study. Supportive Care in Cancer, 26(12), 4207-4216.

Child Behaviour Research Clinic

Enhancing children's wellbeing, preventing problems later in life.

Child Behaviour Research Clinic

Our core business

Child Behaviour Research Clinic

Our team brings together internationally regarded clinicians and researchers in child mental health and development. We work with children 2-8 years of age who present a range of emotional and social development concern, including disruptive behaviour disorders, autism, emotional problems and impulsivity/ hyperactivity.

The Child Behaviour Research
Clinic is a research-based clinic,
offering advanced, evidence-based
treatment programs that provide
families with the latest strategies
in child behaviour management.
Families are considered research
partners, such that we work
alongside parents, forming a
team to maximise learning about
what works best for children with

behaviour problems. Our research aims to identify the mechanisms that contribute to vulnerability, resilience and development in children and their families.

We also offer training internships for clinical psychologists wishing to learn the latest state-of-theart assessments and treatment as part of their masters or doctoral training.

Child Behaviour Research Clinic

Grants / funding



\$1,265,015 An Evidence-based Intervention for Mental Health Disorders in Rural Children. Dadds, Hawes, Brennan. NHMRC Partnership Grant APP1056878 with Royal Far West 2013–2017.

\$2,634,400 Like Father Like Son: A National Approach to Violence, Antisocial Behaviour and the Mental Health of Men and Boys. Dadds et al., Movember Foundation Award 2015–2017.

\$843,495 Transgenerational cycles of violence model in Timor-Leste. Silove, Rees, Steel, Tol, Eapen & Dadds. NHMRC Project Grant 2015 – 2019 APP1086732

\$192,000 The role of oxytocin in attachment patterns and socio-emotional development, Eapen, Silove, Dadds, Barnett, and Kohlhoff. ARC Linkage Grant 2016– 2019 LP160100249

\$1,287,730 Mapping the specific pathways to early-onset mental health disorders. Dadds, Eapen, Frick, Kimonis, Hawes, Moul, Mehta. NHMRC Project Grant 2017–2021 APP1127952.

\$846,110 An integrated model of environmental, neurodevelopmental, and epigenetic resistance and responsiveness to early intervention in childhood psychopathology. Dadds, Hawes, Mehta, Kimonis, Frick. NHMRC Project Grant 2017–2021 APP1123072.

\$849,540 Early childhood mental health: Pathways, treatment, and community literacy. Dadds. NHMRC Research Fellowship APP1136058, 2018–2022.

\$128,000 A novel treatment for childhood autism. Dadds, Tully, Eapen, Hawes, Rotary Health Research Fund. 2019-2020

Child Behaviour Research Clinic Key publications

- 1. Dadds, MR., English, T., Wimalaweera, S., Schollar-Root, O., & Hawes, DJ (2019). Can reciprocated parent-child eye gaze and emotional engagement enhance treatment for children with conduct problems and callous-unemotional traits; A proof-of-concept trial. Journal of Child Psychology and Psychiatry. This is a landmark paper showing for the first time that reciprocated parent-child eye gaze can be used within an early intervention program to remediate pathways to severe conduct problems in children.
- 2. Moul, C., Hawes, D.J., & Dadds, M.R. (2018). Mapping the developmental pathways of child conduct problems through the neurobiology of empathy. Neuroscience and Biobehavoral Reviews, 91, 34–50. This is a major review of neurodevelopmental systems involved in empathy and its disturbance in child psychopathology.
- 3. Dadds, M. R., Moul, C., Hawes, D. J., Mendoza Diaz, A., & Brennan, J. (2016). Individual Differences in Childhood Behavior **Disorders Associated With** Epigenetic Modulation of the Cortisol Receptor Gene. Child Development, 86, 1311-1320. This paper integrates, replicates and extends 3 previous studies providing tentative evidence that epigenetic changes to the DRD4 gene are associated with symptom profiles in young children. It provides clear evidence of a specific mechanism in dopamine regulation that can be used to index ADHD profiles and be targeted for future drug and other treatment development.
- 4. Dadds MR, Allen JL, McGregor K, Woolgar M, Viding E, & Scott, S. (2014). CU traits in children and mechanisms of impaired eye contact during expressions of love: A treatment target? Journal of Child Psychology and Psychiatry, 55, 771-780. This paper represents the culmination of several lead up studies identifying a specific treatment target for early intervention with children showing the most virulent and biologically-driven form of early-onset conduct disorder.
- 5. Dadds, M.R., Moul, C., Cauchi, A., Dobson-Stone, C., Hawes, D.J., Brennan, J., & Ebstein, R. (2014). Methylation of the oxytocin receptor gene and oxytocin blood levels in the development of psychopathy. Development and Psychopathology, 26, 33-40. Related to paper (2) above, this was the first study to show that children with a virulent form of conduct disorder are in part driven by problematic regulation of the oxytocin receptor gene. The findings have now been replication in a 13 year longitudinal study in the UK.
- 6. Fay-Stammbach, T., Hawes,
 D. J., Meredith, P. (2017). Child
 maltreatment and emotion
 socialization: Associations
 with executive function in the
 preschool years. Child Abuse
 & Neglect, 64, 1-12. The first
 study to report that parenting
 practices based on emotion
 socialization may protect
 against the neurocognitive
 (executive function) deficits
 exhibited by children exposed
 to substantiated maltreatment
 in the preschool years.

- 7. Imm Sng, K., Hawes, D. J.,
 Raine, A., Ang, R.P., Yoon Phaik
 O., Fung, D.S.S. (2018). Callous
 unemotional traits and the
 relationship between aggressive
 parenting practices and conduct
 problems in Singaporean
 families. Child Abuse & Neglect,
 81; 225-234. The first study to
 show that CU traits differentially
 moderate associations between
 parenting and proactive/
 reactive aggression in
 children with clinic-referred
 externalising problems.
- 8. Johnson, A. M., Hawes, D. J.,
 Eisenberg, N., Kohlhoff, J.,
 Dudeney, J. (2017). Emotion
 socialization and child conduct
 problems: A comprehensive
 review and meta-analysis.
 Clinical Psychology Review,
 54, 65-80. The first study to
 provide meta-analytic evidence
 that unsupportive emotion
 socialization parenting practices
 are significantly associated with
 severity of conduct problems.
- 9. Fairchild, G., Hawes, D. J., Frick, P. J., Copeland, W. E., Odgers, C. L., Franke, B., Freitag, C. M., & De Brito, S. A. (in press). Conduct disorder. Nature Reviews Disease Primers. This major review of the current state of evidence for conduct disorder spans epidemiology, disease mechanisms, diagnosis, screening, prevention, and treatment, and like all Nature Reviews Disease Primers is authored by scientists recognised as international leaders in the field of the respective disease:

Gambling Treatment and Research Clinic

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Working to reduce the impact of problem gambling in the community.

Gambling Treatment and Research Clinic

Our core business

We strive to better understand the psychology of gambling and to minimise gambling-related harms in the community, through high-quality research and evidence-based therapies, and the training and education of clinicians in the gambling treatment sector. We collaborate with consumers, industry partners, government and NGOs to apply our research in the real world.



Professor Alex Blaszczynski and Dr Sally Gainsbury

The Gambling Treatment and Research Clinic (GTRC), situated within the School of Psychology and the Brain and Mind Centre, is Australia's only university-affiliated gambling treatment provider. Led by Co-Directors Professor Alex Blaszczynski and Dr Sally Gainsbury, the GTRC has attracted funding of \$4 million over four years for a clinical service and \$1.2 million over the past three years for research. Our psychologists and clinical psychologists offer cognitivebehavioural based counselling services to individuals experiencing gambling-related difficulties.

Gambling Treatment and Research ClinicResearch

Research is central to the operation of the clinic. We focus on understanding the psychology of gambling behaviours, defining concepts of recovery and harm, and the effectiveness of interventions and prevention strategies, in order to provide bestpractice treatment. Our research includes venue-based gambling, including electronic gaming machines, or "pokies", which have the greatest contribution to harms. We are also investigating the rapidly rising impact of emerging technologies on gambling harms, and behavioural addictions more broadly, including online gaming.

Gambling harms significantly impact individuals, families and the Australian community, as around 1% of adults experience severe gambling problems and a further 1.4-2.1% experience moderate harms. Gambling is highly accessible in Australia through venues and online websites and apps and there is a high comorbidity between gambling and other mental health disorders.

The GTRC and its leaders are recognized internationally for their research excellence and are frequently invited to contribute to government, industry and community policy and practice to minimize gambling-related harms. Our research has a strong focus on stakeholder engagement, including working closely with state, national, and international governments, industry operators,

communities, and treatment professionals. Strong international collaborative links also support the multidisciplinary research.

All members of the research team routinely present research findings at local and international conferences and have recently been asked to share their work at government forums including the NSW Gambling Help Forum, and gambling industry conferences such as the Australian Gaming Expo and the Gaming, Racing and Wagering Australia conference. Several members of the research team are active committee members of the National Association for Gambling Studies, and PhD students are active members of the Brain and Mind Centre HDR Student Committee.

Our research objectives are to expand our expert research on gambling to include other behavioural addictions, with a strategic focus on problematic risk-taking related to emerging technologies, including online gaming, social media, mobile and wearable devices, virtual reality, and digital currency. We seek to be recognized as world leaders in these areas and are focusing on issues pertaining to mental health and well-being and prevention of harms. These are growing fields with strong social and economic impacts, but which currently lack the research to inform theoretical conceptualisation, policy and practice.

Gambling Treatment and Research Clinic Clinical practice

Over the past two years, the Gambling Treatment and Research Clinic (GTRC) has made significant progress in clinical treatment services, internship training and research into the psychology of gambling. With locations in Camperdown, Campbelltown, Lidcombe and Parramatta, our team have worked diligently to establish the GTRC at the forefront of innovation, treatment and training. Funded by the NSW Government through its Responsible Gambling Trust, the GTRC has treated a large number of individuals presenting with issues related to excessive gambling and its negative consequences. Over three years, we have offered approximately 3,126 sessions and in 2018, we saw our 2000th client. This substantial increase was largely as a result of effective use of the internet to promote our services.

Problem gambling has a huge impact on families and personal relationships. We have developed a manual for significant others to guide them in helping a loved one regain control of their behaviours and/or encourage them to seek treatment. We also offer couples counselling to help couples address their concerns and deal with loss of trust within the relationship.

We complement our core cognitive and behavioural treatment program with dialectical behaviour therapy (DBT) groups. While standard treatments result in significant reductions in gambling behaviour for many clients, other clients struggling with emotion regulation do not fare so well. DBT groups focus on teaching clients emotion regulation and distress tolerance skills. These groups also encompass clients with other substance and impulse control disorders.

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Gambling Treatment and Research Clinic Cultural outreach and education

Our counselling practices are culturally sensitive. Staff members attend training in cultural awareness, understanding and appreciation of the diversity of Aboriginal and Torres Strait Islander culture. Recognising the prevalence of gambling-related problems among Aboriginal communities, we have forged strong links with Marin Weejali Aboriginal Corporation in the Western Sydney region. We are proud to also be building partnerships with the Emerton Men's Shed and Ngallu Wal Aboriginal Child and Family Centre. In the first 12 months of our Aboriginal community outreach activities, we treated around 90 clients. Owing to the great demand, in late 2017, we expanded the DBT program at Marrin Weejali to include an advanced group.

In addition to the provision of clinical services, we place a strong emphasis on education and professional development for students and counsellors.

A significant initiative by Senior Clinician Dr Fadi Anjoul has been the development of a treatment manual. We offer internship placements and supervision for provisional psychologists including

Clinical Masters students. To date, we have trained 36 interns from various universities. We host regular presentations and discussion forums with gambling counsellors from across Sydney to ensure that relevant research findings are translated into clinical practice.

The GTRC places a strong focus on research training and offers supervision for PhD, Masters, and Honours students. The GTRC further hosts international students currently undertaking postgraduate research. A research internship program has been very successful with 15 interns supervised in 2017 and 2018. The internships have been highly successful with outcomes including joining the GTRC as research assistants or postgraduate students, peer-review publications, gaining competitive scholarships and awards and placement into clinical programs.

Gambling Treatment and Research Clinic Industry engagement

The GTRC's research team has worked closely with both industry and government stakeholders to carry out policy-relevant research with real-world impact in gambling venues. The research team has worked with industry partners ClubsNSW to develop a comprehensive, responsible gambling staff training program, which will be empirically evaluated in venues across NSW later this year. The research team has also collaborated with ClubsNSW to collect data for evaluation of their multi-venue self-exclusion program, which allows gamblers to ban themselves from multiple gambling venues under a single registration procedure. Research from this project commenced in 2015 and is ongoing with the collection of longitudinal data. Since commencement, the research has already resulted in 2 large industry reports, 2 peer-reviewed academic publications, 2 industry magazine publications, and the presentation of findings at national and international gambling conferences.



Gambling Treatment and Research ClinicHighlights

Grants awarded

Responsible Gambling Fund - University of Sydney Campbelltown. Camden

Led by: Blaszczynski, A.

Granting body: NSW Government

Department of Industry Years: 2017-2018 Amount: \$227,610

Responsible Gambling Fund – University of Sydney – Darlington

Led by: Blaszczynski, A.

Granting body: NSW Government

Department of Industry Years: 2017-2018 Amount: \$485,709

Responsible Gambling Fund - University of Sydney Lidcombe Aboriginal

Led by: Blaszczynski, A.

Granting body: NSW Government

Department of Industry Years: 2017-2018 Amount: \$129,643

Responsible Gambling Fund – University of Sydney – Lidcombe/Cumberland

Led by: Blaszczynski, A.

Granting body: NSW Government

Department of Industry Years: 2017-2018 Amount: \$39,750.90

The influence of features of the online environment on risk taking

Led by: Gainsbury, S.
Granting body: Australian

Research Council Years: 2016-2020 Amount: \$373,401

Developing online risk taking models in multiple domains

Led by: Gainsbury, S. and Pinkus, R. **Granting body:** School of Psychology, University of Sydney

Years: 2017 Amount: \$15,000

Risky gambling and customer wellbeing: The role of financial institutions

Led by: Gainsbury, S.

Granting body: Commonwealth Bank Australia, University of Sydney – Industry and Community Engagement Seed Fund & Linkage

Incubator funding Years: 2017-2018 Amount: \$55,725

Investigation of the impact of the Interactive Gambling Amendment Bill 2016

Led by: Gainsbury, S., Angus, D. and Blaszczynski, A.

Granting body: Australian Communication and Media Authority

Years: 2018 Amount: \$88,946

Increasing engagement with responsible gambling tools among customers of online wagering sites

Led by: Gainsbury, S. and

Blaszczynski, A.

Granting body: Responsible

Wagering Australia Years: 2018-2019 Amount: \$159,925

Awards

- Dr Sally Gainsbury was awarded a University of Sydney Vice-Chancellor's Award for Outstanding Early Career Research (2018). Dr. Gainsbury was also nominated as one of the Top 25 People to Watch in the gambling field by Global Gaming Magazine (2018) and awarded the Franklin Women 2017 Carer's Travel Scholarship to support her in travelling to London to deliver a keynote address at the GambleAware conference.
- Out of 60 abstract submissions presented at the Brain and Mind Centre Symposium, PhD Candidate Dylan Pickering was awarded the best poster prize for his research titled "What does it mean to recover from a gambling disorder?"

International visits

The GTRC has hosted numerous international academics including from the University of Geneva, University of Hamburg, and the University of Macau. Several international students have completed internships at the GTRC as part of their postgraduate studies to gain further experience in gambling research and be involved with the GTRC team.

Media

The GTRC team is frequently featured in mainstream national and international media related to gambling, online gaming, and addictions. Notable appearances include on the Jim Jefferies Show (broadcast in 13

countries), the Today Show, ABC News, Weekend Sunrise, SBS Insight, ABC Radio National, Triple J Hack, A Current Affair, Studio 10, ABC Life, and ABC Drive.

Gambling Treatment and Research Clinic Key publications

- Ladouceur, R., Shaffer, P., Blaszczynski, A., & Shaffer, H.J. (2018). Brief report: Responsible gambling research and industry funding biases. *Journal of Gambling Behavior*. doi:10.1007/ s10899-018-9792-9
- Adolphe, A., Khatib, L., van Golde, C., Gainsbury, S., & Blaszczynski, A. (2018). Crime and gambling disorders: A systematic review. Submitted Journal of Gambling Studies, doi.org/10.1007/ s10899-018-9794-7
- Gainsbury, S.M., Tobias-Webb, J., & Slonim, R. (2018). Behavioural economics and gambling: A new paradigm for approaching harm-minimisation. Gaming Law Review. doi:10.1089/ glr2.2018.22106
- 4. Blaszczynski, A. (2108).
 Responsible gambling: The need for collaborative government, industry, community and consumer involvement. SUCHT, 64, 64, 307-315. https://doi.org/10.1024/0939-5911/a000564

- Gainsbury, S. & Blaszczynski, A. (2017). How blockchain and cryptocurrency technology could revolutionize online gambling. *Gaming Law Review*, 21(7), 482-492. doi:10.1089/ glr2.2017.2174
- Pickering, D., Keen, B., Entwistle, G., & Blaszczynski, A. (2017). Measuring treatment outcomes in gambling disorders: A systematic review. *Addiction*. doi: 10.1111/add.13968
- Pickering, D, Blaszczynski, A., & Gainsbury, S. (2017). Multi-venue self-exclusion for gambling disorders: A retrospective process investigation. *Journal of Gambling Issues*.
- Baggio, S. Gainsbury, S.M., Starcevic, V., Richard, J-B., Beck, F., & Billieux, J. (2018). Gender differences in gambling preferences and problem gambling: A network-level analysis. *International Gambling Studies*, 18(3), 512-525. doi:10.108 0/14459795.2018.1495750

ForeFront Ageing and Neurodegeneration

At the forefront of research into ageing and neurodegeneration.

ForeFront Ageing and NeurodegenerationOur core business

The ForeFront Ageing and Neurodegeneration team is committed to discovering early detection methods, identifying new treatments and understanding the underlying mechanisms of neurodegenerative disease.

Neurodegenerative diseases are becoming increasingly prevalent in our ageing population. They have a devastating impact on those affected and their families, and have a huge economic and social impact on our society. Our research groups work together to help reduce this impact by improving the services offered to those affected, enhancing support for carers and offering new hope through clinical trials and the development of novel treatments.

Our research covers most neurodegenerative disorders, including frontotemporal dementia, motor neurone disease, Parkinson's disease, dementia with Lewy bodies, and Alzheimer's disease, as well as healthy brain ageing. Our long-term research aims are to be able to improve and expedite diagnosis and to better understand how neurodegenerative processes work so that we can treat and potentially halt these debilitating diseases.

Our collaborative research program incorporates several research groups and laboratories, all focused on different but interrelated aspects of ageing and neurodegeneration.



Finding solutions to world health problems

ForeFront Ageing and NeurodegenerationForeFront research teams

Clinical research on ageing and dementia

Healthy Brain Ageing Program, led by Professor Sharon Naismith

We aim to determine whether changes in vascular risk factors, mood, sleep and lifestyle can effectively reduce cognitive decline, symptoms of depression and dementia-related brain changes in later life. Our research targets modifiable risk factors by providing early identification, intervention and prevention programs for people at risk for dementia. We evaluate clinical interventions, including brain-training programs, groupbased psychoeducation programs to improve sleep disturbance, home-based exercise programs for people with early-stage dementia, and the development of internetbased tools to improve health and wellbeing, reduce depression and minimise vascular risk factors in older adults.

Frontier Frontotemporal Dementia Research Group, led by Professor John Hodges and Professor Olivier Piguet

Frontotemporal dementia is the second-most common degenerative disease that causes dementia in younger adults. Our research group is dedicated to identifying better ways to diagnose frontotemporal dementia, finding the cause and developing effective treatments for the condition. Our multidisciplinary research examines the neurological, psychological and biological brain function in frontotemporal dementia, as well as how the disease impacts on the lives of patients and their families.

Clinical research on motor neurone disease

Motor Neurone Disease Research Group, led by Professor Matthew Kiernan

We are a multidisciplinary team focused on clinical neurology. We work to understand the mechanisms behind neurodegenerative diseases, develop novel diagnostic tools and trial new treatment strategies. We are currently investigating mechanisms, biomarkers and possible prevention strategies for neurodegeneration in motor neurone disease, frontotemporal dementia, chemotherapy-induced neurotoxicity, stroke, Machado-Joseph disease, spinal muscular atrophy and other inherited neuropathies. We also conduct clinical trials to investigate potential treatments for motor neurone disease, chronic inflammatory demyelinating polyneuropathy and other disorders.

Neurodegenerative and Neuromuscular Diseases Group at the Westmead Institute, led by Professor Steve Vucic

We research the underlying mechanisms behind neurodegenerative disorders such as motor neurone disease, frontotemporal dementia and amyotrophic lateral sclerosis (ALS), as well as neuromuscular diseases like multiple sclerosis.

A key issue for many patients is that treatment is delayed due to the lack of reliable diagnostic tests. In collaboration with Professor Matthew Kiernan, we are commercialising our novel threshold-tracking transcranial magnetic stimulation (TMS) technique, which has been shown to be sensitive in diagnosing motor neurone disease and has the potential to be used to identify biomarkers in multiple sclerosis and other degenerative disorders.

Clinical research on Parkinson's disease and dementia with Lewy bodies

Clinical Parkinson's Disease and Dementia with Lewy Bodies Research Group, led by Professor Simon Lewis

Our research is dedicated to improving the quality of life for people with Parkinson's disease, dementia with Lewy bodies and related disorders and, ultimately, to finding a cure for these diseases. By working with people with parkinsonism, we aim to find ways to predict the disease and to stem its progression. We work closely with other researchers who focus on brain conditions related to Parkinson's disease. We participate in NeuroSleep, the Centre for Translational Sleep and Circadian Neurobiology, which ran until 2018 and sought to better understand the relationship between sleep and a healthy brain. From 2019, we are participating in the Centre of Research Excellence to Optimise Sleep in Brain Ageing and Neurodegeneration (CogSleep).

Genetic research on Neurodegeneration

Genetics of Movement Disorders Group, led by Professor Carolyn Sue

Our research aims to improve diagnostic methods and genetic testing for patients with Parkinson's disease and other inherited forms of movement disorders. By identifying causative genes involved in these disorders, we are able to create patient-derived cell models with biologically relevant levels of abnormal proteins to further understand pathogenic mechanisms of disease. Our experiments have led to the discovery of novel disease pathways and new treatment approaches.

Neurogenetics and Epigenetics Research Group, led by Associate Professor John Kwok

Our group studies the relationship between genetic changes and features of dementia and related disorders. We also examine lifestyle and epigenetic factors in these diseases. Our research studies genetic variants in specific genes that have been implicated in sporadic and heritable forms of dementia and other neurodegenerative diseases. We focus on understanding how genetic mutations cause or increase the risk of disease in order to work towards better treatment strategies.

Laboratory-based research on neurodegeneration

Dementia and Movement Disorders Laboratory, led by Professor Glenda Halliday

Our laboratory studies the origin and development of neurodegenerative dementias and movement disorders. Our focus is on how neurodegeneration manifests when symptoms first show and how this relates to genetic makeup, changes identified in the brain, and blood markers of different pathologies. The aim is to identify and validate biomarkers that could be used in the diagnosis of neurodegenerative diseases and/or to monitor responses to new classes of drugs for these debilitating disorders.

Neurodegeneration Research Laboratory, led by Associate Professor Kay Double

Our research is focused on understanding the cause and neurodegenerative processes in Parkinson's disease and other movement disorders so that we can better treat and, ultimately, prevent these conditions. Our laboratory-based research focuses on understanding how degenerative disorders such as Parkinson's disease, dementia with Lewy bodies and motor neurone disease damage brain and nerve cells. We are also researching how we can achieve slower disease progression and better quality of life for patients. We work to develop better and earlier diagnostic tools and targeted treatment strategies for Parkinson's disease.

In November 2018, Sydney hosted the 11th International Conference on Frontotemporal Dementias, which was a huge success. Hosting 770 delegates over three days, the conference brought together global leaders in frontotemporal dementia (FTD) research. The conference was chaired by Professor Olivier Piguet and provided a fantastic opportunity for the ForeFront researchers to showcase their work on FTD with the international experts. It also ran a carer's day, which was a great opportunity for carers of research participants to get expert advice from all over the world.

Representing the Brain and Mind Centre, and in collaboration with the University of Sydney, the ForeFront team has established the Sydney Dementia Network, linking dementia researchers with Local Health Districts, particularly Sydney Local Health District, and researchers in other fields, as well as providing a forum for more direct public engagement and partnerships. The network is expected to aid in the identification of important gaps in dementia research, guiding the University's research priorities.

The University of Sydney

ForeFront Ageing and Neurodegeneration Highlights

Fellowships awarded

The excellent scholarship produced Motor Neurone Disease Research by the ForeFront Ageing and Neurodegeneration team continues to attract support, including the following nine fellowships awarded to researchers.

National Health and Medical Research Council (NHMRC) Fellowships:

- Professor Sharon Naismith: Novel assessment and intervention for dementia: an inter-disciplinary translational approach (NHMRC **Boosting Dementia Research** Leadership Fellowship)
- Dr Carol Dobson-Stone: Discovery of novel neurodegeneration genes via next-generation sequencing technologies and highthroughput cellular assays (NHMRC Boosting Dementia Research Leadership Fellowship)
- Dr Fiona Kumfor: Social and Behavioural disturbances in dementia: optimising detection and treatment (NHMRC Career Development Fellowship)
- Dr Sicong Tu: Neural signatures of disease spread and evolution in motor neurodegenerative syndromes (NHMRC Early Career Fellowship)

Institute of Australia (MNDRIA) Postdoctoral Fellowships:

- Dr Emma Devenney: Behaviour, cognition, eye-movements and psychiatric disease in C9orf72 MND and FTD; a cross modal-approach to facilitate early and accurate diagnosis
- Dr William Huynh: A multimodal approach combining novel electrophysiological and neuroimaging techniques to explore the pathophysiological mechanisms and disease spread in motor neurone disease

Sydney Research Accelerator (SOAR) Fellowships, 2018:

- Associate Professor Muireann Irish: Managing memory loss in dementia
- Dr James Shine: Cognition and attention in dementia
- Dr Carol Dobson-Stone: Uncovering the genetics of dementia

Grants awarded

NHMRC FTD and MND program grant

Led by: Halliday, G., Mattick, J., Hodges, J., Kiernan, M., Piguet, O., Kril, J., Ittner, L., Kassiou, M., Loy, C. **Granting body: NHMRC Program**

grant

Years: 2018-2022 Amount: \$17,069,580

Motor Neurone Disease: Patientcentred care for a progressive neurological disease evidence driving policy

Led by: Kiernan, M. and Vucic, S. Granting body: NHMRC Partnership

Project

Years: 2018-2023 Amount: \$771,042

Inflammatory markers in GBA carriers with and without Parkinson's disease

Led by: Dzamko, N.

Granting bodies: Shake it Up Australia Foundation, The Michael J Fox Foundation for Parkinson's Research and the University of Sydney

Years: 2018-2019 Amount: \$272,514

Are there peripheral changes in GBA protein/activity in idiopathic Parkinson's disease patients?

Led by: Halliday, G., Dzamko, N.,

and Lewis, S.

Granting bodies: Shake it Up Australia Foundation and The Michael J Fox Foundation for Parkinson's Research

Years: 2018-2019 Amount: \$232,300

Testing posterior parietal cortex contributions to human episodic memory

Led by: Irish, M. and Hodges, J. **Granting body:** ARC Discovery

Project

Years: 2018 -- 2020 **Amount:** \$358,912

The role of mutant CYLD in frontotemporal dementia and motor neurone disease

Led by: Dobson-Stone, C. and

Kwok, J.

Granting body: NHMRC Project

Grant

Years: 2018 -- 2021 **Amount:** \$963,216

Nix mediated mitophagy: A new therapeutic approach to Parkinson's disease

Led by: Sue, C. and Fu, Y. **Granting body: NHMRC Project**

Grant

Years: 2018 - 2020 **Amount:** \$674,428

BRAIN-MEND: Biological Resource Analysis to Identify New Mechanisms and Phenotypes in **Neurodegenerative Diseases**

Led by: Kwok, J.

Granting body: NHMRC Boosting Dementia Research Grants

Years: 2018-2021 Amount: \$529,967

The economic impact of providing precision medicine through whole-genome sequencing

Led by: Sue, C. and Davis, R. **Granting body: NHMRC Partnership**

Project

Years: 2018 - 2022 **Amount:** \$1,144,787

Pathophysiology, site of disease onset and mechanisms of spread in amyotrophic lateral sclerosis

Led by: Vucic, S., Menon, P and

Huynh, W.

Granting body: NHMRC Project

Grant

Years: 2017 - 2021 Amount: \$704,270

Healthy gums and muscles for a healthy brain program

Led by: Erberhard J, Naismith SL,

Duffy SL, Ruiz K

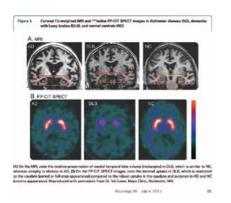
Granting body: Royal Freemasons

Benevolent Institution Years: 2018-2020 **Amount:** \$180,000

ForeFront Ageing and Neurodegeneration Key publications



Pages from Diagnosis and management of dementia with Lewy bodies: Fourth consensus report of the DLB Consortium



Dementia

- 1. McKeith, I.G., Boeve, B.F., Dickson, D.W., Halliday, G., Taylor, J.P., Weintraub, D., Aarsland, D., Galvin J., Attems, J., Ballard, C.G., Bayston, A., Beach, T.G., Blanc, F., Bohnen, N., Bonanni, L., Bras, J., Brundin, P., Burn, D., Chen-Plotkin, A., Duda, J.E., El-Agnaf, O., Feldman, H., Ferman, T.J., Ffytche, D., Fujishiro, H., Galasko, D., Goldman, J.G., Gomperts, S.N., Graff-Radford, N.R., Honig, L.S., Iranzo, A., Kantarci, K., Kaufer, D., Kukull, W., Lee, V.M.Y., Leverenz, J.B., Lewis, S., Lippa C., Lunde, A., Masellis, M., Masliah, E., McLean, P., Mollenhauer, B., Montine, T.J., Moreno, E., Mori, E., Murray, M., O'Brien, J.T., Orimo, S., Postuma, R.B., Ramaswamy, S., Ross, O.A., Salmon, D.P., Singleton, A., Taylor, A., Thomas, A., Tiraboschi, P, Toledo, J.B., Trojanowski, J.Q., Tsuang, D., Walker, Z., Yamada, M., & Kosaka, K. (2017). Diagnosis and management of dementia with Lewy bodies: Fourth consensus report of the DLB Consortium, Neurology, 89(1):88-100.
- van Hummel, A., Chan, G., van der Hoven, J., Morsch, M., Ippati, S., Suh, L., Bi, M., Asi, P.R., Lee, W.S., Butler, T.A., Przybyla, M., Halliday, G.M., Piguet, O., Kiernan, M.C., Chung, R.S., Ittner, L.M., & Ke, Y.D. (2018). Selective spatiotemporal vulnerability of central nervous system neurons to pathologic TAR DNA-Binding Protein 43 in aged transgenic mice. American Journal of Pathology, 188(6):1447-1456.

Motor neurone disease

- 1. Mathey, E.K., Garg, N., Park, S.B., Nguyen, T., Baker, S., Yuki, N., Yiannikas, C., Lin, C.S., Spies, J.M., Ghaoui, R., Barnett, M.H., Vucic, S., Pollard, J.D., & Kiernan, M.C. (2017). Autoantibody responses to nodal and paranodal antigens in chronic inflammatory neuropathies. *Journal of Neuroimmunology*, 309:41–6.
- 2. van Rheenen, W., Shatunov, A., Dekker, A.M., McLaughlin, R.L., Diekstra, F.P., Pulit, S.L., van der Spek, R.A., Võsa, U., de Jong, S., Robinson, M.R., Yang, J., Fogh, I., van Doormaal, P.T., Tazelaar, G.H., Koppers, M., Blokhuis, A.M., Sproviero, W., Jones, A.R., Kenna, K.P., van Eijk, K.R., Harschnitz, O., Schellevis, R.D., Brands, W.J., Medic, J., Menelaou, A., Vajda, A., Ticozzi, N., Lin, K., Rogelj, B., Vrabec, K., Ravnik-Glavač, M., Koritnik, B., Zidar, J., Leonardis, L., Grošelj, L.D., Millecamps, S., Salachas, F., Meininger, V., de Carvalho, M., Pinto, S., Mora, J.S., Rojas-García, R., Polak, M., Chandran, S., Colville, S., Swingler, R., Morrison, K.E., Shaw P.J., Hardy, J., Orrell, R.W., Pittman, A., Sidle, K., Fratta, P., Malaspina, A., Topp, S., Petri, S., Abdulla, S., Drepper, C., Sendtner, M., Meyer, T., Ophoff, R.A., Staats, K.A., Wiedau-Pazos, M., Lomen-Hoerth, C., Van Deerlin, V.M., Trojanowski, J.Q., Elman, L., McCluskey, L., Basak, A.N., Tunca, C., Hamzeiy, H., Parman, Y., Meitinger, T., Lichtner, P., Radivojkov-Blagojevic, M., Andres, C.R., Maurel, C., Bensimon, G., Landwehrmeyer,

B., Brice, A., Payan, C.A., Saker-Delye, S., Dürr, A., Wood, N.W., Tittmann, L., Lieb, W., Franke, A., Rietschel, M., Cichon, S., Nöthen, M.M., Amouyel, P., Tzourio, C., Dartigues, J.F., Uitterlinden, A.G., Rivadeneira, F., Estrada, K., Hofman, A., Curtis, C., Blauw, H.M., van der Kooi, A.J., de Visser, M., Goris, A., Weber, M., Shaw, C.E., Smith, B.N., Pansarasa, O., Cereda, C., Del Bo, R., Comi, G.P., D'Alfonso, S., Bertolin, C., Sorarù, G., Mazzini, L., Pensato, V., Gellera, C., Tiloca, C., Ratti, A., Calvo, A., Moglia, C., Brunetti, M., Arcuti, S., Capozzo, R., Zecca, C., Lunetta, C., Penco, S., Riva, N., Padovani, A., Filosto, M., Muller, B., Stuit, R.J., PARALS Registry, SLALOM Group, SLAP Registry, FALS Sequencing Consortium, SLAGEN Consortium, NNIPPS Study Group, Blair, I., Zhang, K., McCann, E.P., Fifita, J.A., Nicholson, G.A., Rowe, D.B., Pamphlett, R., Kiernan, M.C., Grosskreutz, J., Witte, O.W., Ringer, T., Prell, T., Stubendorff, B., Kurth, I., Hübner, C.A., Leigh, P.N., Casale, F., Chio, A., Beghi, E., Pupillo, E., Tortelli, R., Logroscino, G., Powell, J., Ludolph, A.C., Weishaupt, J.H., Robberecht, W., Van Damme, P., Franke, L., Pers, T.H., Brown, R.H., Glass, J.D., Landers, J.E., Hardiman, O., Andersen, P.M., Corcia, P., Vourc'h, P., Silani, V., Wray, N.R., Visscher, P.M., de Bakker, P.I., van Es, M.A., Pasterkamp, R.J., Lewis, C.M., Breen, G., Al-Chalabi, A., van den Berg, L.H., & Veldink, J.H. (2016). Genome-wide association analyses identify new risk variants and the genetic architecture of amyotrophic lateral sclerosis, Nature Genetics, 48(9):1043-8.

Parkinson's Disease

- Postuma, R.B., Poewe, W., Litvan, I., Lewis, S., Lang, A.E., Halliday, G., Goetz, C.G., Chan, P., Slow, E., Seppi, K., Schaffer, E., Rios-Romenets, S., Mi, T., Maetzler, C., Li, Y., Heim, B., Bledsoe, I.O., & Berg, D. (2018). Validation of the MDS clinical diagnostic criteria for Parkinson's disease, Movement Disorders, 33(10):1601-1608.
- 2. Guerreiro, R., Ross, O.A., Kun-Rodrigues, C., Hernandez, D.G., Orme, T., Eicher, J.D., Shepherd, C.E., Parkkinen, L., Darwent, L., Heckman, M.G., Scholz, S.W., Troncoso, J.C., Pletnikova, O., Ansorge, O., Clarimon, J., Lleo, A., Morenas-Rodriguez, E., Clark, L., Honig, L.S., Marder, K., Lemstra, A., Rogaeva, E., St George-Hyslop, P., Londos, E., Zetterberg, H., Barber, I., Braae, A., Brown, K., Morgan, K., Troakes, C., Al-Sarraj, S., Lashley, T., Holton, J., Compta, Y., Van Deerlin, V., Serrano, G.E., Beach, T.G., Lesage, S., Galasko, D., Masliah, E., Santana, I., Pastor, P., Diez-Fairen, M., Aguilar, M., Tienari, P.J., Myllykangas, L., Oinas, M., Revesz, T., Lees, A., Boeve, B.F., Petersen, R.C., Ferman, T.J., Escott-Price, V., Graff-Radford, N., Cairns, N.J., Morris, J.C., Pickering-Brown, S., Mann, D., Halliday, G.M., Hardy J., Trojanowski, J.Q., Dickson, D.W., Singleton, A., Stone, D.J., & Bras, J. (2018). Investigating the

- genetic architecture of dementia with Lewy bodies: a two-stage genome-wide association study, *The Lancet Neurology*, 17(1):64-74.
- Walton, C., Mowszowski, L., Gilat, M., Hall, J., O'Callaghan, C., Muller, A., Georgiades, M., Szeto, J., Ehgoetz Martens, K., Shine, J., Naismith, S., & Lewis, S. (2018). Cognitive training for freezing of gait in Parkinson's disease: a randomized controlled trial. NPJ Parkinson's Disease, 4(15).
- 4. Trist, B.G., Davies, K.M., Cottam, V., Genoud, S., Ortega, R., Roudeau, S., Carmona, A., De Silva, K., Wasigner, V., Lewis, S.J.G., Sachdev, P., Smith, B., Troakes, C., Vance, C., Shaw, C., Al-Sarraj, S., Ball, H., Halliday, G., Hare, D.J., Double, K.L. (2017) Amyotrophic lateral sclerosislike superoxide dismutase 1 proteinopathy is associated with neuronal loss in Parkinson's disease brain. *Acta Neuropathol*. 134(1):113-127.

Ageing

 Naismith, S., Pye, J., Terpening, Z., Lewis, S., & Bartlett, D. (2018). "Sleep Well, Think Well" group program for mild cognitive impairment: A randomized controlled pilot study. Behavioral Sleep Medicine, 24:1-12.



Researcher Spotlight

Dr Carol Dobson-Stone

Dr Carol Dobson-Stone is a molecular geneticist interested in genes that are mutated in dementia and related diseases. She completed her PhD in human genetics at the University of Oxford, UK, in 2004, and shortly thereafter moved to Sydney to work on brain function genetics, at the Garvan Institute. Carol then worked at Neuroscience Research Australia and in 2017, she joined the Brain and Mind Centre as a Senior Research Fellow, working on the genetics of dementia.

"Our cognitive capabilities are what make us uniquely human", says Carol, "and dementia robs people of this humanity. The greatest risk factor for dementia is age and so as the population ages, more and more people will become affected." It is predicted that by the year 2050, around 950,000 Australians will have dementia, for which there is currently no effective treatment. Carol's research aims to uncover the genes involved in the pathogenesis of different forms of dementia, as the first step on the pathway towards designing treatments for these disorders. "We recently identified a mutation in a gene that is responsible for disease in a large

Australian family with several people affected with dementia", Carol explains. "This gene encodes an enzyme involved in autophagy, a process by which the cell breaks down unwanted or misfolded proteins. This is the first time that this enzyme has been implicated in brain disease, and no-one has yet examined its pathogenic role".

In January 2018, Carol was awarded a Sydney Research Accelerator (SOAR) Fellowship to help expand her research into this gene. She is examining how the gene mutation affects cell functions to cause nerve cell death, using cutting-edge cell and mouse models of disease. Carol aims to find out whether people who have more common variants of this gene are at greater risk of developing dementia. "I hope that my research into this and other genes will provide crucial knowledge for diagnosing and developing new treatments for this debilitating group of disorders", she says.

"The greatest risk factor for dementia is age and so as the population ages, more and more people will become affected"

Dr Carol Dobson-Stone



Dr Carol Dobson-Stone

Developing new ways to detect and treat neurological disease.

Our core business

Our neuroimmunology research focuses on improving our understanding of neurological and psychiatric diseases. It has become clear that many of them are associated with a dysregulation of the immune system.

Sydney Neuroimmunology's team of internationally-renowned clinicians and researchers are at the forefront of research into diseases affecting the brain and mind that are associated with an immune dysfunction. These so-called 'neuroimmunological' disorders include subsets of diseases, such as:

- Autoimmune encephalitides
- Autism
- Youth mental health
- Multiple sclerosis
- Motor neurone disease
- Movement disorders
- Myasthenia gravis
- Immune-mediated neuropathy
- Dementia

Our work includes developing novel diagnostic biomarkers, exploring the biological mechanisms that lead to the development of diseases, and implementing new and innovative treatments for some of the most debilitating disorders.

Partnering the Brain and Mind Centre with the Local Health Districts of Sydney, Western Sydney, Northern Sydney and Nepean Blue Mountains, as well as the Sydney Children's Hospital Network, this initiative is the first joint initiative of its magnitude in Australia. Our interdisciplinary team combines discovery research and clinical research programs with specialist clinical care, maximising our capacity to rapidly progress new discoveries into standard clinical practice.

Bringing together our collective expertise, we offer specialist diagnostic immunology services that expedite the assessment of neurological disorders and improve specialist access for physicians.

We are also working to fast-track research into neurological disorders by establishing a shared data repository for collating and comparing data. This repository is providing unprecedented opportunities to develop novel diagnostic biomarkers of disease and develop new treatments.

By integrating clinical neuroimmunology diagnostic services with cutting-edge research, we are facilitating public access to and participation in clinical trials. We are also working towards better patient outcomes by improving treatment options and the surveillance of therapy.

Research areas



Professor Russell Dale, Paediatric Neurologist, Neuroimmunology team

Our discovery work involves identifying novel immune biomarkers, exploring the role of the immune response in pathogenesis, and linking data in order to support and enable population research.

Clinically, we are working to define clinical phenotypes and treatment outcomes, and conduct both longitudinal clinical studies across the lifespan and trials aimed at improving diagnosis and treatment.

Highlights



Professor Steve Vucic, Neurologist, Neuroimmunology team

Grants awarded

SREI II: Neuroimmunology and neuroinflammation: from biomarker and pathogenesis to patient diagnosis and improvement of clinical outcome

Led by: Brilot-Turville F, Dale R, Brown D, Kiernan M, Marais B, Barnett M, Britton P, Guastella A, Halliday G, Harris A, Hickie I, Lewis S, Nassar N, Ramanathan S, Vucic S, Wood N

Granting body: DVC Research/Sydney Research Excellence Initiative 2020 (SREI).

Years: 2018-2019 Amount: \$300,000

Nodal function in peripheral neuroinflammatory disorders: Target antigens, functional significance and treatment response

Led by: Kiernan, M.

Granting body: National Health and Medical Research Council Project Grants

Years: 2016-2019 **Amount:** \$623,975

Defining the basis of autoimmune attacks against myelin to better target treatment of demyelinating disorders

Led by: Brilot-Turville F, Dale R

Granting body: National Health and Medical

Research Council Project Grants

Years: 2018-2021 Amount: \$913,216

The effectiveness of tecfidera in amyotrophic lateral sclerosis: A phase II multicentre randomised placebocontrolled study (TEALS)

Led by: Kiernan, M. and Vucic, S. **Granting body:** FightMND

Years: 2018-2019 Amount: \$4.7 million

Understanding the induction of disease quiescence by immunomodulating drug in multiple sclerosis

Led by: Grau G, Hawke S, Byrne S, Zinger A,

Barnett M, Hodgkinson S

Granting body: MS Research Australia

Years: 2018 -- 2020 Amount: \$225,000

Novel approaches to mitigating heat-related fatigue in individuals with multiple sclerosis

Led by: Jay O, Barnett M, Davis S, Filingeri D,

Carlsen T, Boyd D

Granting body: MS Research Australia

Years: 2018 -- 2020 Amount: \$176,000

Does somatic mutation in the brain drive progressive MS?

Led by: Rubio J, Leslie S, Barnett M **Granting body:** MS Research Australia

Years: 2018-2020 Amount: \$229,000

Fellowships awarded

SOAR Fellowship: Michael Barnett ECF fellowship: Sudarshini Ramanathan,

4 years, NHRMC

Publications

- Ramanathan, S., Mohammad, S., Tantsis, E., Nguyen, T.K., Merheb, V., Fung, V.S.C., White, O.B., Broadley, S., Lechner-Scott, J., Vucic, S., Henderson, A.P.D., Barnett, M.H., Reddel S,W., Brilot, F., Dale, R.C. & Australasian and New Zealand MOG Study Group (2018). Clinical course, therapeutic responses and outcomes in relapsing MOG antibody-associated demyelination, Journal of Neurology, Neurosurgery, and Psychiatry, 89(2):127-137. doi: 10.1136/ jnnp-2017-316880
- Kieseier, B.C., Mathey, E.K., Sommer, C. & Hartung, H.P. (2018). Immunemediated neuropathies, *Nature Reviews Disease Primers*, 4(1):31. doi: 10.1038/ s41572-018-0027-2
- You, Y., Graham, E.C., Shen, T., Yiannikas, C., Parratt, J.D.E., Gupta, V., Barton, J., Dwyer, M.G., Barnett, M.H., Fraser, C.L., Graham, S.L., and Klistorner, A. (2018). Progressive inner nuclear layer dysfunction in non-optic neuritis eyes in multiple sclerosis. Neurol Neuroimmunol Neuroinflamm,5:e427
- Chaseling, G.K., Filingeri, D., Barnett, M., Hoang, P., Davis, S.L., Jay, O. (2018). Cold-Water Ingestion Improves Exercise Tolerance of Heat-Sensitive People with MS. Medicine and science in sports and exercise. *Med Sci Sports Exerc*. 50(4):643-648.
- Fragoso, Y.D., Spelman, T., Boz, C., Alroughani, R., Lugaresi, A., Vucic, S., et al. (2018). Lymphocyte count in peripheral blood is not associated with the level of clinical response to treatment with fingolimod. *Multiple sclerosis and related* disorders. 19:105–8.
- Garber, J. & Barnett, M.H. (2018)
 Controversies in MS: "We should focus more on finding therapeutic targets for the non-inflammatory damage in MS". Invited commentary. Mult Scier. 24(10):1272-1274.

- 7. Christogianni, A., Bibb, R., Davis, S.L., Jay, O., Barnett, M., Evangelou, N., & Filingeri, D., (2018) Temperature sensitivity in multiple sclerosis: an overview of its impact on sensory and cognitive symptoms *Temperature*, 5(3):208–223.
- 8. Reddel, S.W., Barnett, M.H., Riminton, D.S., Dugal, T., Buzzard, K.A., Wang, C., Fitzgerald, F., Beadnall, H.N., Erickson, D., Gahan, D., Wang, D., Ackland, T., Thompson, R. (2018). Successful implementation of an automated electronic support system for patient safety monitoring the Alemtuzumab in Multiple Sclerosis Safety Systems (AMS3) study. *Mult Scler*. doi: 10.1177/1352458518783673. [epub ahead of print]
- Triplett, J. D., Yiannikas, C., Barnett, M. H., Parratt, J., Barton, J., Graham, S. L., ... Klistorner, A. (2018). Pathophysiological basis of low contrast visual acuity loss in multiple sclerosis. *Annals of clinical and* translational neurology, 5(12), 1505–1512.
- Tantsis, E.M., Prelog, K., Alper, G., Benson, L., Gorman, M., Lim, M., Mohammad, S.S., Ramanathan, S., Brilot, F., Dale, R.C. (2018). Magnetic resonance imaging in enterovirus-71, myelin oligodendrocyte glycoprotein antibody, aquaporin-4 antibody, and multiple sclerosis-associated myelitis in children. Paediatric Myelitis Mri Study Group. *Dev Med Child Neurol*. doi: 10.1111/dmcn.14114. [epub ahead of print]
- 11. Brilot, F. (2018). Relapsing ADEM followed by optic neuritis in children; a clinical entity associated with anti-MOG antibody. *Eur J Neurol*. 25(8):1003-1004 (invited editorial)
- 12. Berridge G, Menassa DA, Moloney T, Waters PJ, Welding I, Thomsen S, Zuberi S, Fischer R, Aricescu AR, Pike M, Dale RC, Kessler B, Vincent A, Lim M, Irani SR, Lang B. (2018). Glutamate receptor δ2 serum antibodies in pediatric opsoclonus myoclonus ataxia syndrome. Neurology 91(8):e714e723

- 13. Dale RC, Nosadini M. (2018). Infectiontriggered autoimmunity: The case of herpes simplex virus type 1 and anti-NMDAR antibodies. *Neurol Neuroimmunol Neuroinflamm*. 5(4):e471.
- Kothur K, Bandodkar S, Chu S, Wienholt L, Johnson A, Barclay P, Brogan PA, Rice GI, Crow YJ, Dale RC. (2018). An open-label trial of JAK 1/2 blockade in progressive IFIH1-associated neuroinflammation. Neurology. 90(6):289-291.
- 15. Tsai VW, Brown DA, Breit SN. Targeting the divergent TGFβ superfamily cytokine MIC-1/GDF15 for therapy of anorexia/cachexia syndromes.(2018) Curr Opin Support Palliat Care. 12(4):404-409.
- 16. Atashrazm, F., Hammond, D., Perera, G., Dobson-Stone, C., Mueller, N., Pickford, R., Kim, W.S., Kwok, J.B., Lewis, S.J.G., Halliday, G.M., Dzamko, N. (2018). Reduced glucocerebrosidase activity in monocytes from patients with Parkinson's disease. *Sci Rep*.8(1):15446. doi: 10.1038/ s41598-018-33921-x.
- Barton J, Hardy T, Riminton S, Reddel SW, Barnett Y, Coles A and Barnett MH. (2017). Tumefactive demyelination following treatment for relapsing multiple sclerosis with alemtuzumab. *Neurology*. 88(10):1004-1006.
- Dale, R.C., Barnett, M.H. & Kiernan, M.C. (2017). Maternal autoimmunity: risk of neurodevelopmental and neuropsychiatric outcomes, *Journal of Neurology*, *Neurosurgery*, and *Psychiatry*, 88(9):713-714. doi: 10.1136/jnnp-2017-315724
- Kalincik, T., William, J., Brown, L., Robertson, N. et al. (2017). Treatment effectiveness of alemtuzumab compared with natalizumab, fingolimod, and interferon beta in relapsing-remitting multiple sclerosis: a cohort study. *Lancet Neurol*. 16(4):271-281.

- 20. Filingeri, D., Chaseling, G., Hoang, P., Barnett, M., Davis, S.L., Jay, O. (2017). Afferent thermosensory function in relapsing-remitting Multiple Sclerosis following exercise-induced increases in body temperature. *Experimental* physiology 102 (8), 887–893.
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- 22. Kalincik et al. (2017) Towards personalised therapy for multiple sclerosis: prediction of individual treatment response. *Brain*. 140(9):2426-2443
- 23. Swee et al. (2017). Vestibulo-ocular reflex deficits with medial longitudinal fasciculus lesions. *Journal of Neurology*. 264: 2119.
- 24. Khani, S.E., Vafaee, F., Suter, C., Hawke, S., Beadnall, H., Devenney, E. (2017) Exosomal microRNA signatures in multiple sclerosis reflect disease status. Scientific Reports (Nature). 7: 14293.
- 25. Weissert, R., Brilot, F. (2017). Induction of Central Nervous System Disease by the Adaptive Immune Response. *Front Immunol.* 8:1218. doi: 10.3389/fimmu.2017.01218.
- 26. Chen, K.A., Brilot, F., Dale, R.C., Lafferty, A.R., Andrews, P.I. (2017). Hashimoto's encephalopathy and anti-MOG antibody encephalitis: 50 years after Lord Brain's description. *Eur J Paediatr Neurol.* 21(6):898-901. doi: 10.1016/j. ejpn.2017.06.002.
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- 30. Korff, C. M., & Dale, R. C. (2017). The immune system in pediatric seizures and epilepsies. *Pediatrics*, *140*(3), doi: 10.1542/peds.2016-3534.
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Patient spotlight

Lauren's story

It's a shock to learn you have a chronic condition. When Lauren was diagnosed with multiple sclerosis at 25, gaining control of her health and pursuing a career were her priorities.



Lauren

Lauren had just landed a prestigious job with a top-tier law firm in Sydney. Soon after arriving, this journey came to a standstill after she paid a visit to her GP.

"He said I was showing signs of multiple sclerosis," Lauren says. "To be honest, I thought he was crazy. I was doing triathlons, working more than full time and I'd just moved to Sydney for a great career opportunity."

Later, when Lauren lost movement in one of her arms, she realised something was wrong. She was taken straight to the emergency department and hospitalised for a week.

It was while in the hospital that a doctor sat with Lauren and asked her about herself, her career and what she did outside work. "He was the one who thought Michael Barnett at the Brain and Mind Centre would be the perfect neurologist for me," Lauren says. "That's how I got the referral."

It has been seven years since Lauren first saw Professor Michael Barnett, a neurologist and multiple sclerosis specialist at the University of Sydney's Brain and Mind Centre. He has helped Lauren throughout her journey, from navigating the initial diagnosis to treatment and ongoing management. His clinic is the only multiple sclerosis facility in Australia that is based within a university and therefore integrated with the latest research.

"The thing with multiple sclerosis is that if you stop it when you're young, you don't have that damage going forward," says Lauren. "So, it's really important to get in early and stop it in its tracks and that's exactly what Michael did for me."

Lauren has not had any relapses or degeneration so far, and she has gone on to lead a successful career as an academic lawyer at one of Australia's top law schools.

Understanding the links between sleep and brain health.

Our core business

Inadequate or poor-quality sleep and sleep disorders such as insomnia, circadian rhythm disorders and obstructive sleep apnoea are major health problems. Our team are focused on leading world-class efforts in delineating the role of sleep and circadian (sleep-wake) disorders for brain and mental health.

In 2016–17, 40% of Australians reported insufficient sleep and 20% complained of excessive daytime sleepiness. According to a 2017 report by Deloitte Access Economics for the Sleep Health Foundation, the cost of inadequate sleep in Australia was \$26 billion in 2016–17 through loss of productivity and healthcare costs. Sleep–wake disturbance also significantly impacts our mental health and wellbeing and contributes to accelerated brain ageing and neurodegeneration.

In 2018, the Sleep and Circadian Biology team was launched at the Brain and Mind Centre, bringing together researchers from the Woolcock Institute and the University of Sydney faculties of Science, Medicine and Health, Engineering, Information Technologies, and Nursing, as well as University multidisciplinary initiatives, including the Charles Perkins Centre. Our highly integrated, multidisciplinary team has already demonstrated success and attracted funding in recognition of our work, including NHMRC Fellowships and a highly competitive NHMRC grant for the Centre of Research Excellence to Optimise Sleep in Brain Ageing and Neurodegeneration (CogSleep CRE).

Current research

Priority areas for our research include child development, youth mental health and dementia, which contribute significantly to the global burden of disease. At an individual level, mental health problems and neurodegenerative diseases both have deleterious impacts on the brain, as well as hindering wellbeing and contributing to disability. Sleep-wake disturbance is a prodromal feature of depression,

dementia and Parkinson's disease, and the persistence of sleep disturbances predicts the recurrence of depressive illness as well as cognitive decline.

It is therefore likely that better efforts to understand and treat sleep-wake disturbance in these diseases will have an impact on early intervention and prevention approaches, as well as optimising wellbeing, productivity and functioning. Our team works across various diseases and collaborates closely with existing Brain and Mind Centre teams to pursue this cross-cutting research, including the Youth Mental Health, Forefront Ageing and Neurodegeneration and Child Neurodevelopment and Mental Health teams.

The Sleep and Circadian Biology team is co-led by Professor Sharon Naismith, Professor Ron Grunstein and Professor Simon Lewis, who are establishing the team as world leaders in research linking sleep and circadian systems and disorders of the brain and mind, by fostering national and international collaborations.



Sleep and Circadian Biology Highlights

Grants awarded

CogSleep Centre of Research Excellence: Sleep-wake disturbance in ageing and neurodegenerative disease

Led by: Naismith, S., Grunstein, R., Lewis, S., Phillips, C., D'Rozario, A., Hoyos, C., Rajaratnam, S., Halliday, G., Martins, R., Lagopoulos, J.

Granting body: National Health and Medical Research Council (NHMRC)

Years: 2018 - 2023 Amount: \$2.5m

"Local Sleep" in the awake brain: An underlying cause of neurobehavioural deficits in sleep apnea?

Led by: Grunstein, R., D'Rozario, A., Phillips, C., Wong, K., Hoyos, C., Naismith, S., Vakulin, A. &Eckert, D. Granting body: National Health and Medical Research Council (NHMRC) Project Grants

Years: 2018 - 2020 Amount: \$582,330

Cannabinoids and sleep: A randomised, placebo-controlled crossover pilot study of 20:1 CBD:THC for insomnia.

Led by: Grunstein. R., & Hoyos, C.M. **Granting body:** Lambert Initiative Research Grant, University

of Sydney Years: 2018 - 2021 Amount: \$255,712

The Australian Dementia Network (ADNeT): Bringing together Australia's dementia stakeholders

Led by: Rowe, C., Sachdev, P., Naismith, S.L., Breakspear, M., Brodaty, H., Anstey, K., Martins, R., Ward, S., Vickers, J., & Masters, C..

Granting body: NHMRC **Years:** 2018 - 2023 **Amount:** \$18,000,000

Awards

- Professor Sharon Naismith received the 2018 Society for Mental Health Research Oration Award for outstanding commitment to and achievements in psychiatric research.
- Dr Angela D'Rozario was awarded the Helen Bearpark Scholarship, one of the most prestigious awards from the Australasian Sleep Association, the national peak professional body for sleep research and medicine.
- Dr Loren Mowszowski was awarded one of six inaugural Brain and Mind Centre Research and Development Grants for early- or midcareer researchers.
- Dr Camilla Hoyos was recognised with three prestigious national and international awards:
 the Sleep, Respiratory and
 Neurobiology Assembly James
 Skatrug New Investigator Award at the American Thoracic Society meeting, the BUPA Health
 Foundation Emerging Health
 Researcher Commendation
 Award, and the Young
 Researcher Award from Sydney
 Health at the Sydney Innovation and Research Symposium.

2019 and beyond

The Sleep and Circadian
Biology team will investigate
new biomarkers of sleep-wake
disturbance that predict cognitive
decline, neurodegenerative disease
and poor mental health. We will
undertake novel clinical trials for
sleep-wake disturbance in order
to improve cognition and mental
health and optimise healthy
brain ageing. We will employ new
technology and data science
approaches to surveil symptoms
in real-time, and test new
e-health interventions.

Our focus for 2019 also includes increasing the visibility of our international leadership in the field of sleep and chronobiology. We will be co-leading new global initiatives in sleep and dementia, which will feature at the Alzheimer's Association International Conference in Los Angeles and the World Sleep conference in Vancouver.



Sleep and Circadian BiologyKey publications

- Naismith, S.L. & Mowszowski, L. (2018). Sleep disturbance in mild cognitive impairment: a systematic review of recent findings. Current Opinion in Psychiatry, 31(2):153-159.
- Cross, N.E., Memarian, N., Duffy, S.L., Paquola, C., LaMonica, H., D'Rozario, A., Lewis, S.J.G., Hickie, I.B., Grunstein, R.R. & Naismith, S.L. (2018). Structural brain correlates of obstructive sleep apnoea in older adults at risk for dementia. European Respiratory Journal, 52(1): 1800740.
- 3. D'Rozario, A.L., Bartlett, D.J., Wong, K.K.H., Sach, T., Yang, Q., Grunstein, R.R. & Rae, C.D. (2018). Brain bioenergetics during resting wakefulness are related to neurobehavioral deficits in severe obstructive sleep apnea: a 31P magnetic resonance spectroscopy study. Sleep, 41(8).
- 4. D'Rozario, A.L., Field, C.J., Hoyos, C.M., Naismith, S.L., Dungan, G.C., Wong, K.K.H., Grunstein, R.R. & Bartlett, D.J. (2018). Impaired neurobehavioural performance in untreated obstructive sleep apnea patients using a novel standardised test battery. Frontiers in Surgery, 18(5): 35. doi:10.3389/fsurg.2018.00035.



L-R Inventor of the CPAP machine, Colin Sullivan, Professor Sharon Naismith and Professor Ron Grunstein

"Working at the Brain and Mind Centre offers the opportunity to collaborate with leading researchers with different clinical and scientific expertise across a range of research fields"

Dr Shantel Duffy



Dr Shantel Duffy

Researcher Spotlight

Dr Shantel Duffy

A postdoctoral research fellow with the discipline of Exercise and Sport Science in the Faculty of Health Sciences, Dr Shantel Duffy works with the Sleep and Circadian Biology team at the Brain and Mind Centre. With a background as an accredited (and practising) exercise physiologist and nutritionist, and bringing advanced neuroimaging expertise to the team, Dr Duffy currently holds a prestigious NHMRC-ARC Dementia Research Development Fellowship. Her research aims to explore the mechanisms underpinning cognitive decline and depression in older adults at risk for dementia.

She also examines the effect of interventions on markers of inflammation and oxidative stress. Dr Duffy has pioneered work exploring a Magnetic Resonance Imaging (MRI)-derived marker of oxidative stress in individuals at risk for dementia and/or mood disorders. Internationally, she was the first researcher to show changes in this marker in people with sleep-disordered breathing.

Dr Duffy is also currently leading a series of studies exploring the effect of exercise interventions on mood and cognition in individuals living with cognitive impairment, as well as residents in aged-care facilities.

"Working at the Brain and Mind Centre offers the opportunity to collaborate with leading researchers with different clinical and scientific expertise across a range of research fields. In this way, we are uniquely placed to explore complex, multidisciplinary research questions that have real-world implications", says Dr Duffy. "The most rewarding aspect of my work is interacting every day with individuals who are living with cognitive impairment and having the opportunity to translate our research findings in to my own clinical practice."

"A key strength of our work is our capacity for translation: we work closely with Dementia Australia and regularly provide seminars for both the community and clinicians to disseminate our research findings. In this way, I believe we are making a truly meaningful impact in the area of dementia-prevention research."

Computational Neuroscience

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Using artificial intelligence to gain insight into the cause and progression of neurological diseases.

Computational Neuroscience

Our core business

Comprising experts in neuroimaging science, deep learning and clinical neurology, the Brain and Mind Centre's recently established Computational Neuroscience Team is building a library of algorithms that, when applied to large imaging datasets, will provide insights into the cause and progression of neurological diseases. New imaging biomarkers derived from this work will be used in neuroimaging research, clinical trials and clinical practice.

Funded by a 2018 Australian government Cooperative Research Centre project grant, the Team has developed an exciting partnership with I-MED Radiology and the Sydney Neuroimaging Analysis Centre to accelerate the translation of their work in imaging science and machine learning to clinical medicine and industry, with a focus on inflammatory, degenerative and vascular diseases of the brain.

The team has also been substantially bolstered by an influx of enthusiastic early-career researchers, including imaging scientist Dr Chenyu Wang, recently appointed as Senior Lecturer and the inaugural Nerve Research Foundation Fellow, and a team of three artificial intelligence scientists, including Dr Hao Xiong, a postdoctoral scientist supported by the Brain and Mind Centre.

Computational Neuroscience Highlights

The team's expansion in 2018 supported three PhD candidates in neuroimaging science and the creation of two scholarships for students in imaging artificial intelligence. The team made significant strides in biomarker research, particularly for patients with multiple sclerosis (MS). Specifically, this work used new analysis techniques and algorithms to demonstrate previously undocumented changes within established brain MS lesions over time. These changes have been adapted into biomarkers that can be used in clinical trials of emerging neuroprotective and pro-reparative medicines.

In 2018, the University also signed a memorandum of understanding with MSBASE Foundation to develop an imaging repository and analysis platform for the largest MS registry in the world (with upwards of 70,000 patients).

The Computational Neuroscience team's unique mix of clinicians, imaging scientists and deep-learning experts, together with access to large-scale datasets such as the MSBASE repository, has the potential to drive the development of next-generation biomarkers for precision medicine across the spectrum of neurological diseases.

Fellowship success

Professor Fernando Calamante was awarded an NHMRC Research Fellowship:

Novel methods to study structuralfunctional connectivity in Epilepsy and Schizophrenia

Our team also received two three-year fellowships from MS Research Australia:

- Dr Chenyu Wang: Developing multimodal quantitative imaging biomarkers in multiple sclerosis
- Dr Justin Garber: Postgraduate Scholarship - connectomics and other imaging aspects of progressive multiple sclerosis

Grants awarded

Members of the team received the following research grants:

Al: new smarts for the medical imaging industry

Led by: Sydney Neuroimaging Analysis Centre, in partnership with the Computational Neuroscience team and I-MED Radiology Network

Granting body: Cooperative Research Centre Project (CRC-P) Program

Years: 2018-2021 Amount: \$2.36 million

This study aims to improve diagnostic neuroimaging of brain ailments such as multiple sclerosis and dementia. The CRC-P program supports industry-led, outcomesfocused partnerships between industry, researchers and the community: this project funding results from a successful and longstanding partnership between the Brain and Mind Centre, Sydney Neuroimaging Analysis Centre and I-MED Radiology Network.



Professor Michael Barnett at the Computational Neuroscience Team announcement

NVIDIA Medical Imaging Computational and Artificial Intelligence Platform

Led by: Calamante, F., Tao, D. and Barnett, M. **Granting body:** University of Sydney/NHMRC equipment grant, with in-kind support

from NVIDIA Years: 2018

Amount: \$180,000

This equipment grant provided funds for infrastructure and support for a NVIDIA DGX supercomputer, boosting the Computational Neuroscience team's capability in developing artificial intelligence technologies and their application into neurological and neuroinflammatory disease states.

Cladribine: a multicentre Longterm efficacy Biomarker Australian Study (CLOBAS)

Led by: Hunter New England Local
Health District, in partnership with the
Computational Neuroscience team and
Sydney Neuroimaging Analysis Centre
Collaborators: Sydney Neuroimaging Analysis
Centre & Computational Neuroscience team
Granting body: Merck Serono Australia

Years: 2018 - 2027 Amount: \$3.25 million

Implemented in ten sites across Australia, this study investigates longitudinal clinical, genetic, epigenetic and imaging data in a large cohort of multiple sclerosis (MS) patients. The study is expected to uncover further insights into the causes and underlying biology of MS. The Brain and Mind Centre will be one of the clinical trial sites for the study and the Computational Neuroscience team and Sydney Neuroimaging Analysis Centre will additionally lead the imaging analysis for all of the centres involved.

Computational NeuroscienceKey Publications

- Zhang, C., Song, Y., Liu, S., Lill, S., Wang, C., Tang, Z., You, Y., Gao, Y., Klistorner, A., Barnett, M. & Cai, W. (2018). MS-GAN: GANbased semantic segmentation of multiple sclerosis lesions in brain magnetic resonance imaging, Digital Image Computing: Techniques and Applications (DICTA), Canberra, Australia. doi: 10.1109/DICTA.2018.8615771
- Tang, Z., Wang, C., Hoang, P., Liu, S., Cai, W., Soligo, D., Oliver, R. & Barnett, M. (2018) Automatic segmentation of thigh muscle in longitudinal 3D T1-weighted magnetic resonance (MR) images. In: A. Melbourne et al. (Eds.) PIPPI 2018, DATRA 2018. Lecture Notes in Computer Science: Vol 11076. Data Driven Treatment Response Assessment and Preterm, Perinatal, and Paediatric Image Analysis. Granada, Spain: Springer.
- 3. Ting Shen, T., You, Y.,
 Arunachalam, S., Fontes, A.,
 Liu, S., Gupta, V., Parratt, J.,
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 & Yiannikas, C. (2018). Differing
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 in multiple sclerosis and
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 L., & Barnett, M.H. (2018).
 White matter tract-specific
 quantitative analysis in multiple
 sclerosis: Comparison of
 optic radiation reconstruction
 techniques, *PLoS ONE*, 13(1): 1-19.
- 7. Lu, G., Beadnall, H.N., Barton, J., Hardy, T.A., Wang, C., & Barnett, M.H. (2018). The evolution of 'No Evidence of Disease Activity' in multiple sclerosis, Multiple Sclerosis and Related Disorders, 20: 231–38.
- 8. Triplett, J.D., Yiannikas, C., Barnett, M.H., Parratt, J., Barton, J., Graham, S.L., You, Y. & Klistorner, A. (2018). Pathophysiological basis of low contrast visual acuity loss in multiple sclerosis. *Annals of Clinical and Translational Neurology*, 5(12): 1505–1512.
- Garber, J.Y. & Barnett, M.H. (2018). We should focus more on finding therapeutic targets for the non-inflammatory damage in MS – Yes. Multiple Sclerosis, 24(10): 1272-1274.
- Destefano N, Silva DG, Barnett MH. Effect of Fingolimod on Brain Volume Loss in Patients with Multiple Sclerosis. CNS Drugs. 2017 Apr;31(4):289-305.

- 11. Klistorner et al. Progression retinal ganglion cell loss in multiple sclerosis is associated with new lesions in the optic radiations. Eur J Neurol. 2017 24(11):1392-1398
- 12. Klistorner et al. Diffusivity in the core of chronic multiple sclerosis lesions. PLoS One. 2018 13(4):e0194142.
- 13. Min M, Spelman T, Lugaresi
 A, Boz C, Spitaleri D, Pucci E,
 Grand'Maison F, Granella F,
 Izquierdo G, Butzkueven H,
 Sanchez-Menoyo JL, Barnett M,
 Girard M, Trojano M, Grammond
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 imaging Shifting goal posts for
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Dr Chenyu (Tim) Wang

"I am extremely excited to be applying my basic science and engineering skills to clinical questions and problems that will ultimately directly help patients with multiple sclerosis and other neurological disorders".

Dr Chenyu (Tim) Wang

Researcher Spotlight

Dr Chenyu (Tim) Wang

Dr Chenyu (Tim) Wang is the inaugural Nerve Research Foundation and Multiple Sclerosis Research Australia Research Fellow at the Brain and Mind Centre. He completed his PhD at the Brain and Mind Centre under the supervision of Professor Michael Barnett and was awarded the 2018 Peter Bancroft Prize by the Faculty of Medicine and Health, a prize given to a graduate whose thesis was passed by all three examiners without requiring any emendations or amendments. He is currently leading the development of imaging and imaging-electrophysiological biomarkers and researching artificial intelligence solutions for clinical radiology with the Computational Neuroscience team at the Brain and Mind Centre.

"I am fortunate enough to have the opportunity to work with people from many different backgrounds at Brain and Mind Centre on almost a daily basis, including neurologists, radiologists, pathologists, clinical scientists, imaging physicists, computer scientists and engineers. The unique expertise of these individuals often exposes many different perspectives on the same problem, which frequently results in innovative thoughts and wild ideas."

With a background in electronic engineering, neuroimaging and neuroscience, Dr Wang is currently focusing his research on neurological disease, aiming both to clarify underlying disease pathomechanisms and to develop tools for use in monitoring subclinical disease progression.

"I am extremely excited to be applying my basic science and engineering skills to clinical questions and problems that will ultimately directly help patients with multiple sclerosis and other neurological disorders".

Aside from co-authored publications in peerreviewed journals and scientific conferences, his work has also been recognized with travel grant awards from world-leading conference committees for the last four years (including the International Society for Magnetic Resonance in Medicine and the European Committee for Treatment and Research in Multiple Sclerosis).

Dr Wang is also the Director of Operations at the Sydney Neuroimaging Analysis Centre, which, co-located with the Brain and Mind Centre, provides imaging central reading services for phase 2 and 3 clinical trials.

Technical Facilities

Sydney Imaging, Neuropathology, Microscopy and Neurology lab.

Technical Facilities

Sydney Imaging

Sydney Imaging is one of the University of Sydney's core research facilities. Bringing together researchers and clinicians through the provision of exceptional biomedical imaging infrastructure and technical expertise, we tackle frontier questions in healthcare and medical research.

Sydney Imaging has a base at the Brain and Mind Centre and provides a comprehensive suite of preclinical and clinical imaging modalities in collaboration with partners such as I-MED and Australia's Nuclear Science and Technology Organisation (ANSTO).

Preclinical Imaging

The Brain and Mind Centre is home to the University of Sydney and ANSTO joint Node of the Australian National Imaging Facility. This shared facility provides researchers with access to state-of-the-art imaging capabilities. Together with Sydney Imaging, the preclinical imaging platform includes micro-PET, PET-CT, PET/SPECT/CT and 3T MRI/PET scanners, as well as autoradiography, radiometabolite analysis and tissue-counting facilities.

Our imaging researchers are focused on developing new technologies for non-invasive imaging and imaging-biomarker development. We collaborate with a large group of colleagues, both at the Brain and Mind Centre and more broadly nationally and internationally, to develop new imaging methods and test new drugs and interventions for various brain disorders, including neurodegenerative diseases, mood disorders and cancers.

Our imaging scientists have an outstanding track record of innovation in both clinical and preclinical imaging, developing novel technologies for the advancement of neuroimaging research and understanding of disease processes.

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Clinical Imaging

The I-MED Radiology Network is a leading provider of radiological services across Australia, operating a network of radiology practices across the country, including an imaging research facility at the Brain and Mind Centre. This facility houses a stateof-the-art 3 Tesla Magnetic Resonance Imaging (MRI) scanner, capable of running structural, diffusion, functional and spectroscopic imaging for research as well as for patient care. A subspecialist neuroradiologist reports all scans and is based on site, providing the highest standards of imaging reporting for patients attending our multidisciplinary clinics and for subjects participating in clinical trials at the Brain and Mind Centre, as well as further afield.

Through our collaboration with I-MED Radiology, Brain and Mind Centre researchers have developed a sophisticated multinuclear spectroscopy program that provides the ability to image a range of spectroscopic nuclei. The technique, known as magnetic resonance spectroscopy (MRS), is used to study the metabolic changes associated with diseases that affect the brain. It also provides additional information on top of the structural information that is obtained from standard MRI sequences alone. I-MED Radiology Network has also partnered with the Sydney Neuroimaging Analysis Centre and the Brain and Mind Centre's Computational Neuroscience Team to deliver improved diagnostics and patient monitoring through artificial intelligence applied to neuroimaging.

Sydney Neuroimaging Analysis Centre

Also housed at Brain and Mind Centre's Mallett Street campus is the Sydney Neuroimaging Analysis Centre, a cutting-edge facility that uniquely integrates in-house neuroimaging research with a dedicated, regulatory-compliant commercial image analysis facility for Phase 2, 3 and 4 clinical research trials. Sydney Neuroimaging Analysis Centre is also a major partner in the Brain and Mind Centre's Computational Neuroscience team, supporting a range of imaging and artificial intelligence projects and providing infrastructure and support for higher degree (Doctoral and Masters) students.

Technical Facilities

Highlights

Welcome Professor Fernando Calamante

Sydney Imaging welcomes Professor Fernando Calamante to the role of Academic Director. Professor Calamante specialises in novel Magnetic Resonance Imaging (MRI) techniques that enable the investigation of brain structure, function and network connectivity, as well as how these are affected in disease. Since joining us in 2018, Professor Calamante has been working closely with a number of teams at the Brain and Mind Centre, including the Computational Neuroscience team.

Imaging brain behaviour

In 2017-18, our team has further enhanced and exploited an innovative technique first developed at the Brain and Mind Centre, which images the brains of conscious, freely-moving small laboratory animals with positron emission tomography (PET). This technique allows us to study the chemical changes that take place in the brain as a result of learning and other behaviours, and how these normative changes are affected by brain abnormalities and disease. In recent developments, we have extended this unique research tool to deliver images with better spatial resolution, and the ability to produce voxel-wise maps of 3D neurotransmitter responses to stimuli during imaging experiments.

Total-body PET technology

We have strengthened our collaboration with Professor Simon Cherry's team at the University of California, Davis (UC Davis), on applications of the innovative total-body PET technology, having

held externally funded international total-body PET workshops at UC Davis and the University of Sydney in 2017–18.

Patient motion can degrade the excellent spatial resolution achievable with this system. As such, we are working together to develop methods for motion tracking and correction. We have implemented a whole-body optical motion-tracking system on an EXPLORER total-body PET scanner mock-up at UC Davis and are using this to study the motion of volunteers under a range of imaging conditions.

We have been successful in attracting \$6.3 million in funding from the National Collaborative Research Infrastructure Strategy (NCRIS) towards Australia's first total-body PET facility and we are seeking a clinical partner to host and operate the system.

CT brain imaging without motion artifacts

Patient head motion causes artifacts that hamper accurate diagnosis in patients undergoing computed tomography (CT) scans to assess trauma, stroke and other brain conditions. Our team, in collaboration with Professor Johan Nuyts and his team at the KU Leuven in Belgium, has developed and applied for a patent on a data-driven motion estimation/ correction algorithm to eliminate these artifacts. Current clinical evaluation suggests that it may find its most valuable application in CT perfusion imaging, where accurate images of the core infarct and its penumbra are critical in selecting the optimal treatment for patients with acute stroke.

Grants awarded

Motion-adaptive PET technology for brain imaging of freely moving mice

This project aims to develop new technology for imaging the brain of a freely moving mouse while analysing its learned behaviours. The new technology will, for the first time, enable scientists to study the fundamental mechanisms of the brain that regulate behaviour and decision making in mammals, with future applications to human brain disorders.

Led by: Professor Steven Meikle Collaborators: Professor Simon Cherry (UC Davis) & Dr Andre Kyme (University of Sydney Faculty of Engineering & IT)

Granting body: ARC Years: 2019-21 Amount: \$486,000

Total-Body PET technology and methods for biological systems research in metabolic disorders and mental illness

This project aims to establish the first total-body PET facility in Australia and to develop motion-correction and kinetic-modelling methodology for this new technology which will enable imaging of physiological function in all tissues of the body simultaneously with extremely high sensitivity.

Led by: Professor Steven Meikle **Collaborators:** Professor Simon Cherry (UC Davis)

Granting body: University of Sydney–University of California, Davis Priority Partnership Collaboration Awards Program

Years: 2017-18 Amount: \$40,000

Technical Facilities Key publications

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Technical Facilities

Neuropathology

Our extensive expertise in clinical and research neuropathology allows us to analyse the molecular and cellular bases of neurological diseases, including brain tumours and neurodegenerative conditions.

In doing so, we can identify new ways of diagnosing these disorders when the disease first manifests, allowing patients to benefit from the most effective interventions available, as early as possible. By increasing our knowledge of the underlying bases of these diseases, we can help progress the development of new and more effective treatments.

We are working on developing novel blood tests that enable early detection of major diseases, including brain tumours and multiple sclerosis. We are also investigating brain tumour tissue to learn more about its complex genetic makeup and how brain tumours manipulate their surroundings in order to grow.

Our neuropathology research program is part of the Royal Prince Alfred Hospital Department of Neuropathology, the only neuropathology department in New South Wales and one of only two in Australia and New Zealand. We provide a broad suite of specialist diagnostic expertise, including:

- tissue-based diagnostic services for the Royal Prince Alfred Hospital and Chris O'Brien Lifehouse (including brain biopsies for a wide variety of brain disease and brain tumour resections)
- a second-opinion service for complex brain biopsy cases from across NSW and overseas
- a comprehensive NATAaccredited molecular testing service for brain tumours, including massively parallel sequencing
- a NSW state referral laboratory for biopsy and autopsy diagnosis of atypical/rapidly progressive dementias, including Creutzfeldt-Jacob

- disease (CJD) diagnosis
- statewide forensic neuropathology services for all three NSW forensic hubs
- non-coronial-autopsy neuropathology for complex neurological disease
- muscle biopsy pathology in conjunction with the Neurology laboratory at the Royal Prince Alfred Hospital.

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Technical FacilitiesHighlights

- 2018 saw the NATA-accreditation of Neuropathology's massively parallel sequencing service for clinical diagnostic use with brain tumours: an Australian first. The service receives over 500 brain tumour specimens annually from across Australia and New Zealand for molecular analysis. In gliomas, the most common intrinsic brain tumours, adding molecular information on top of the microscopic diagnosis has led to marked refinement of diagnostic accuracy.
- In March 2018, we launched the Australian Sports Brain Bank (brainbank. org.au) to better understand the links between sporting head injuries and neurodegenerative disease. Over 80 sportspeople have committed to donating their brains for study after their deaths, and three brains have already been retrieved. Our results on our first brain examination were widely reported in the media. Read more at https://www.theage.com.au/sport/afl/study-of-concussed-footballer-s-brain-yields-surprising-results-20190314-p51481.html
- Our research into a new blood test for brain tumours is accelerating, with the findings of our promising pilot study published in NPJ Precision Oncology (Ebrahimkhani et al., 2018).

Technical Facilities

Key publications

- Ebrahimkhani, S., Vafaee, F., Hallal, S., Wei, H., Lee, M.Y.T., Young, P.E., Satgunaseelan, L., Beadnall, H., Barnett, M.H., Shivalingam, B., Suter, C.M., Buckland, M.E. & Kaufman, K.L. (2018). Deep sequencing of circulating exosomal microRNA allows non-invasive glioblastoma diagnosis. NPJ Precision Oncology 2:28.
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- S. Hallal, S., Mallawaaratchy, D. M., Wei, H., Ebrahimkhani, S., Stringer, B. W., Day, B. W., Boyd, A. W., Guillemin, G. J., Buckland, M. E. & Kaufman, K.L. (2018). Extracellular vesicles released by glioblastoma cells stimulate normal astrocytes to acquire a tumor-supportive phenotype via p53 and MYC signaling pathways. Molecular Neurobiology. doi: 10.1007/s12035-018-1385-1





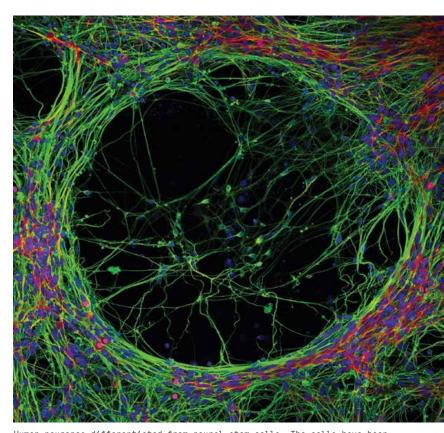
Technical FacilitiesMicroscopy

The Brain and Mind Centre's microscopy facilities provide researchers with access to sophisticated technology to observe diseases of the brain and mind at a micro level.

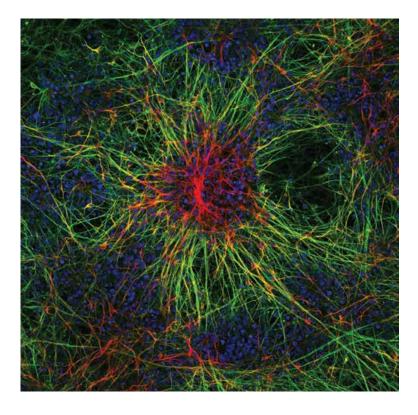
The microscopy facility based at the Brain and Mind Centre forms part of Sydney Microscopy and Microanalysis (SMM), the University of Sydney's largest core facility, which is run by the Australian Centre for Microscopy and Microanalysis. This crossdisciplinary research centre is one of the most comprehensive microscopy centres in the world, with world-class instrumentation and technical expertise available for all researchers. An SMM-wide facility management booking system allows users to seamlessly book any microscopy platform across the Brain and Mind Centre, the Madsen building and the Charles Perkins Centre.

Over the past few years we have purchased new, state-of-the-art equipment, including a Leica DIVE multiphoton system, which will allow the 3D observation of complex biological processes occurring in live tissues.

Human skin cells that have been reprogrammed and differentiated into neurones. The cells have been stained with markers depicting the nuclei of the neurones (blue), the connections between the neurones as a network (green), abnormal protein aggregates (yellow) and the mechanism of autophagy (red). The cells can be used as a tool to study neurodegenerative diseases. This image was awarded an Image of Distinction at the Nikon Small World 2018 Photomicrography Competition. Provided by Jianqun Gao, PhD student, ForeFront Ageing and Neurodegeneration Team.



Human neurones differentiated from neural stem cells. The cells have been stained with markers showing the nuclei of the neurones (blue) and their networks (green and red). Experiments conducted using these neurones hope to unravel the mechanisms of neurodegenerative diseases, such as Parkinson's disease. This image was the winner of the NHMRC Science to Art 2019 Award. Provided by Jianqun Gao, PhD student, ForeFront Ageing and Neurodegeneration Team.



Technical Facilities

Neurology Laboratory

The Brain and Mind Centre's Neurology Laboratory is one of the world's leading centres for diagnosis and research into nerve and muscle diseases.

A collaboration between the University of Sydney and Royal Prince Alfred Hospital, the Neurology Laboratory is a state reference laboratory for peripheral nerve and muscle histopathology (NATA/RCPA Accreditation Number 2146). Established in the late 1960s, the laboratory was the first specialised neuromuscular pathology unit in Australia, and has maintained its position at the forefront of work in this specialisation.

The laboratory, managed by Dr Min-Xia Wang, Senior Principal Hospital Scientist at RPAH, holds one of the largest curated nerve and muscle archives in the world. This repository is an invaluable resource for research and teaching across brain and mind sciences. The laboratory has produced more than 300 original research publications and trained numerous PhD and other higher-degree students.

In 2018, we validated a novel approach to the diagnosis of neuropathy using minimally invasive skin biopsy, a collaboration with the Mayo Clinic, and hope to begin offering this as clinically available tool in 2019.



Technical FacilitiesKey publications

- Mathey EK, Garg N, Park SB, Nguyen T, Baker S, Yuki N, Yiannikas C, Lin CS, Spies JM, Ghaoui R, Barnett MH, Vucic S, Pollard JD, Kiernan MC. Autoantibody responses to nodal and paranodal antigens in chronic inflammatory neuropathies. *J Neuroimmunol*. 2017 Aug 15;309:41-46. doi: 10.1016/j.jneuroim.2017.05.002.
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- Sutrave G, Maundrell A, Keighley C, Jennings Z, Brammah S, Wang MX, Pamphlett R, Webb CE, Stark D, Englert H, Gottlieb D, Bilmon I, Watts MR. Anncaliia algerae Microsporidial Myositis, New South Wales, Australia. *Emerg Infect Dis*. 2018 Aug;24(8):1528–1531.
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Lambert Initiative

Exploring the medicinal potential of cannabinoid therapeutics.

Lambert Initiative

Our core business

The Lambert Initiative for Cannabinoid Therapeutics, based at the Brain and Mind Centre, is a long-term research program exploring the medicinal potential of the cannabis plant. Our vision is to conduct the high-quality research required to discover, develop and optimise safe and effective cannabinoid therapeutics in Australia and beyond.

The Lambert Initiative was founded in 2015, thanks to an unprecedented pledge of \$33.7 million to the University by Barry and Joy Lambert – the largest single gift in the history of the University of Sydney. The Initiative now provides national and international leadership in the science of medicinal cannabinoids and in the discovery and development of cannabis-based medicines.

Our activities span a wide spectrum of basic science and clinical activities - from plant science to cellular and preclinical pharmacology to medicinal chemistry and drug discovery -with the ultimate goal of producing cannabinoid-based medicines and ensuring their availability to patients.

Advocacy and education

In parallel with our scientific endeavours, the Lambert Initiative also acts in an advocacy and educational capacity, targeting consumers, health professionals and politicians and influencing regulatory approaches and public health policy.

For many patients and families, the future of medicinal cannabis is one of hope: hope that legislation will change to make medical cannabis and future cannabinoid drugs more accessible. Hope that attitudes change to encourage practitioners to prescribe medicinal cannabis. A key aspect of the Lambert Initiative's vision is to provide tangible scientific evidence to help translate hope into reality.

Lambert Initiative

Highlights

Methamphetamine addiction research

Lambert Initiative scientists have recently shown that there is potential for Cannabidiol (CBD) to be used in the treatment of methamphetamine addiction.

Methamphetamine, also known as "ice" or "crystal meth", is highly addictive, and people who develop a dependence on it find it very difficult to kick their habit. Binge use of methamphetamine is common, wherein users repeatedly take the drug and do not eat or sleep for days. Long-term use is particularly problematic because it is associated with anorexia, severe dental problems ("meth mouth"), aggression and paranoid psychosis (hallucinations and delusions). The use of methamphetamine by truck drivers is associated with road fatalities.

There are few treatment options available to curb methamphetamine use or prevent relapse into drug use. Lambert Initiative researchers Professor Iain McGregor and Associate Professor Jonathon Arnold, in collaboration with Associate Professor Jennifer Cornish at Macquarie University, recently published a paper in the Journal of Psychopharmacology (Hay et al., 2018 – see key publications) showing that a single exposure to CBD reduced the motivation to seek and consume methamphetamine in rats. Moreover, CBD reduced relapse to methamphetamine use; this is important as drug relapse is crucial in explaining the chronic nature of drug addiction.

The team is now exploring the possibility of mounting a clinical trial assessing the relative success of using CBD in the treatment of methamphetamine addicts.





Professor Iain McGreggor, Dr Michael Bowen and the research team

World Health Organisation review and recommendations

Associate Professor Jonathon
Arnold was one of four cannabis
experts selected world-wide
to assist the World Health
Organisation (WHO) at their 40th
meeting of the Expert Committee
of Drug Dependence (ECDD) in
Geneva in June 2018. This meeting
may have huge ramifications for
the restricted status of cannabis
under international drug control
treaties, as this committee makes
rescheduling recommendations to
the United Nations which are then
voted on by member states.

Currently, the cannabis plant and extracts are included in the most restricted schedules of the world's international drug-control treaties. For example, cannabis is included in the Single Convention on Narcotic Drugs in schedules I and IV, which deems cannabis to be highly liable to abuse and particularly dangerous.

The 40th ECDD meeting attended by Associate Director Associate Professor Arnold was a historic meeting for two reasons:

- It marked the first time in history that the WHO reviewed the risks and benefits of the cannabis plant and cannabisrelated substances.
- It recommended that cannabidiol not be subjected to international drug control.

At the time of writing, the recommendations made will be voted on at the upcoming UN's Commission of Narcotic Drugs in Vienna. If the UN adopts the recommendations, this will end international cannabis prohibition and ease country-level restrictions on medicinal cannabis and the use of cannabis for scientific research.

Cannabis as Medicine Survey

In 2016, researchers at the Lambert Initiative conducted the first Australia-wide survey of individuals self-reporting the use of cannabis for medical reasons: the Cannabis As Medicine Survey 2016 (CAMS:16).

This survey captured the experiences of 1744 Australians before the implementation of new regulations in October 2016, and so represents a 'before' snapshot of medical cannabis use in Australia. Representing the largest survey of medical cannabis users in Australia, the CAMS:16 results were published in the Medical Journal of Australia in August 2018.

The research identified a number of key findings:

- Cannabis was most commonly used for chronic pain, mental health (anxiety, depression and post-traumatic stress disorder), sleep and neurological conditions. Medical cannabis was largely illicitly sourced and used by inhaled routes, such as "bongs/water pipes" (42 percent) or "joints" (20 percent), although most people indicated they would prefer to use safer approaches, such as oral routes.
- Overall, people reported that their cannabis use had been effective in helping to manage their health conditions.

- A range of side effects were also identified, including increased appetite, drowsiness, eye irritation, lethargy, and memory impairment.
- People also reported concerns stemming from the illegal status of their cannabis use, citing concerns about employment, irregular access to cannabis and the highly variable quality of cannabis accessed illegally.
- Most people expressed a strong preference for medical cannabis to be integrated into mainstream healthcare and for products to meet quality and safety standards.

The research team repeated the survey in 2018 (publication pending) and will do so again in 2020, to look at how patterns of use have changed since new regulations have taken effect. CAMS:18 and CAMS:20 will provide us with a unique opportunity to examine the impact of the regulatory and community changes regarding medical cannabis over time.

GP Survey

In late 2017, the Lambert Initiative conducted a survey of 640 Australian general practitioners (GPs) regarding the use of medicinal cannabis in patient treatment. The results, which were published in the British Medical Journal Open (Karanges et al., 2018 – see key publications) revealed that GPs strongly support prescribing medical cannabis to help people cope with cancerrelated pain, palliative care and epilepsy. Additionally, almost two thirds (61.5 percent) of the GPs surveyed have had patients ask about the drug.

As the ABC reported in July 2018, the survey results indicate a clear need for GPs to be more educated about medicinal cannabis, in addition to being authorised to prescribe it. Most doctors said they felt they did not have enough knowledge about the drug to be comfortable discussing it with patients.

Paediatric epilepsy (PELICAN) study

This study examined the experiences and attitudes of parents of children with epilepsy on the use of cannabis oils to treat their child's illness. The team conducted interviews with families of children with diverse forms of epilepsy to explore their attitudes towards and experiences with, using cannabis extracts, including families who have tried and stopped using medicinal cannabis, and families who had never used cannabis-derived treatments. For those using cannabis, extracts were analysed for cannabinoid content.

This study produced some interesting results, including that children given cannabis extracts tended to have more severe epilepsy

and had trialled more anticonvulsants than those that had never received cannabis extracts. The team also discovered there was high variability in the cannabinoid content and profile of cannabis extracts. Contrary to families' expectations, many samples did not contain CBD, while THC was present in nearly every sample.

These findings highlight profound variation in the illicit cannabis extracts being currently used in Australia and warrant further investigations into the value of cannabinoids, either alone or in combination, in epilepsy.



ambert Initiative

Lambert Initiative

Grants awarded

Associate Professor Jonathan Arnold has been awarded a National Health and Medical Research Council (NMHRC) Project Grant for the preclinical development of cannabis-derived medicines for drug-resistant epilepsy. Many childhood epilepsies are refractory to current treatment options and patients have a large seizure burden, often including a reduced lifespan and developmental delays. Through this project, our aim is to further develop our understanding of the role of the endocannabinoid system in childhood epilepsy and undertake preclinical development of candidate cannabinoids as anticonvulsants.

Key publications

- Hay, G., Baracz, S., Everett, N., Roberts, J., Costa, P., Arnold, J., McGregor, I., Cornish, J. (2018). Cannabidiol treatment reduces the motivation to self-administer methamphetamine and methamphetamine-primed relapse in rats. *Journal of Psychopharmacology*, 32(12), 1369-1378.
- Karanges, E., Suraev, A., Elias, N., Manocha, R., McGregor, I. (2018).
 Knowledge and attitudes of Australian general practitioners towards medicinal cannabis: a cross-sectional survey.
 BMJ Open, 8(7), e022101.
- Suraev, A., Todd, L., Bowen, M., Allsop, D., McGregor, I., Ireland, C., Lintzeris, N. (2017). An Australian nationwide survey on medicinal cannabis use for epilepsy: History of antiepileptic drug treatment predicts medicinal cannabis use. *Epilepsy and Behavior*, 70, 334–340.
- Suraev, A., Lintzeris, N., Stuart, J., Kevin, R., Blackburn, R., Richards, E., Arnold, J., Ireland, C., Todd, L., Allsop, D., McGregor, I. (2018). Composition and Use of Cannabis Extracts for Childhood Epilepsy in the Australian Community. Scientific Reports, 8(1), 28127.

University of Sydney

Brain and Mind Centre

Our donors

Our goal is to translate research into real-world outcomes that improve patient care and treatment, transforming the lives of the individuals and families affected by disorders of the brain and mind. This transformative work would not be possible without the support of our donors.

As the multidisciplinary home for mental health and neuroscience at the University of Sydney, we are part of an institution with a proven track record of research excellence, and their families. Philanthropy which benefits communities near and far.

Our donors have a profoundly significant impact on advancing mental health and neuroscience research. One hundred per cent of donations received go directly to funding research that may otherwise not have been supported through traditional grant schemes. Over the past two years, we have received more than \$13 million in donations to support research, scholarships and services across child development, youth mental health and addiction and ageing and neurodegeneration.

There has never been a more promising time to support mental health and neuroscience research. The advancements that will emerge in this field over the

next five to 10 years, in particular, will transform knowledge and practice, ultimately helping to improve outcomes for patients will remain an essential part of our success and ability to realise these breakthroughs and discoveries.

We deeply value relationships with all supporters and partners who understand the role that high-quality, multidisciplinary and translational research plays alongside clinical services in driving real outcomes. The impact of their support is immeasurable and increasingly pivotal to our success.

To find out more about how you can support our work, please visit

sydney.edu.au/ brain-mind/donate

Brain and Mind CentreSupporting research

As government funding continues to decrease, philanthropy is critical in order for us to make major research breakthroughs and health advances. A generous gift of \$240,000 has enabled the Frontier Research Group to establish a vital Research Assistant position to accelerate their crucial work in improving Frontotemporal Dementia diagnosis, finding its cause, developing effective treatments for the condition and working towards a cure.

"Without this generous gift, we would not have been able to hire James, who offers the perfect balance between the clinical and the technical. He is improving and streamlining all our systems," explained Professor Oliver Piguet, Co-Director of the Frontier team.

"He ensures that the practice runs to its best, allowing the team to be dynamic and our research translational. He plays a key role in driving our research agenda forwards at a quicker pace than would have been otherwise possible.

"Gifts like this not only have a profoundly positive impact on our patients and their families, but on the future health of all Australians."



Brain and Mind Centre

Supporting early-career researchers



EMCR L-R Dr Rachel Tan, Dr Loren Mowszowski, Dr Petra van Nieuwenhuijzen, Dr Samuel Banister (L-R. Not pictured Dr Kaylena Engoetz Martens and Dr Rebekah Ahmed)

Philanthropy is vital to funding our early- "Lenity is honoured to be a partner career researchers (ECRs). In the field of mental health and neuroscience, ECRs often struggle to gain the vital research experience necessary to win grant funding. A philanthropic gift allows ECRs to continue to work in their chosen field without having to turn to other research areas where grant funding is perhaps more easily available.

Lenity Australia, for example, has donated \$1.25 million to support a five-year research fellowship, the Lenity Research Fellow, in the field of neurodegenerative diseases at the Brain and Mind Centre.

in this vital area of research", Geoff Henry from Lenity Australia said. "This donation compliments our portfolio of humanitarian and medically focused projects in Australia and Oceania."

Professor Matthew Kiernan, Co-Director of the Brain and Mind Centre, says philanthropy is a vital avenue of support for research. "Gifts like this one from Lenity Australia allow us to attract the brightest talent and expand into new areas of focus, significantly contributing to our already important work in ageing and neurodegeneration."

Brain and Mind Centre

Thanks to our donors

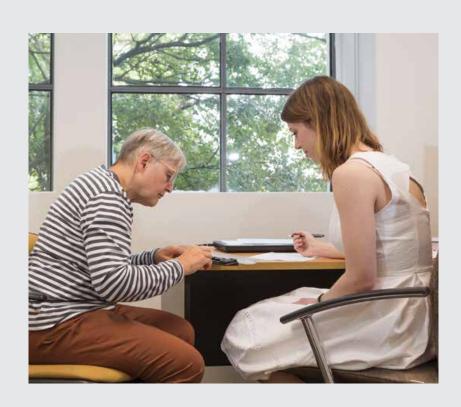
The Brain and Mind Centre wishes to thank all of our donors. Your generosity keeps our work possible and together we raised over \$13 million in donations between January 2017 and December 2018.

No gift is too small and we welcome contributions of any size. We wish to particularly thank the following people, who donated \$1000 or more. Our thanks also go to our donors who wish to remain anonymous and to all those who have contributed over the last two years.

Mr Alastair Griffin, Dr Alexander Bela Leslie Hunyor, Alleasing Pty Ltd, Australian & New Zealand Association of Neurologists, Mrs Annabel Williamson, Mrs Anne Osborne Sullivan, Balverona Pty Ltd, Bluesand Foundation Pty Ltd, Dr Brian John Shaw OAM, Ms Cara Chriqui, Mrs Carole

Roussel, Ms Catherine Abbott, Mr Charles Reynolds, Mrs Christine Windeyer, ClubsNSW, , Colorectal Surgical Society of Australia and New Zealand, Conversely, Mr Craig Whitworth, Cure for MND Foundation Inc, Mrs Cveta Lillyman, Mr David E Landa OAM, Ms Debbie Seidler, Diamond Blue Financial Services, Ms Diane Chaffey, Ms Elaine Chang, Dr Eleanor Jew, Ms Eleanor Sydney-Jones, Estate of the Late Christopher J Wood, Fireglobes Australia, Fredmarch Pty Ltd, Future Generation Investment Company, Ms Gail Hayman, The Goodridge Foundation, Harper Bernays Charitable Trust, Mrs Helen Breekveldt, Mrs Hilary Marion Cairns, Mr Ian William Jew, Ironshore Australia Pty Ltd, Mrs Jacqueline A Hiller, Mr James Rebbeck, Ms Jane Dean, Mr Jeff Hauser, Dr Jill M Hawker, The Jim McIntyre Foundation, Mr Joseph Vucetic, JR Darling Foundation,

Kildare Road Medical Centre, Lenity Australia, Mr Leslie P Pongrass, Mr Luke Watson, Ms Maria Valos, Dr Marion G Maxwell, Mr Marty Shaw, The Michael J. Fox Foundation for Parkinson's Research, Mr Michael R Johnston, Mr Miles Prosser, The Mill House Foundation, Motor Neurone Disease Research Institute of Australia Inc., The Negri Family, Mr Otto and Mrs Judy Appenzeller, Mr Paul Rosin, Mr Peter J Burgess, Mr Peter McAuliffe, Mrs Rae Cottle, Mr Robert Phillips, Mrs Robyn Winifred Smith, Dr Roslyn Jolly, Shake It Up Australia Foundation, Ms Silvana d'Iapico-Bien, St Vincent's Hospital Sydney Limited, St Vincent's Private Hospital Sydney, Dr Steven K C Lee, Mrs Susan Hauser, Dr Suzanne Lewis, Dr Terence J Wiesner, The University of Sydney USA Foundation Inc, Ms Vanessa Pearson, Dr Vincent V Phung, Mr William Sweeney, The Yulgilbar Foundation.



Brain and Mind Centre

Our teams

Our unique teams consist of academics, researchers, students and professional staff. They are the lifeblood of Brain and Mind Centre. We acknowledge and give thanks for their tireless hard work, diligence and dedication to their research, which can, and is, changing the world.

Child Neurodevelopment and Mental Health Team

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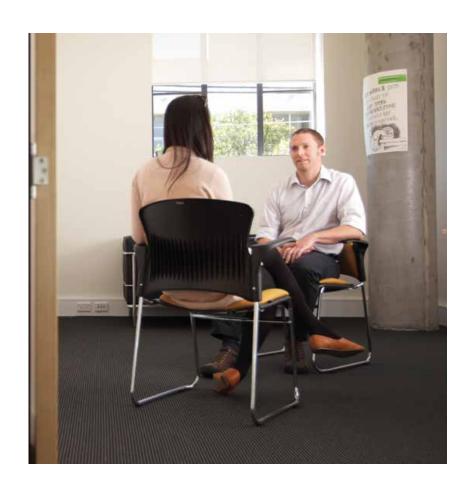
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