brainWAVES

The Newsletter of the Brain Foundation

Summer 2023/24

Each year I have the absolute pleasure of contacting those researchers who were awarded a research grant by the Brain Foundation's independent scientific committee. The scientific committee has the almost impossible task of judging the hundreds of applications received from researchers across Australia. Sadly there are always more applications than funds available.

Inside these pages we showcase the research grant recipients for 2023. Their various research projects are exciting, inspirational and provide hope that better treatments and cures are on the horizon for many brain disorders, diseases and injuries which touch so many families.

You can help fast-track our research efforts by spreading the word amongst your friends, colleagues, patients and corporate contacts to help raise funds.

Put simply; there can be no cure without research and there can be no research without the generosity of individuals, corporate sponsors and Gifts in Wills.

Trevor Thompson
CEO

Migraine & Headache Awareness Week 2023

Every year we host Migraine & Headache Awareness Week to support people living with migraine or headache disorders. From September 4-7, we invited people to participate in webinars featuring Australia's leading headache specialists. It was once again a fantastic week and it was great to hear positive feedback from so many people in our community.

This year the theme was **#MakeMigraineMatter**, which is about recognising that migraine is a legitimate neurological condition. It's much more than just a bad headache. Until it is treated seriously low diagnosis rates will persist, denying thousands of Australians the ability to effectively treat and manage their condition.

Recent research commissioned by Migraine & Headache Australia shows that women at work with migraine experience particularly high levels of stigma and discrimination. The nationally representative survey found almost 1 in 4 Australian women with migraine have quit a job due to lack of support, undermining efforts to achieve workplace gender equality.

We also took polls during the webinars which showed that:

- Nearly three quarters (73%) of attendees felt that migraine has significantly affected their career prospects.
- 62% of people had experienced discrimination or stigma in the workplace.

Through events like Migraine & Headache Awareness Week and other advocacy efforts, we are working to change this. We hope that everyone who participated in this year's event found the information helpful and felt welcomed in the community. If you didn't see the presentations this year, you haven't missed out - there is information on how to view the webinar recordings on page 4.

Migraine & Headache Awareness Week

OVER $6,000,000 IN **GRANTS GIVEN** FROM **2010** TO **TODAY.** WE CAN'T WAIT TO SEE WHAT THE COMING DECADES HAVE IN STORE

OVER 50 YEARS OF RESEARCH
• MAKING A DIFFERENCE SINCE 1970 •

Contact the Brain Foundation
PO Box 579, Crows Nest NSW 1585
Telephone: 02 9437 5967 or 1300 886 660
Email: info@brainfoundation.org.au
Visit our websites **brainfoundation.org.au** and **headacheaustralia.org.au**

News

Sedentary lifestyle linked to dementia

Adults aged 60 and older who spend more time engaging in sedentary behaviours like sitting or driving may be at increased risk of developing dementia, according to a new study published in the Journal of the American Medical Association (JAMA).

The researchers found that dementia risk increased significantly if people spent more than 10 hours a day being sedentary. Contrary to popular belief, they also found that it didn't matter as much if the sedentary time was all in one block or if it was broken up throughout the day. The important factor was the total amount of sedentary time.

More research will be needed to confirm if this can be counteracted by exercise or furniture such as standing desks.

Source: Science Daily

Brain biometrics can help identify sports concussions

Research from the University of South Australia has found that new brain biometrics could help inform whether an athlete is ready to return to play following a concussion. They measured changes in micro-movements of the brain – termed 'headpulses' – to detect the lasting impacts of a concussion.

The researchers used a custom-designed headset which detected brain abnormalities in 81% of players who had a concussion. These headpulse alterations lasted 14 days beyond concussion symptoms and were exacerbated by return-to-play or unsupervised physical activity.

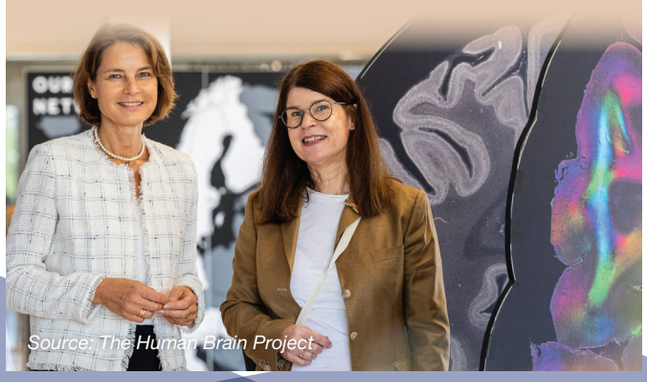
"We discovered that almost all players who received a concussion had a 'disconnect' between their symptoms and the headpulse," says UniSA Professor of Exercise Science Kevin Norton. "Even when the players said they felt good, the headpulse still showed evidence of brain injury."

Source: University of South Australia

The Human Brain Project ends after 10 years

Between 2013 and 2023, researchers from 155 institutions and 19 countries worked together on the Human Brain Project (HBP). The HBP has pioneered digital neuroscience, a new approach to studying the brain based on multidisciplinary collaborations and high-performance computing. It produced more than 3000 academic publications and more than 160 digital tools.

In particular, the EBRAINS research infrastructure will allow for more collaboration, higher quality research, and better access to data. Researchers can sign up to use EBRAINS for free, where they can access comprehensive data & powerful research tools. Thank you to everyone who contributed towards the HBP. Your work will impact neuroscience for many years to come.



Source: The Human Brain Project

Study shows deep brain stimulation encouraging for stroke patients

A first-in-human trial of deep brain stimulation (DBS) for post-stroke rehabilitation patients has shown that using DBS to target a specific part of the brain is safe and feasible. The researchers target the dentate nucleus, which is a region that regulates fine-control of voluntary movements, cognition, language, and sensory functions in the brain.

The EDEN trial (Electrical Stimulation of the Dentate Nucleus for Upper Extremity Hemiparesis Due to Ischemic Stroke) found that the majority of participants demonstrated improvements in both motor impairment and function. We look forward to seeing further research in this area, which could revolutionise stroke rehabilitation & significantly reduce stroke-related disability.

Source: Science Daily

Principal investigators, Dr Andre Machado and Dr Kenneth Baker.

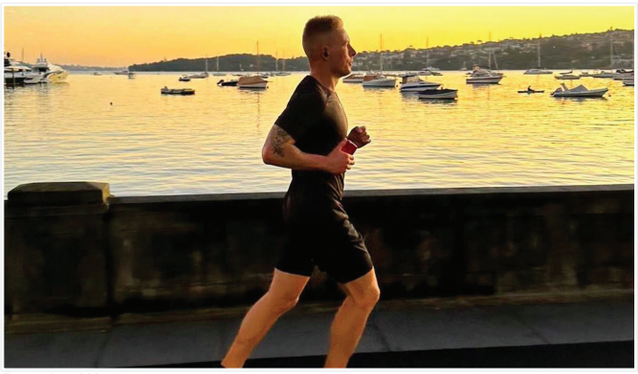
Fundraisers

52 Marathons in 52 Days for AVM

The incredible Brendan Wyatt is taking on his biggest challenge yet, running 52 marathons in 52 weeks throughout 2024 to raise funds and awareness for arteriovenous malformation (AVM) and cerebrovascular disease. You might remember Brendan from his fundraiser earlier this year, when he ran 160km in 17 hours in memory of Lily Pacheco, raising an incredible $19,300.

"To say I'm nervous, anxious and yet excited for this would be selling it short," he says. "The consistency, dedication and commitment this will take is something I'll have to confront myself and dig deep to find. In doing so, I hope to continue to be able to spread awareness, fund valuable research and help positively change the narrative and lives of those impacted by AVM and other cerebrovascular diseases."

We look forward to sharing more once the challenge begins. Until then, we hope you will support us and Brendan in raising awareness & research funds for AVM. You can find his fundraising page at https://bit.ly/52MarathonsAVM.



Brendan Wyatt

Nia and her husband crossing the finish line

Half marathon for PSP

In October, Nia Johnston ran in the Melbourne Marathon in memory of her father, Brian. He passed away in April of this year from progressive nuclear palsy (PSP), a neurodegenerative disease that causes progressive lack of coordination, stiffness, cognitive dysfunction and difficulty moving.

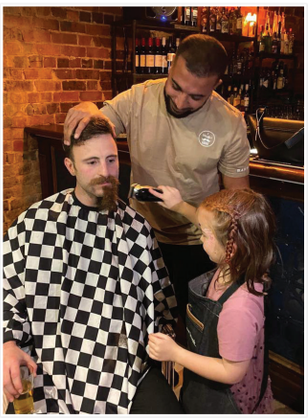
"My dad (Brian) was a much-loved Husband, Dad and Grandad who was always active and ultra fit," she told us. "He taught PE for most of his working life and inspired many to keep moving and be the best physical version of themselves."

Nia shared more about her father and the impact of PSP in an interview which is on our website. Thank you so much Nia for raising much-needed research funds and awareness for PSP. You can read her story at https://bit.ly/BrianJohnstonPSP

Shave for Teddy

Thank you so much to Vito, who shaved his beard earlier this year to raise funds and awareness for brain tumour research in memory of his friend, Teddy.

"Teddy was my absolute best mate, and losing him was a really challenging time in my life," Vito says. "Keeping his memory alive and making sure that his family is a part of my life and Teddy's friends lives, is what the fundraiser was all about."



Vito's fundraiser raised nearly $10,000, which will go on to help so many people by funding vital research. We are so thankful to Vito, his community, and everyone who knew Teddy for helping to raise awareness & research funds for this devastating type of cancer.

Tamworth Fair: 20th anniversary

The Tamworth Fair took place on the 19th of November with a fantastic array of local products, food, and live music. We are so thankful to the organisers, who have been hosting this event in support of the Brain Foundation for 20 years.

This year, the proceeds from the fair will fund Amirali Popat's research into brain cancer treatments. You can read more about this project on page 7.

If you're interested in attending the fair next year, you can follow their Facebook page to stay in the loop for next year's date. www.facebook.com/BFTCF/

Migraine & Headache Australia Updates

Migraine & Headache Awareness Week 2023

Thank you to everyone who attended this year's Migraine & Headache Awareness Week! The topics covered this year included:

- New Treatments - Dr Bronwyn Jenkins
- Triptans Without a Prescription - Dr Jacinta Johnson
- Research on Headache Disorders - Dr Faraidoon Haghdoost
- Concussion Interview - Dr Rowena Mobbs & Brett Kearney (retired NRL star)
- Migraine at Work (Panel) - Ellee Lines, Georgia Spencer, Megan Chapman & Sarah Abdou (Solicitor)
- Event Highlights and General Q&A - Carl Cincinnato & Anniek Grundy, Migraine & Headache Australia.

Speakers from top left: peakers from top left: Dr Bronwyn Jenkins, Dr Jacinta Johnson, Dr Faraidoon Haghdoost, Dr Rowena Mobbs, Brett Kearney, Sarah Abdou, Georgia Spencer, Ellee Lines, and Megan Chapman.

If you missed the talks this year and wanted to catch up on the event recordings, they are uploaded on our website. You can find them in our menu under 'Resources', where you can also find recordings from previous years.

Event feedback from participants

"I would like to congratulate you on the excellent recordings … Having Australia-only treatments discussed was great. I have some new ideas now on how to manage my migraine and I feel a sense of hope. Thank you … Although I am a migraineur myself, I am also a social worker, working in the area of disability and injury. When I speak to clients who have migraine I always inform them of Migraine and Headache Australia and the corresponding social media. Keep up the good work!"

- Cheryl

"It was great, I really enjoyed it. It gave me strength and a positive attitude toward not feeling so alone and isolated in my suffering. Hearing others' stories made me feel less pain for myself and I was able to feel better about my condition and gain confidence for moving forward with it from all the info gained and topics discussed. Definitely glad I made it!"

- Jess

"Thank you for all you and your team have done and continue to do in this invisible field."

- Kay

Shades for Migraine winners

Alicia Hines looking fabulous in her shades

Back in June we reached out to the Migraine & Headache Australia community to participate in Shades for Migraine, a global initiative to raise awareness and show support for people living with migraine. We invited you to "show you care and wear a pair", and once again it was fantastic to see all of your creative photos in your sunglasses. Thank you to everyone who participated!

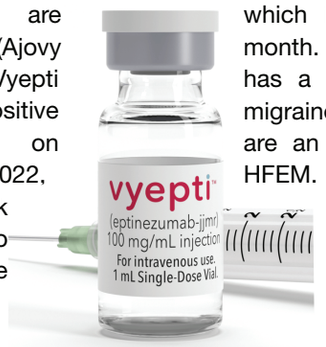
Five lucky participants won our migraine hamper packs, which included over $250 worth of self-care products for people living with migraine. You can check out one of the winning photos below.

If you didn't get a chance to participate this year, we'll be providing more opportunities to raise awareness in the future - subscribe to the e-newsletter to be the first to know.

New treatment updates:

Vyepti added to the PBS: Vyepti is a calcitonin gene-related peptide (CGRP) monoclonal antibody that is administered intravenously once every 3 months, or four times per year.

We are excited to report that it was added to the Pharmaceutical Benefits Scheme (PBS) as of August 1st, 2023. This was a faster timeline than the other two CGRP monoclonal antibodies that are listed on the PBS (Ajovy and Emgality) – Vyepti received a positive recommendation on August 19th 2022, meaning it took less than a year to be added to the PBS.



Increased PBS access for Ajovy: Ajovy is another CGRP monoclonal antibody which has been available on the PBS for people with chronic migraine since August 2021. Chronic migraine is defined as having 15 or more headache days per month.

In exciting news, Ajovy is now available on the PBS for people with high-frequency episodic migraine (HFEM), which is 8-14 headache days per month. Research shows that HFEM has a lot in common with chronic migraine, and preventive treatments are an important part of managing HFEM.

Update on the new gepants: Gepants are a new type of acute migraine treatment that work by targeting the CGRP pathway. In our last issue of Brainwaves, we told you that two gepants were on the July 2023 Pharmaceutical Benefits Access Committee (PBAC) agenda for PBS listing. These were atogepant (for migraine prevention) and rimegepant (for acute treatment).

Unfortunately, neither of these were added to the PBS in the July meeting. Atogepant also has not been approved yet by the TGA. We are encouraging a resubmission by the manufacturers, so they can work with PBAC to find a common ground that considers all stakeholders including patients. We hope that a future submission for PBS listing will be successful.

Supporting women with migraine at work

Back in August we hosted an event in Parliament House about 'Keeping Women With Migraine In The Workforce'. Migraine is a complex neurological disease that can be debilitating, interfering with a person's life at home, with friends, and in the workplace. Women are disproportionately affected by migraine, making up 72% of migraine sufferers.

The event allowed us to advocate for the migraine community directly to key stakeholders, policy makers and government officials. Speakers included co-hosts Peta Murphy & Bridget Archer (co-chairs of the Parliamentary Friends of Women's Health Group), Ged Kearney (Assistant Minister of Health and Aged Care), Dr. Bronwyn Jenkins, and a woman who was pushed to leave her job and ultimately the workforce due to migraine.

If you'd like to learn more about our advocacy work and how you can help, please visit brainfoundation.org.au/migraine-at-work/

Headache researchers and some of the Brain Foundation team. Attendees from left: Anniek Grundy, Dr Faraidoon Haghdoost, Dr Bronwyn Jenkins, Carl Cincinnato, Dr Elspeth Hutton, Dr Emma Foster, Trevor Thompson.

JOIN MIGRAINE AND HEADACHE PRIVATE SUPPORT GROUP ON FACEBOOK TODAY

Join the community to connect with other patients, keep up to date with news, and discover upcoming events.

Migraine & Headache Australia support - **Facebook.com/groups/headacheaustraliasupportgroup/**

Follow us on Twitter @HeadacheAus

Follow our Instagram @migraineandheadacheaustralia

Disclaimer: Migraine & Headache Australia is not a medical office and cannot offer medical advice. We encourage you to discuss any issues you have with your medical practitioner

2023 Research Grant Awards

For over 50 years, our primary objective has been to support the highest quality Australian research into brain diseases, disorders, and injuries. There are always so many fantastic applications each year which showcase the talent and dedication of Australian researchers.

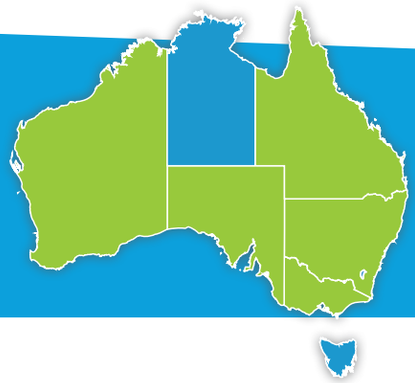
We are excited to announce our 2023 grant recipients, whose work has the potential to make a real impact in the lives of people living with neurological conditions. Thank you to the members of our Scientific Committee for volunteering your time and expertise to assess these applications.

This year we have funded 14 projects across a wide range of research areas. While this is more than the past two years, we know there's still more work to be done. There are always many worthy applicants that miss out on grants due to funding constraints. But we are working to bring our funding back to regular levels so that we can continue to give out more grants each year. We will always strive to do more to support researchers, patients, and their loved ones.

Finally, we extend our sincere thanks to our donors, fundraisers, and corporate sponsors. Almost everyone has been touched in some way by a brain disease, disorder, or injury. Your support makes research possible so that we can improve our understanding of these conditions, and work towards finding new treatments and cures.

You can read all about the 2023 research grants on the following pages.

DID YOU KNOW?
5 STATES WERE REPRESENTED IN THIS YEAR'S **GRANT AWARDS**



THE BRAIN FOUNDATION IS A NATIONAL CHARITY, AND **FUNDING** RESEARCH **ACROSS THE COUNTRY** IS AN **IMPORTANT** PART OF **OUR MISSION**

▼ ALZHEIMER'S DISEASE & OTHER DEMENTIAS

Comparing familial Alzheimer's disease and Sanfilippo syndrome childhood dementia at single cell resolution

Chief Investigator:
Dr Karissa Barthelson, Flinders University

Co-Investigators:
Dr Michael Lardelli,
Dr Luciano Martelotto

Dementia is not only a disease of the elderly. Every 1 in 2,800 children are born with a genetic disorder which causes childhood dementia. Sanfilippo syndrome, among these genetic disorders, is particularly tragic and currently has no cure. Children born with Sanfilippo syndrome seem to develop typically during their early years, only to face a loss of developmental milestones from approximately two years of age. In the years following, neurodegeneration begins to onset which ultimately leads to a heartbreaking loss of life. At the cellular level in the Sanfilippo brain, many problems are occurring. Some of these problems appear similar to those which occur in Alzheimer's disease, the most common form of dementia. However, a thorough comparison of these diseases has not been performed.

This study will utilise our zebrafish models of these diseases to compare the brain gene expression changes at the level of single cells. To do this, we will use a cutting-edge technique called single-nuclei transcriptomics. This is one of the most sensitive and powerful methods of examining the molecular state of the brain. We will dissect how each of the brain's many different cell types are altered in these diseases, and whether there are commonalities between them. Identification of common cellular changes between the Alzheimer's disease and Sanfilippo syndrome models will suggest novel therapeutic approaches which could be beneficial for both diseases.

▼ BRAIN TUMOUR INCL. ACOUSTIC NEUROMA

Nanoparticles for Treatment of Brain Cancer

Chief Investigator:
A/Prof Amirali Popat,
University of Queensland

Co-Investigators:
Dr Taskeen Janjua,
Prof Kristofer Thurecht,
Prof Maria Kavallaris

Approximately 1900 individuals in Australia receive a diagnosis of brain cancer each year, sadly resulting in around 1500 annual fatalities from this relentless disease. Despite substantial advancements in therapies designed to combat glioblastoma multiforme (GBM), it remains a daunting challenge, characterised by a grim prognosis and no permanent cure. Temozolomide (TMZ) stands out as the only orally available FDA approved chemotherapy for GBM treatment. However, it grapples with challenges, including inadequate oral bioavailability, limited tumour penetration (below 20%), and susceptibility to resistance. While other therapeutic options, such as intravenous administration of targeted therapies like Bevacizumab, may come into play when glioblastoma recurs or fails to respond to alternative treatments, they, too, fall short of delivering curative or long-lasting effects. This underscores the urgent need for the development of innovative treatment approaches, particularly those that enhance the efficient delivery of established chemotherapeutic drugs like TMZ.

Hence, our primary objective revolves around encapsulating TMZ within biodegradable, clinically applicable smart nanoparticles. This pioneering approach holds promise in safeguarding TMZ within the bloodstream, enhancing its bioavailability, and augmenting its ability to infiltrate tumour cells through active targeting mechanisms. We firmly believe that our strategy will significantly elevate TMZ's bioavailability within tumours through a multi-modal approach. Our strategy holds the promise of reducing the effective dosage and dosing frequency of TMZ, which, in turn, has the potential to mitigate or delay drug resistance while simultaneously improving the clinical outcomes and overall quality of life for GBM patients.

▼ MOVEMENT DISORDERS INCL. PARKINSON'S, DYSTONIA, HUNTINGTON'S, PSP

Bilateral MRI guided focused ultrasound intervention for tremor

Chief Investigator:
Dr James Peters,
St Vincent's Campus
Sydney

Co-Investigators:
A/Prof Stephen Tisch,
Dr Benjamin Jonker

The commonest form of tremor, essential tremor, affects approximately 3% of the population. Despite best medical management, 30-50% of these patients have persistent disability with activities of daily living, which often prompts the consideration of surgical intervention. MRI-guided focused ultrasound (MRgFUS) is an incision-less technique, where ultrasound beams are delivered transcranially to create therapeutic lesions in highly specific locations within the brain. Its application in movement disorders and tremor is to target and disrupt the neural circuitry that is propagating tremor (thalamotomy). In the last 5 years, treatment to one side of the body has become routine clinical practice in medication refractory tremor and is of particular interest to those who have contraindications to invasive forms of neurosurgical interventions. Despite the success of unilateral MRgFUS thalamotomy, many patients continue to have trouble with the 'untreated' side and have shown interest in bilateral treatments. In light of the improved technology, the safety and effectiveness of bilateral MRgFUS treatments have been proven in prospective studies. Thus, this project aims to verify the effectiveness and safety of this treatment in a real-world setting and to explore if the procedure provides a synergistic improvement in quality of life compared to a single side treatment. Further, the team at St Vincent's Hospital Sydney will continue the collaborative work with the computational neuroscience research team at the Brain and Mind Centre, to determine if the degree of neural circuitry interruption specific to tremor is associated with clinical benefit and/or side-effects, and if this differs from a unilateral treatment.

DID YOU KNOW?

There are over 40 major types of primary brain tumours, which can start anywhere in the brain or spinal cord. They are classified based on what type of cell they start in and how they are expected to behave (i.e. slow or fast growing, likelihood of recurrence, etc).

2023 Research Grant Awards

▼ CEREBROVASCULAR INCL. STROKE, ANEURYSMS, AVM

Computerised calculation of ruptured brain aneurysm wall tension at admission predicts the risk of aneurysm re-rupture before treatment within 24 hours

Chief Investigator:
Dr Arosha Dissanayake,
Sir Charles Gairdner Hospital

Co-Investigators:
Prof Graeme Hankey,
A/Prof Kwok Ming Ho,
Dr Timothy J Phillips,
Mr Stephen Honeybul,
Prof Karol Miller

Each year approximately 1 in 12 Australians who suffer brain bleeding from the rupture of an aneurysm experience re-rupture of the same aneurysm within the first 24 hours. This is devastating as re-bleeding greatly increases the risk of death and severe disability. Whilst this could be prevented by treating everyone as soon as they are admitted to hospital; aneurysm treatment requires expert teams using specialised equipment. Having such teams and equipment available 24/7, 365 days of the year at every hospital throughout Australia is too costly and logistically burdensome to make it viable. For these reasons predicting who is likely to suffer re-bleeding is critical but to date; no tool has proven to be useful. Our earlier research showed that internationally described scoring systems which predict re-bleeding for European and Chinese patients are not accurate for Australian patients. In this study, we investigate whether the tension on the wall of an aneurysm is different between Australian patients who suffered re-bleeding and those who did not when matched for all other known predictors. To estimate wall tension, we will use a newly developed computer program which needs only the size and shape of the aneurysm from brain scans together with blood pressure readings at the time of scanning. If this study finds wall tension is different between the groups, in the future this technique could be used to predict which patients with a ruptured brain aneurysm are at increased risk of re-bleeding and would benefit the most from emergency aneurysm treatment.

A novel molecular pathway that mediates constriction after aneurysms rupture

Chief Investigator:
Dr Matilde Balbi,
University of Queensland

Co-Investigator:
Dr Louis-Philippe Bernier

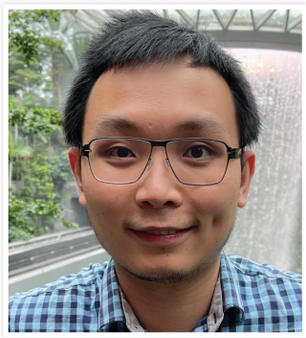
Brain aneurysms form when a weak area of a blood vessel in the brain bulges out, often leading the vessel to rupture and blood to leak into the brain and the subarachnoid space (vascularised space between the brain and the skull). This condition known as aneurysmal subarachnoid haemorrhage (aSAH) affects more than 10,000 patients per year in Australia. Of patients who experience an aSAH, roughly a quarter to half will then suffer from cerebral vasospasm, a debilitating complication of aSAH. What triggers vasospasms is unknown and there are no effective treatments available. Our project directly investigates a signalling pathway that we hypothesise is responsible for the cerebral vessel constriction causing vasospasm. Our objective is to find what triggers vasospasms. Using advanced imaging techniques in animal models of vasospasm, we will build on robust preliminary data showing that our target pathway triggers constriction of brain vessels by activating newly described receptors on vascular cells.

WHAT IS VASOSPASM??

Vasospasm occurs when a brain blood vessel narrows, blocking blood flow. It can occur in the two weeks following a subarachnoid haemorrhage.

▼ CEREBROVASCULAR INCL. STROKE, ANEURYSM, AVM

HEAD-START 2: Improving blood pressure during acute stroke to assist brain reperfusionstroke



Chief Investigator:
Dr Rudy Goh,
Royal Adelaide Hospital

Co-Investigators:
Prof Timothy Kleinig,
Prof Jim Jannes,
Dr Stephen Bacchi,
Dr Felix Ng

Acute ischaemic stroke is a common, disabling, but treatable condition requiring urgent treatment. In 2020, there were 445,087 stroke survivors in Australia and 27,428 Australians newly diagnosed with stroke. This is predicted to increase to 50,600 annual strokes and 819,000 Australian stroke survivors by 2050. When ischaemic stroke happens, a blood vessel supplying the brain becomes blocked and cuts off oxygen supply to the brain. This causes brain tissue to die. However, brain tissue death occurs faster in areas with less blood flow, and slowly in areas of more blood flow.

We propose that increasing blood pressure with a medication called metaraminol may temporarily improve blood flow to the brain as a complementary treatment to other standard treatments. Although metaraminol is sometimes given in stroke, it is uncertain whether blood flow to the brain improves with this treatment, or to what degree. This study tests this theory directly and briefly as a 'proof of concept'. CT perfusion accurately detects the size and region of brain tissue that will most likely die without restoration of blood flow. We aim to repeat CT perfusion to show whether brain blood flow improves after increasing blood pressure with metaraminol. If we prove that brain blood flow improves by increasing blood pressure, this may improve outcomes for patients undergoing long distance transfer for clot retrieval therapy ('thrombectomy').

▼ MND / ALS & OTHER NEURODEGENERATIVE DISEASES

The Role of Clinical, Electrophysiological, Molecular, and Imaging Biomarkers in the Management of Motor Neuronopathies in Adults

Chief Investigator:
Dr Aicee Calma,
Concord Repatriation General Hospital

Co-Investigator:
Dr Katrina Morris

Spinal Muscular Atrophy (SMA) and Motor Neuron Disease (MND) are neurodegenerative motor neuronopathies that result in motor neuron loss leading to progressive weakness. In the last decade, there have been significant developments in the care of both SMA and MND patients – with rapidly expanding areas of research into more targeted therapies.

In SMA, both nusinersen and risdiplam, which are disease modifying therapies, have now been approved for use in adults. Similarly, management of MND continues to evolve with the advent of more targeted therapies. This era of evolving therapies has highlighted the need to establish ways to measure disease progression and response to therapy. In addition, it also raises the question of how tools initially validated in the paediatric SMA population can be applied in adult SMA patients.

With support from the Brain Foundation, we will explore the role of clinical, electrophysiological, biochemical, and imaging parameters in a longitudinal study of adult SMA and MND patients. This will involve assessing functional outcomes through standardised clinical assessments; measuring serum neurofilament to assess neuronal injury; ultrasound assessment of muscle architecture; and neurophysiological assessments to examine the degree of motor neuron loss.

2023 Research Grant Awards

▼ CONCUSSION & TRAUMATIC BRAIN INJURY

Biomarkers to diagnose concussion when patients are under the influence of alcohol and/or other drugs

Chief Investigator:
Dr Jennifer Makovec Knight, Monash University

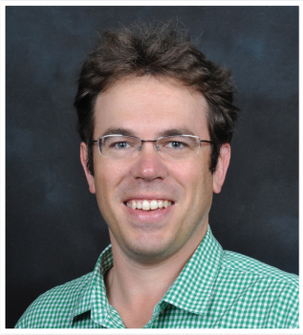
Co-Investigators:
Dr Stuart McDonald,
Dr William O'Brien,
Prof Biswadev Mitra

Concussion can be a serious diagnosis exposing patients to both short-term and long-term morbidity. The diagnosis of concussion relies on self-reported symptoms and tests of cognitive function. In Australia, a substantial number of patients sustain head strikes while under the influence of alcohol and other drugs. In these cases, the acute impacts of intoxication render it difficult to obtain a reliable account of the injury event or effectively diagnose concussion. Without reliable diagnoses, patients are at higher risk of repeat injury, and worse outcomes.

Objective markers of brain injury (i.e. biomarkers), can be a valuable adjunct to clinical judgement. We have recently shown that a panel of blood-based biomarkers can distinguish between individuals with and without concussion with high accuracy, however, these markers have not been validated in the setting of exposure to alcohol and/or other drugs.

This study aims to improve diagnostic certainty and outcomes of concussion among patients presenting to the emergency department with signs and symptoms of head injury, but are unable to be assessed using standard subjective reports and cognitive testing because they are under the influence of alcohol or other drugs. We will collect blood from these patients in the Emergency Department and quantify levels of blood biomarkers. Our hypothesis is that the levels of blood biomarkers on the day of injury will correlate to symptom severity, and therefore provide evidence on potential utility of biomarkers to predict post-concussion symptoms.

Evaluation of novel pharmacological supplements for prevention of concussion trauma in a preclinical model



Chief Investigator:
Dr Andrew Fenning, CQ University

Co-Investigator:
Dr Anna Balzer, Ms Katy Li

Repetitive mild traumatic brain injury (rmTBI) or concussion trauma, accounts for the majority of TBI cases worldwide and is currently a major focus in the public consciousness around many of our sporting codes. Its effects are far-reaching and include populations such as military personnel, domestic violence victims and athletes of contact-based sports. There is now an established link between rmTBI and the susceptibility for acquiring chronic traumatic encephalopathy (CTE), a longer term, more severe neurological disorder characterised by scarring, remodelling and plaque formation within the brain. Despite this, a clear understanding of how CTE develops from rmTBI is yet to be conclusively identified, and effective treatments for those suffering from or at risk of developing CTE are not available.

Our research, through the generous support of the Brain Foundation and their donor network, will enable our team to examine brain wide genetic changes following concussion trauma in a pre-clinical model. This analysis will allow us to identify key injury pathways which we can then treat with novel drugs such as rapamycin, berberine or guanidinoacetic acid to hopefully chart a course toward the development of further treatments for this debilitating condition. These drugs direct their action at cellular damage and encourage the brain cells to engage in cleaning and targeted repair processes. If these treatments prove successful, we will have a greater understanding of the how, where and why of concussion injury and avenues to prevent further damage.

DID YOU KNOW

Concussion is considered a 'mild' traumatic brain injury (TBI) because it is not usually life-threatening - but it can still have serious implications or long-term effects. Some patients experience symptoms for weeks or even months after the initial injury, and research has linked repeated concussions to chronic traumatic encephalopathy (a neurodegenerative disease).

▼ EPILEPSY

PLASMA Study: Understanding and improving antiseizure medication management

Chief Investigator:
Dr Emma Foster,
Alfred Hospital

Co-Investigators:
Prof Patrick Kwan,
Dr Sandra Reeder,
Ms Alison Conquest,
Dr Sameer Sharma,
Dr Nicholas Lawn,
Ms Carol Ireland,
Ms Lisa Todd,
Dr Lisa Wait,
Ms Emma Withoff

Epilepsy is a neurological disorder that causes recurrent seizures. More than 150,000 Australians live with epilepsy, and it can start at any age. Epileptic seizures can cause serious injuries (e.g., broken bones), accidents (e.g., falls, drowning), affect people's quality of life, and can even lead to death. The primary aim of epilepsy treatment is to control seizures. Two out of every three people living with epilepsy can become seizure free on antiseizure medications. However, antiseizure medications will not work if they are not taken. Distressingly, recent studies report that half of all Australians living with epilepsy do not take their antiseizure medications as prescribed. Similar findings have been reported internationally. With the generous support of Brain Foundation, our research team will conduct interviews and focus groups with key stakeholders (people living with epilepsy and healthcare providers). We aim to understand why people may or may not take antiseizure medications when they are first recommended, or why they may choose to discontinue antiseizure medications months or years after starting them. We will also find out what information about antiseizure medications is important to people living with epilepsy. We will workshop this information into the existing resources provided by national patient advocacy groups Epilepsy Action Australia and the Epilepsy Foundation. This study's targeted approach centres around people's lived experience, aiming to improve antiseizure medication adherence, and reduce otherwise avoidable seizures, seizure-related injuries, accidents, and death. We sincerely thank the Brain Foundation for their support, and are honoured to have received this prestigious award.

▼ MIGRAINE & HEADACHE

The effect of CGRP monoclonal antibodies on bone health

Chief Investigator:
Dr Jason Ray,
Monash University

Co-Investigators:
Prof Manjit Matharu,
Dr Elspeth Hutton,
Dr Shoshana Sztal-Mazer

CGRP monoclonal antibodies are an effective new class of medications used in Australia and worldwide for the prevention of migraine, a condition that affects 1 in 7 people. They work by blocking either the CGRP molecule, which is involved in the initiation of a migraine, or its receptor. While these medications have been found to be well tolerated in clinical trials, because CGRP has other roles in the body, there is an ongoing need to study these medications to ensure there are no 'off-target' effects from their use.

Our research project is expanding on earlier clinical observations by investigating any effect that these medications have on the immune system. To do this, we are collecting blood samples from volunteers prior to, and after commencing these medications, and analysing the level and pattern of expression of immune cytokines – proteins involved in signalling in the immune system.

This research will further inform clinical practice worldwide by either confirming the safety of these medications, or identifying an area that may require particular monitoring to ensure the ongoing safe use of the medication. We would like to sincerely thank the scientific committee, sponsors and donors of the Brain Foundation for their support of this project.

2023 Research Grant Awards

▼ MULTIPLE SCLEROSIS & OTHER INFLAMMATORY DISEASES

Neuroimaging analysis in patients with Susac's syndrome

Chief Investigator:
A/Prof Todd Andrew Hardy,
University of Sydney

Co-Investigators:
Dr Heidi Beadnall,
Prof Michael Barnett,
Dr Chenyu Wang,
Dr Linda Ly

Susac's syndrome is an autoimmune disease where a person's immune system mistakenly attacks the small blood vessels of the brain, cochlea of the ear, and the retina of the eye causing brain damage and hearing and visual loss.

Early corticosteroid treatment helps to suppress the immune system and limit damage from the disease. Often, other high powered immune therapies are added but this may not be appropriate for all due to the risk of adverse effects, such as infection.

Data are limited as to whether patients with Susac's syndrome acquire progressive brain shrinkage (atrophy) over time and whether it might relate to poorer cognitive and disability outcomes. Furthermore, no studies have looked at whether the volume, location and burden of areas of brain magnetic resonance imaging (MRI) abnormality (or "lesions") predicts outcomes later in life.

We will investigate lesion characteristics and brain shrinking in Susac's syndrome by reviewing sequential MRI scans of the brain performed as part of usual clinical monitoring in patients with the condition. Brain MRI scans will be analysed using software developed to assess for brain lesion measurements (such as lesion volume and distribution), and atrophy (evaluating the change in volume of different brain regions over time).

The results of the study will help clinicians to understand whether high powered therapies should be used from the outset in all, or a subset of, Susac's syndrome patients and whether chronic immune treatments are required for long periods to minimise ongoing lesion formation, brain shrinkage and disability.

Improving diagnosis and monitoring of autoimmune encephalitis

Chief Investigator:
Dr Robb Wesselingh,
Monash University

Co-Investigators:
A/Prof Mastura Monif,
Ms Sarah Griffith,
Dr Nabil Seery

Your immune system exists within the human body to protect you against microscopic invaders such as bacteria and viruses. In some people this system instead incorrectly targets elements of your own body instead (autoimmunity). In the case of autoimmune encephalitis (AE) the immune system targets the brain causing damage and swelling called inflammation. This results in severe symptoms such as seizures, involuntary movements, poor memory and even coma.

This condition can be treated by dampening down or suppressing the immune system to prevent ongoing inflammation. At present patients with AE are treated until their symptoms have diminished. However, a significant number of patients will continue to have ongoing symptoms that can cause significant impairment and prevent them from returning to their previous life or employment. These symptoms can include memory issues, physical disability, low mood and difficult to manage seizures.

My research aims to use samples of blood from patients with AE and look at the way their immune cells are acting at a genetic level. This can help guide us to find previously unrecognised blood proteins that are associated with AE, particularly patients who have poor recovery from their illness. If we can identify these proteins, we may help doctors to diagnose patients more quickly, identify those with ongoing inflammation, and those that may continue to do poorly. This information is crucial for patients, their care givers and it assists with future development of tools for improved disease diagnosis, monitoring, patient counselling and treatment options.

Recessive titinopathy patient muscle analyses to inform therapy development

Chief Investigator:
Dr Emily C. Oates,
University of New South Wales

Co-Investigators:
Dr Michaela Yuen,
A/Prof Mark Raftery,
Prof Marc Wilkins

Recessive titinopathy has recently emerged as one of the most common childhood-onset muscle disorders. It is caused by disease-causing variants within an enormous gene called TTN (titin) and results in weakness of the voluntary skeletal muscles of the body, such as the arm, leg, and breathing muscles, and the heart muscle. This results in physical disability and sometimes early death, usually due to breathing or heart complications. There are no effective treatments to prevent or reduce the significant and often-progressive weakness caused by this condition.

Differences in the amount of titin protein expressed in patient muscle are likely contributing to the striking differences in clinical severity observed within this patient group (some succumb during pregnancy/infancy, others survive into adulthood). We anticipate that patients who express more titin are less severely affected. Therefore, increasing titin expression is likely to improve patient outcomes. However, existing titin quantification methods are notoriously inaccurate.

We currently have funding to develop two different treatment strategies (CRISPR-on and exon skipping) aimed at increasing titin expression. This project will complement these treatment development endeavours by enabling us to develop and apply a novel mass spectrometry-based method to accurately quantify titin expression in patient muscle from mildly and severely affected individuals and compare this to expression in healthy muscle. This will increase our understanding of how much additional titin is needed to improve clinical outcomes. The project will also allow us to characterise the impact of disease-causing variants at the protein recipe (RNA) level to better understand which patients would benefit most from our exon skipping therapies. Overall, this project will advance our goal of becoming a world leading recessive titinopathy treatment development centre.

You've seen the exciting projects that we are funding in our 2023 grants, but what about the results from past research? In most issues of Brainwaves, we include research report summaries to highlight some of the projects from previous years. Unfortunately we didn't have space in this issue, but if you're interested, the reports are all uploaded in full on our website. You could learn about things like…

- **How researchers are trying to identify concussion biomarkers** (Detecting Concussion In The Brain, Dr Remika Mito, 2021)
- **The efficacy of newborn screening programs in improving clinical outcomes for diseases like spinal muscular atrophy** (Does Newborn Screening For Spinal Muscular Atrophy Change Patient Outcomes? Dr Didu Sanduni Kariyawasam, 2021)
- **Investigating new treatment options for stroke, which could possibly be safer or more effective than current treatments** (Identification of New Approaches for the Treatment of Stroke, A/Prof Simone Schoenwaelder, 2019)

The reports are uploaded on each grant page approximately one year after they receive the grant. You can access them by going to brainfoundation.org.au and clicking on 'Research > Funded research by year'.

Healthy brain

Brain-boosting foods

Last issue we wrapped up our three part series on how the brain works. If you missed it, you can catch up on the website by visiting https://brainfoundation.org.au/healthy-brain/how-the-brain-works/

In this issue we're covering one of the frequently asked questions about brain health - which foods are actually good for your brain?

We all know the saying, "You are what you eat." This means the food we put into our bodies affects how we feel, think, and even how our brains work. Just like how a car needs the right fuel to run smoothly, our brains also need the right food to work at their best.

Before we get into it, it's important to remember that these foods can't single-handedly prevent or cure brain diseases, disorders or injuries. They just support brain function because they contain high levels of some of the essential nutrients that your brain requires. There are many other factors that affect your brain health such as genetics, exercise, mental health, environmental factors, and more. Always consult your doctor if you are concerned about your lifestyle or brain health.

Fatty Fish

Fatty fish like salmon, trout, and sardines are loaded with omega-3 fatty acids. Our brains use these fats to build brain and nerve cells, which are super important for learning and memory. Without enough omega-3s, we might feel forgetful or even a bit down.

Blueberries

These tiny fruits are packed with antioxidants. Antioxidants fight against harmful things in our body called 'oxidative stress' and inflammation. By eating blueberries, you're helping your brain fight off these bad guys which can cause brain ageing and other diseases.

Turmeric

You might have seen this yellow spice in your kitchen. Turmeric has curcumin, which can pass through the barrier between our blood and our brain. This helps boost brain-derived neurotrophic factor (BDNF), a growth hormone that helps brain cells grow. It also helps fight brain inflammation and keeps our memory sharp

Broccoli

Broccoli is full of antioxidants and vitamin K. Vitamin K is believed to support brain health by protecting the brain against damage. Plus, it's a relatively affordable and versatile vegetable that is easy to incorporate into lots of different meals.

Pumpkin seeds

These tiny seeds have a lot of powerful stuff: antioxidants, magnesium, iron, zinc, and copper. Magnesium is good for learning and memory, while zinc and copper are important for nerve signalling, which is when your brain cells talk to each other.

Dark chocolate

Dark chocolate has caffeine, which can make you more alert. It also has antioxidants and other chemicals that are good for brain health. Remember to eat in moderation, though!

Nuts

Nuts, especially walnuts, have lots of good fats, antioxidants, and vitamin E. Vitamin E helps protect your brain cells from damage. Eating nuts might also help improve your memory and keep your brain sharp as you get older.

Oranges

Oranges are famous for vitamin C. Did you know that vitamin C helps prevent mental decline? Eating enough vitamin C-packed foods like oranges can help protect your brain as you get older.

Eggs

Eggs are a great source of several nutrients like vitamins B6 and B12, folate, and choline. Choline helps produce a chemical called acetylcholine, which helps regulate mood and memory.

Green tea

Like dark chocolate, green tea has caffeine, which can make you feel more awake and focused. It also has an amino acid that helps you feel more relaxed. Plus, it's full of antioxidants that can keep your brain healthy.

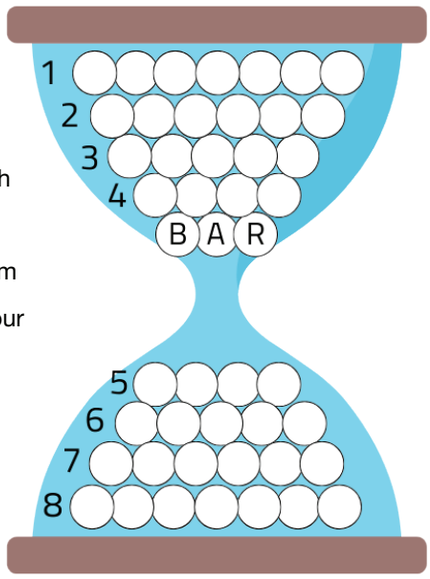
Remember, a well-balanced diet with lots of different foods is the key. These foods are just some of the ways you can help keep your brain happy and healthy. Maybe next time you don't know what to make for dinner, take some inspiration from these brain-boosting foods!

Healthy Brain Games

Hourglass brain teaser

Starting in the middle, each word in the top half has the letters of the word below it, plus a new letter, and each word in the bottom half has the letters of the word above it, plus a new letter.

1. Small army unit
2. Tease
3. Made from dough
4. Lyric poet
5. Short for Abraham
6. Deep yellow colour
7. Sculpture rock
8. Pedestrian



Sudoku

MEDIUM

	9	2		3	8	1		
		5	2				7	
			6					
4			5				8	1
	5			9	4	7		
			1	6			5	9
			3	8				
1		8					3	
5	7		9				2	

Solutions are on the back page.

Leave a lasting gift

Have you written your will yet? Making your will for the first time or changing it to include a gift to the Brain Foundation could be as simple as contacting your legal advisor.

Alternatively, you can now use an online option to create a simple will. We've partnered with Gathered Here, an online Wills and Estates firm, to offer you a free and easy will writing service. The step-by-step form can be completed online in less than ten minutes, and all you have to do is print it out and sign it.

NO MATTER HOW MUCH YOU HAVE, LARGE OR SMALL, IT CAN MAKE A DIFFERENCE. PLEASE CONSIDER MAKING A BEQUEST IN YOUR WILL TO THE BRAIN FOUNDATION. WRITE YOUR FREE WILL NOW AT WWW.GATHEREDHERE.COM.AU/C/BRAIN-FOUNDATION

IN MEMORIAM

A big thank you to the families and friends of the following who donated in memory of their loved ones.

Hazel Bickford

Tom Cullen

Christina Jane Hanks

Michelle Hugo

Brian Johnston

John Robert Meagher

James Mills

Bobbie Shaban

Julie Stonehouse

Michael Ian Turner

Jean Mary Wandoch

John Woodward

Did you know that you can remember your loved ones and make a donation to a specific category of research? Please phone if you would like more details or see our online donation form or scan the QR code.

Thank you to our fundraisers

We didn't have space to fit all of our fundraisers on page 3, but we would like to thank and acknowledge everyone who has helped raise money for research this year.

McCarthy Catholic High School - Cerebrovascular disease

Cynthia Still (Ladies in the Field) - Brain tumours

Sarah O'Donald - Cerebrovascular disease (AVM)

Robert Baker (Finley Car Show and Cruise) - Brain tumours

Lucienne Ruddenklau - Cerebrovascular disease (aneurysm)

Brendan Wyatt - Cerebrovascular disease (AVM)

Vito Midolo - Brain tumours

Rachael Ward - General research

Morgans Financial Limited - General research

Jessica Stankovski - Multiple sclerosis

Kate Bickford - MND/ALS & other Neurodegenerative Diseases

Anahita Shaban - General research

Kacey Hugo - Cerebrovascular disease (aneurysm)

Nicki Cambourn - Cerebrovascular disease (AVM)

Nia Johnston - Movement disorders

Barbara Winkler-Wolff - ALS & FTD

Steph Judd - Dystonia

Amanda Glasson - Cerebrovascular disease (aneurysm)

Tara Cullen - Multiple systems atrophy

Ellie Stonehouse - Cerebrovascular disease

Your support is so appreciated. Thank you for your commitment to raising awareness and research funds. We couldn't do it without you!

THANK YOU!

Healthy Brain Solutions

Hourglass brain teaser

Brigade
Badger
Bread
Bard
Bram
Amber
Marble
Rambler

Sudoku Medium

6	9	2	7	3	8	1	4	5
8	1	5	2	4	9	6	7	3
7	3	4	6	5	1	2	9	8
4	6	9	5	2	7	3	8	1
3	5	1	8	9	4	7	6	2
2	8	7	1	6	3	4	5	9
9	4	6	3	8	2	5	1	7
1	2	8	4	7	5	9	3	6
5	7	3	9	1	6	8	2	4

Brain Foundation

Thank you for supporting brain research through the Brain Foundation

To make a donation please visit our website
brainfoundation.org.au/donation/
or use the donation form on the letter enclosed.

REGISTERED CHARITY acnc.gov.au/charityregister