brainWAVES

The Newsletter of the Brain Foundation

Summer 2022/23

Thank you... Thank you... Thank you... I am absolutely thrilled to report that our research grants program is back in full swing after a tough couple of years. Much of that thanks needs to go to fundraisers across the country. In fact, there were so many we could not fit them all inside these pages!

If you donated or helped raise funds in any way over the past 12 months please read about the researchers who are putting your dollars hard to work, finding better treatments and cures. We have funded 13 amazing projects this year, focusing on many different brain diseases, disorders and injuries. It's a privilege to be able to fund research into such a wide range of conditions.

Your donation, no matter how small, is greatly appreciated and will help so many. To donate, visit our website, phone or write to us. Thank you.

Trevor Thompson
CEO

Migraine & Headache Awareness Week 2022

Every year we host Migraine & Headache Awareness Week to support people living with migraine or headache disorders. From September 19-23, we invited people to participate in webinars featuring Australia's leading headache specialists. Once again we had a fantastic turnout with over 4,500 people joining us for the presentations.

Migraine and headache disorders can take a heavy toll on people when they don't have access to support, information, and appropriate treatments. That's why this event is so important - it's an opportunity for patients & carers to have their questions answered by leading neurologists & experts.

Learning about new treatments and management strategies can empower people to take control of this disease. We know that migraine is…

- **Under-diagnosed & under-treated.** 46% of participants said it took more than 5 years to receive a diagnosis of chronic migraine.
- **Isolating.** Family, friends or colleagues might not realise how debilitating migraine can be. This stigma can make it hard to find support.
- **A highly variable condition.** Everyone's experience with migraine is different, from triggers to treatments. There is no 'magic pill' that works for everyone.

During the webinars, participants were able to chat with each other and share their experiences. While each story was unique, many people were able to connect over similarities in their migraine or headache disorder as well.

We hope that everyone who attended 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

Brain tumour model could help develop personalised treatments

Glioblastoma is a rare but deadly brain cancer. It is very hard to treat because it is resistant to surgery, chemotherapy, and radiation - however, scientists at Virginia Tech are hoping to change that.

They have developed a 3D tissue-engineered model of the glioblastoma tumour microenvironment. This can be used at a patient-specific level to learn why tumours return & test which treatments will be most effective.

Given that many cancer treatments are invasive or have damaging side effects, it can be devastating for a patient's quality of life when they don't work. This model is a major breakthrough that could eliminate the guesswork in treating glioblastoma. We hope to see it in clinical practice in the near future.

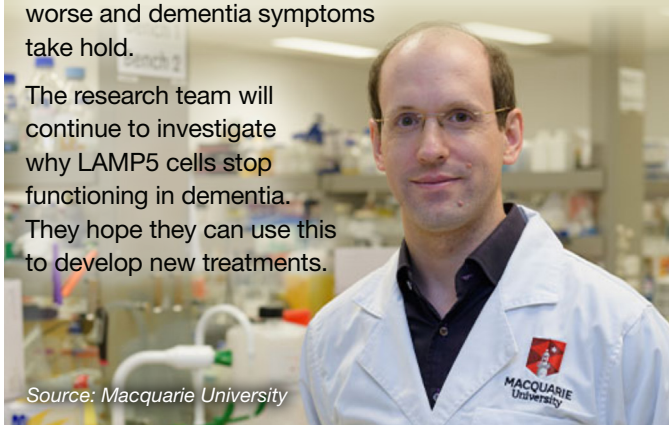
Source: Virginia Tech
Dr Gabriela Mendes holding an example of the 3D model of the glioblastoma tumour microenvironment (Credit: Clayton Metz).

Protein discovered that plays a key role in dementia

Researchers at Macquarie University have discovered that an obscure brain protein plays a role in Alzheimer's disease & other forms of dementia. The protein is called lysosome-associated membrane protein 5, or 'LAMP5'.

Professor Lars Ittner (Centre for Dementia Research) and his team were investigating hyperexcitation in the brain, which has been connected to the development of dementia symptoms. LAMP5 interneurons are particularly important in regulating neuronal activity and preventing hyperexcitation. So when these proteins stop working, hyperexcitation in the brain becomes worse and dementia symptoms take hold.

The research team will continue to investigate why LAMP5 cells stop functioning in dementia. They hope they can use this to develop new treatments.



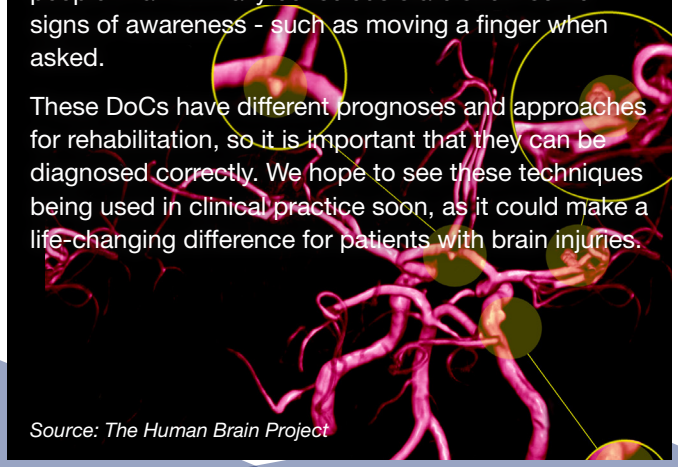
Source: Macquarie University

Improving our understanding of disorders of consciousness

A study by the Human Brain Project has explored new techniques to help differentiate between disorders of consciousness (DoCs). They found ways to differentiate between unresponsive wakefulness syndrome ('vegetative state') and states of minimal consciousness.

Unresponsive wakefulness refers to patients who wake up from a coma but do not respond to their environment or verbal commands. On the other hand, people in a minimally conscious state show some signs of awareness - such as moving a finger when asked.

These DoCs have different prognoses and approaches for rehabilitation, so it is important that they can be diagnosed correctly. We hope to see these techniques being used in clinical practice soon, as it could make a life-changing difference for patients with brain injuries.



Source: The Human Brain Project

An historic moment: successful trial for Alzheimer's drug

A clinical trial in the UK has found that lecanemab can slow the cognitive decline of people with early Alzheimer's disease. The experimental drug was given to people for 18 months, and those on lecanemab declined by 27% less than those on a placebo treatment.

This might not seem groundbreaking, but this is the first time in over 20 years that a drug has shown clinical improvements for Alzheimer's patients. Other anti-amyloid medications have been able to reduce plaque levels in the brain, but they didn't improve peoples' symptoms.

There were some side effects and more research needs to be done to confirm the drug's efficacy. But this is a major step in Alzheimer's research - we look forward to hearing more news.

Source: The Guardian

Fundraisers

Circling the Void' exhibition

Circling the Void was an exhibition at YAVA Art Gallery in Victoria that featured the work of Sally Miller and Bronwyn Ward. Sally passed away in 2015 with multiple systems atrophy (MSA), and in her last few months she made nine beautiful drawings that told the story of how she felt as her disease progressed. Bronwyn's work explores similar themes, reflecting on death, dying, and the void left behind after someone dies.

It was a beautiful exhibition that helped raise awareness for MSA, as well raising funding for research. We would like to thank David Miller (her brother) for donating the profits of Sally's art prints to the Brain Foundation to support research in her memory.

MULTIPLE SYSTEM ATROPHY (MSA) IS A RARE, DEGENERATIVE NEUROLOGICAL DISORDER AFFECTING YOUR BODY'S INVOLUNTARY (AUTONOMIC) FUNCTIONS, INCLUDING BLOOD PRESSURE, AND MOTOR CONTROL.

UNWINDING is about Sally's body unwinding as parts of her brain cease to communicate with her muscles. This leads to a loss of self-esteem as one feels one is losing one's identity.

Trevor meeting the wonderful Tamworth Christmas Fair committee.
Front row left to right: Pip, Sarah, Kate, Paolina.
Back row left to right: Trevor, Susi, Tina, Lisa, Liz, Lisa, Jane.

Tamworth Christmas Fair

The Tamworth Christmas Fair took place on the 20th 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 over 20 years.

This year, the proceeds from the fair will fund Daniel Beard's research into stroke outcomes. You can read more about this project on page 9.

If you missed out on this year's wonderful regional event, you can follow their Facebook page to stay in the loop for next year's date. https://www.facebook.com/BFTCF/

Shaw House Fun Run

Back in September, students and staff from Shaw House at Caulfield Grammar School participated in a fun run to support the Brain Foundation. This is a cause close to their hearts and we are so thankful for their ongoing support. This is their 10th fun run, and in that time they have raised over $40,000 for neurological research!

Thank you for helping us honour those who have suffered from brain diseases, disorders, and injuries. Your dedication will help so many in the future as we continue to fund research.

Fighting TN (Trigeminal Neuralgia) Community Fundraiser

Fighting TN hosted a community fundraising event in October, with a market that showcased businesses from Echuca / Moama (VIC) and surrounds. They had a fantastic day with over 30 stall holders, 5 musicians, a welcome to country and Smoking Ceremony by a local Elder, children's activities, and an art gallery by local kindergartens.

Trigeminal neuralgia is an extremely painful condition causing facial pain on one side of the face. It can be very distressing to live with, particularly if treatments don't work. We are so grateful for the support of Fighting TN - their wonderful event raised over $8,500. Thank you so much for helping us fund much-needed research.

Migraine & Headache Australia Updates

Migraine & Headache Awareness Week 2022

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

- New Treatments - Dr Michael Eller
- Ageing with Migraine - Dr Katherine Spira
- Headache Types: including Vestibular Migraine, Hormonal Migraine, Cluster Headache & NDPH - Dr Jason Ray
- 2022 Research Findings on Headache & Migraine - Dr Bronwyn Jenkins
- Treatment Performance, Hospital Utilisation & Weather - Francois Cadiou, Founder of Migraine Buddy
- Event Highlights and General Q&A - Carl Cincinnato, Migraine & Headache Australia

Speakers from top left: Dr Michael Eller, Dr Katherine Spira, Dr Jason Ray, Dr Bronwyn Jenkins, Francois Cadiou and Carl Cincinnato.

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

"The ability to watch the recordings was great as was the length of the talks and the topics covered. Also, having Australian information was great. I was feeling exhausted and pessimistic and these talks inspired me to pick myself up and keep trying. You are making a positive difference. Thank you."

- Alison

"Thank you for your work and the foundation, it has been a life saver for me and for many others. The webinars helped me to better understand my condition. I hope one day I can help others suffering this condition too."

- Sigrid

"I've enjoyed this week because I now know I'm not alone and what I have been suffering from for years is real and actually quite common. I will be talking more with my doctor!"

- Cheryl

Shades for Migraine winners

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. Thank you to everyone who participated, we loved seeing all your creative photos.

Five lucky participants won our migraine hamper packs, which included over $350 worth of self-care products for people living with migraine. You can check out some of their entries below.

If you didn't get a chance to participate this year, we'll be providing more opportunities to raise awareness in the future. We will announce next year's competition (and more exciting prizes) in our e-newsletter.

Our winning entries from Abeera, Alison, and Geoff.

New Treatment Updates:

New treatment update: Vyepti® recommended for PBS listing

On the 19th of August, Vyepti® received a positive recommendation from the PBAC (Pharmaceutical Benefits Advisory Committee) to be listed on the PBS (Pharmaceutical Benefits Scheme).

Vyepti® is another calcitonin gene-related peptide monoclonal antibody (CGRP), which is the newest type of preventive migraine treatment. This recommendation is very exciting, particularly because Vyepti® was only approved for use in Australia in April.

Once the listing is finalised, Vyepti® will be available with PBS pricing for chronic migraine patients who have found at least three other preventive medications to be ineffective or intolerable. It will be joining two other CGRPs (Ajovy and Emgality) which are already listed on the PBS.

Thank you to everyone who made a PBAC submission to support Vyepti's listing on the PBS. This recommendation wouldn't have been possible without your ongoing support & advocacy. We hope to hear more news soon!

You can learn more about Vyepti® on our website at headacheaustralia.org.au/vyepti/.

Celebrity Apprentice

We were so thankful to have the support of Eloni Vunakece during the 2022 season of Celebrity Apprentice. He is a former international NRL football star who retired from football in 2018 after a particularly bad concussion.

Eloni estimates he suffered 15 concussions over his career and he is now an advocate for players welfare, specifically when it comes to head injuries. He has also registered as a brain donor with the Australian Sports Brain Bank to help advance research into brain injuries.

Despite leaving the show after the eighth challenge, Lord Sugar gave him a donation cheque in recognition of his hard work and effort. Thank you Eloni for your passion & dedication in being an advocate for brain health!

City2Surf

Thank you Sigrid, Andy, and Conor for supporting us in the City2Surf this year! Sigrid has chronic migraine, so her partner (Andy) and his brother decided to run for those who can't. Their fundraising efforts paid off with their team raising over $2,000 from people across the world - donations came from Europe, New Zealand, America, and Australia.

Even more importantly, they raised awareness for this invisible neurological illness. We wholeheartedly agree with Sigrid, who says "even if it's just one more person knowing about it, it makes a difference".

Thank you so much for your dedication and support! If you would like to do the same, you can enter the City2Surf next year, or find other running events via https://runforcharity.com/

Sigrid, Andy & Conor wearing the shirts they designed for this event; and the successful runners after the race.

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

2022 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. The applications this year were, as always, a fantastic insight into the talent, dedication, and curiosity of Australian researchers.

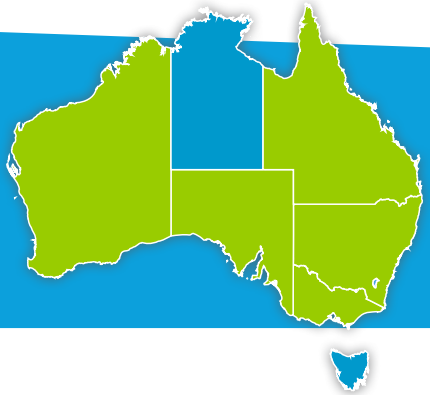
We are excited to announce that our grants program is continuing to rebuild after the challenging events of 2020, and we are able to fund 13 projects this year. We would like to thank the members of our Scientific Committee for volunteering their time and expertise to assess these applications.

However, the effects of the pandemic, natural disasters, and inflation are still lingering. 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 work to do more to support researchers, patients, and their loved ones.

The recipients of our 2022 grants are representative of the high quality research happening in Australia. You can read all about their projects on the following pages.

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.

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

High-resolution imaging of protein clumps in frontotemporal dementia and motor neuron disease

Chief Investigator:
Dr Adekunle Bademosi, University of Queensland

Co-Investigator:
Dr Adam Walker

Frontotemporal dementia (FTD) and motor neuron disease (MND) are incurable neurodegenerative diseases. Currently, about 30 in 100,000 Australians live with FTD while 8 in 100,000 live with MND and their prevalence is projected to increase annually. A key feature that drives the progression of both diseases is abnormal clumping of a protein known as 'TDP-43' within nerve cells. Physiologically, TDP-43 binds to diverse DNA and moves between the part of the nerve where DNA is abundant and the areas with little DNA. However, in FTD and MND, this shuttling of TDP-43 stops, and the structure of the protein is modified in such a way that increases its propensity to clump. This clumping induces toxicity and death within the affected nerves. It is therefore of vital importance to identify how these changes alter the function of TDP-43.

This project will use recently developed advanced microscopy tools that allow for imaging of single proteins such as TDP-43 within nerves. Dr Bademosi who is an expert in using these advanced imaging tools will attempt to provide very high and precise localisation, yielding resolutions about 10 million times higher than the camera of a standard smart phone. This project therefore has the potential to uncover new and precise mechanisms through which the different changes in the structure of TDP-43 alters its dynamics and therefore function in disease. It is important to pinpoint these early changes in TDP-43 protein dynamics that are conducive to clumping to be in a position to prevent them.

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

MRI guided focused ultrasound (MRgFUS) for focal hand dystonia

Chief Investigator:
Dr Joel Maamary,
St Vincent's Public Hospital

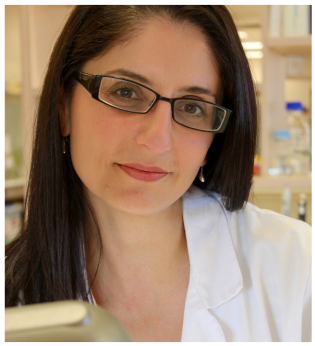
Co-Investigators:
A/Prof Stephen Tisch
Dr Yael Barnett

Dystonias are a group of movement disorders that are characterised by sustained or intermittent muscle contractions that result in abnormal movements, postures or both. Focal dystonias are a subgroup of dystonia where the abnormal movements are isolated to a single body part. In the upper limb, these are referred to as focal hand dystonia and are commonly task-specific, triggered by a particular motor task. The most well-known forms of focal hand dystonia are 'writers cramp' and 'musicians dystonia.' Individuals with focal dystonia are often disabled and unable to perform these tasks with subsequent implications on their profession or livelihood.

Current treatment options are limited to short term symptom relief with low efficacy oral medications or local treatment with botulinum toxin. Physical therapies and rehabilitation have been reported to provide some improvement, but this evidence is not definitive. Our trial aims to assess the safety and efficacy of MRI guided focused ultrasound, a new minimally invasive neurosurgical treatment method, in individuals with focal hand dystonia. This treatment utilises high frequency ultrasound beams to interrupt the pathways involved in generating the dystonia without requiring a surgical incision or open neurosurgery. Further, we aim to better define the abnormal neural pathways and brain changes associated with this condition as well as outline the effect of this minimally invasive treatment on upper limb strength, coordination and function.

▼ PAEDIATRIC NEUROLOGY

"Mini-brains" as personalised medicine tools for cerebral palsy



Chief Investigator:
A/Prof Mary Tolcos,
RMIT University Bundoora

Co-Investigator:
Dr Anita Quigley
A/Prof Atul Malhotra
Dr Bobbi Fleiss

Cerebral palsy is a brain disorder that affects an individual's movement, posture, and balance, and is the most common movement disability in childhood. Babies born too early, or preterm, are at a greater risk of sustaining brain injury that can then lead to the development of cerebral palsy. The precise processes that occur in the infant brain to lead to cerebral palsy are not fully understood, and there are no widely available treatments to prevent or correct the brain injury to improve neurological outcomes.

In this initial study, we will recruit two infants who are at high-risk of cerebral palsy due to preterm birth from the Early Neurodevelopment Clinic at Monash Children's Hospital, led by Associate Professor Atul Malhotra. With ethics approval and parental consent, blood will be collected from each of the two infants who have been identified as having early signs of cerebral palsy due to being born preterm to generate two separate sets of stem cells i.e., cells with the special ability to develop into any type of cell in the body. We will then generate brain organoids using these stem cells from the two high-risk preterm infants and using commercially available stem cells derived from individuals with no known brain disorder for comparison. Brain organoids will be grown, and we will study their structure and function to identify the mechanisms that may contribute to the development of cerebral palsy, with the intention of establishing a personalised medicine tool for future therapeutic testing.

WHAT IS CEREBRAL PALSY?

Cerebral palsy (CP) is a physical disability that affects movement and posture. It is caused by an injury to the developing brain either during pregnancy or shortly after birth. Around 34,000 people in Australia are living with CP, making it one of the most common brain disorders in Australia.

2022 Research Grant Awards

▼ BRAIN TUMOUR INCL. ACOUSTIC NEUROMA

Repurposing FDA-approved drugs for the treatment of glioblastoma

Chief Investigator:
Dr Stanley Stylli,
Royal Melbourne Hospital

Co-Investigators:
Prof Christopher Hovens
Dr Theo Mantamadiotis

Each year, approximately 2000 Australians are diagnosed with brain cancer and approximately 1600 will die from this disease. Glioblastoma (GBM) is the most common form of brain cancer and it is the most aggressive and lethal primary brain tumour due to its highly invasive and neurologically destructive nature. The current clinical approach involves surgery, radiotherapy (RT) and chemotherapy with temozolomide (TMZ) resulting in a median survival of approximately 15 months and a poor 5-year survival rate of only 4.6%. During this treatment, changes can occur in the GBM cells allowing them to survive multiple rounds of treatment. Our unique approach involves the generation of patient derived GBM cells that have survived multiple rounds of RT/TMZ treatment designated as 'treatment resistant cells' (long term treated). This project will examine the genetic fingerprint of untreated, single treatment and long term treated cells providing a comprehensive overview of the RT/TMZ treatment response versus genetic fingerprint before being treated with adjuvant therapies. This project will utilize a number of FDA-approved drugs that we have previously determined as potential agents for targeting GBM cells, as a single drug or in a 'polytherapeutic combination' repurposing approach to reduce the viability and invasive capacity of the different GBM cell groups. Determining the most effective adjuvant drug treatment especially against the 'long-term treatment resistant' GBM cells and correlating this with their genetic fingerprint will allow us to potentially determine which patients in the future may respond to this treatment when used post-RT/TMZ treatment.

Target therapies for the treatment of acoustic neuroma

Chief Investigator:
A/Prof Rebecca Lim,
University of Newcastle

Co-Investigators:
Prof Hubert Hondermarck
A/Prof Robert Eisenberg
A/Prof Phillip Jobling
Prof Alan Brichta

Nerve cells responsible for transmitting balance and hearing information from the inner ear to the brain are protected and insulated by a special type of cell called a Schwann cell, that wrap around nerve cells. Sometimes there is an unrestrained growth of Schwann cells, which results in the growth of a tumour. We call this an acoustic neuroma or vestibular schwannoma. People that develop a vestibular schwannoma may develop hearing loss, ringing in the ear, imbalance, dizziness, and sometimes numbness in the face. Large tumours can also be life-threatening because they can compress important regions of the brain. There are three main ways of treating a vestibular schwannoma 1) watch and wait, 2) surgical removal, and 3) radiotherapy. At present there are no drug therapies to stop or slow the growth of tumours once diagnosed or to prevent tumour regrowth after surgical removal.

In this project we will develop a brand new therapy for the treatment of vestibular schwannoma. There are a set of proteins in vestibular schwannoma called proNGF, p75NTR, and sortilin. These proteins are essential for the growth and survival of the tumour and there is a high concentration of these proteins in the tumour. We will use new drugs called blocking antibodies, to target these proteins. We propose that reducing the expression of these proteins will stop or slow tumour growth and cause tumour cell death. This new and exciting approach means this is the first targeted therapy for vestibular schwannoma.

Preserving blood flow, preserving brain: improving outcomes after stroke

Chief Investigator:
Dr Daniel Beard,
University of Newcastle

Co-Investigators:
Prof Neil Spratt
Prof Donald Ingber

Increasing blood flow through brain bypass vessels could help save the brain from stroke. Unfortunately, there has been no effective way of enhancing bypass flow using vessel widening (vasodilating) drugs without causing vasodilation of all blood vessels, leading to a drop in blood pressure (analogous to losing water pressure in a hose). We have teamed up with Harvard University who produce vasodilating drugs packaged into nanoparticles. These nanoparticles only release vasodilating drugs when exposed to levels of a frictional force known as shear stress only found in brain bypass vessels. So far, we have shown that these nanoparticles can selectively deliver vasodilators to only bypass vessels and can enhance bypass flow in our experimental stroke model, significantly reducing stroke severity without a dropping in blood pressure. In this project we aim to confirm the safety of NG-NPAs in a range of pre-clinical stroke models that better reflect the complexity of the stroke patient population to be ready for clinical trials to reduce severity of the stroke and improve patient outcome.

DID YOU KNOW?

There were 27,428 Australians who experienced stroke for the first time in their lives in 2020, which equates to one stroke every 19 minutes.

Targeting ischaemia-reperfusion injury following stroke

Chief Investigator:
Dr Annabel Sorby-Adams,
University of Adelaide

Co-Investigator:
Prof Mike Murphy
A/Prof Thomas Krieg
A/Prof William Taylor
Kimberly

Ischaemic stroke is a leading cause of death and disability worldwide. Arising due to arterial occlusion, current treatment involves removing the blockage to rapidly re-establish blood flow to compromised brain tissue, however, this often paradoxically leads to ischaemia reperfusion (I/R) injury.

I/R injury initiates many damaging cellular processes through the production of unstable molecules termed mitochondrial reactive oxygen species (ROS). Previously thought to be a non-specific response, mitochondrial ROS production following reperfusion is now established to arise due to conserved metabolic pathways. Specifically, the accumulation of mitochondrial metabolite succinate has been identified as a key driver in I/R injury, mediating its effects through binding succinate dehydrogenase (SDH).

Malonate, an inhibitor of SDH, has the potential to prevent I/R injury post stroke and markedly improve patient outcomes, with administration leading to a significant reduction in stroke volume in pre-clinical studies. To advance treatment to clinical trial, however, comprehensive evaluation of the efficacy of Malonate administration on stroke volume evolution is required. Neuroimaging is an invaluable tool for the evaluation of I/R clinically, enabling non-invasive assessment of the evolving injury in the same patient following onset of stroke. This project thus seeks to comprehensively evaluate the efficacy of malonate on stroke evolution using neuroimaging tools, specifically magnetic resonance imaging (MRI) and digital subtraction angiography (DSA), in a pre-clinical model of ischaemic stroke. The results of this study aim to support progression of malonate to clinical trial with the ultimate goal to reduce death and disability in ischaemic stroke survivors.

2022 Research Grant Awards

▼ CONCUSSION & TRAUMATIC BRAIN INJURY

Using light stimulation to improve recovery following traumatic brain injury

Chief Investigator:
Dr Jamie Beros,
University of Western Australia

Co-Investigators:
A/Prof Jennifer Rodger
Miss Emily King
Miss Rebecca Ong

The central nervous system, which includes the brain and spinal cord, has limited capacity to repair itself after traumatic brain injury. When damaged brain cells die, they are not readily replaced, and damage can spread to regions next to the injury site, increasing the loss of brain cells and impact of the original injury. Therefore, interventions that promote brain cell survival are essential to improving recovery and preserving quality of life outcomes following injury.

A promising method of keeping brain cells healthy is to increase their supply of neurotrophins, proteins produced and released by active brain cells that can affect neighbouring cells in the brain and improve survival after injury. Our project will use an exciting and cutting-edge neuroscience technique termed optogenetics to control the activity of brain cells using light stimulation following traumatic brain injury. Our goal is to use this technique to activate surviving brain cells at and surrounding the injury site to promote the production of neurotrophins. We will measure the quantity of neurotrophins produced in response to this form of stimulation and whether this intervention can promote the survival of damaged brain cells, prevent the spread of injury and improve brain function and repair. This project will provide important insight into how we can keep brain cells alive after injury to preserve brain function in the short and long-term.

How do changes in brain rhythms contribute to the effects of brain injury?

Chief Investigator:
Dr George Opie,
University of Adelaide

Co-Investigators:
A/Prof John Semmler
Dr Ngee Foo

Within Australia, traumatic brain injury (TBI) is one of the most common forms of acquired brain injury, being associated with more than 22,000 hospitalisations per year. The vast majority (80-90%) of TBIs are classified as mild (mTBI) and are responsible for the bulk of this impact. Although mTBI has long been considered to have only short-lived and mild symptoms, we now know that this is not actually the case. In fact, there is growing recognition of the serious and persistent side-effects experienced by many patients. Unfortunately, though, we still understand very little about the changes within the brain that drive these devastating side-effects. This limits our ability to identify patients that are likely to experience persistent problems, or to provide treatment.

Although limited, our current understanding of mTBI suggests that changes to the way in which different parts of the brain communicate with each other is important in generating long-term side-effects of injury. This process is referred to functional connectivity and underpins how the brain handles information. However, the mechanisms that drive these changes in functional connectivity are not known. Consequently, our project will attempt to better characterise how functional connectivity is altered by mTBI. We will approach this issue from a new perspective that focuses on different types of 'brain waves'. In particular, we will investigate how mTBI changes interactions between different brain waves, and how this relates to the side-effects of injury.

DID YOU KNOW

Every year in Australia more than 3,000 people are hospitalised after being concussed during sport - but triple that number won't seek medical attention. Concussion research can help us better recognise concussion to ensure people get the treatment they need.

▼ EPILEPSY

Testing antiseizure drugs with mini-brains

Chief Investigator:
Dr Alexander Bryson,
The Florey Institute

Co-Investigators:
A/Prof Snezana Maljevic
Prof Steven Petrou

Epilepsy is a common disorder in which episodes of abnormal electrical activity (seizures) arise within the brain. The first-line treatment of epilepsy is with antiseizure medications, yet many patients experience persistent seizures that are refractory to existing drugs.

Although the molecular targets of many antiseizure medications have been identified, it remains unknown how these drugs modify brain activity to prevent seizures, which limits efforts to develop more effective therapies. One reason for this knowledge gap is a lack of tools at our disposal to probe brain activity at sufficient detail to untangle how antiseizure medications work.

This project will tackle this issue using a technique to image brain activity at very fine-grained detail, known as two-photon calcium imaging, and a model of the brain grown in a dish, known as a brain organoid. This approach will enable us to characterise how antiseizure medications modulate brain activity, and may unlock the potential to develop new treatments that are tailored for specific forms of epilepsy.

▼ MIGRAINE & HEADACHE

An evaluation of the impact of CGRP monoclonal antibodies on the immune system in migraine

Chief Investigator:
Dr Jason Ray,
Monash University

Co-Investigator:
Dr Elspeth Hutton

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.

SUPPORT GROUPS WE CAN SUPPORT

Are you part of a support group for another neurological condition that you would like to share with other sufferers.

Please let us know so that we can publish the details. No one should have to go it alone.
Being with others with the same condition offers a great deal of comfort and support!

2022 Research Grant Awards

▼ MND, ALS & OTHER NEURODEGENERATIVE DISEASES

Mapping nutrient-sensing pathways in the brains of people across the ALS-FTD spectrum of disease

Chief Investigator:
Dr Frederik Steyn,
University of Queensland

Co-Investigators:
A/Prof Shyuan Ngo
A/Prof Rebekah Ahmed
Ms Stephanie Howe
Ms Jeryn Chang

Motor Neurone Disease (MND) is a group of incurable diseases of the brain and spinal cord that robs the individual from using their muscles. Amyotrophic Lateral Sclerosis (ALS) is the most common form of MND and is generally associated with more rapid disease progression. For most patients with ALS, death occurs within 3 to 5 years following the onset of symptoms. Our research focus is to develop a greater understanding of factors that impact the rate of disease progression in patients with ALS, with the aim of developing therapies to help slow disease progression and improve quality of life.

Some patients with ALS experience unexplained changes in appetite. In these patients, weight loss due to loss of appetite is associated with faster disease progression and earlier death. There is evidence to suggest that the hypothalamus (a part of the brain that regulates appetite) might be impacted by disease. Using emerging technologies, we will define the impact of disease on cells within brain samples from people with ALS and uncover how ALS impacts hypothalamic cells across different types of ALS. With support from the Brain Foundation, we are now able to conduct the most comprehensive interrogation of this part of the brain – a world first for ALS research and for research in general. Results will improve understanding on how disease might impact areas of the brain that regulate appetite, and with this, provide key insight into how best we can support people living with ALS.

▼ ELIZABETH PENFOLD SIMPSON PRIZE

Motor cortex plasticity and skill acquisition in endurance trained athletes

Author:
Brodie Hand

It is now well understood that exercise provides numerous benefits to the human brain. Importantly, acute exercise has been shown to modify neuroplasticity (the ability of the brain to adapt). However, it has remained unknown how regular exercise interacts with various plasticity-inducing techniques (i.e., skill training and non-invasive brain stimulation). Furthermore, it was unknown whether the benefits of exercise are confined to the areas of the brain responsible for controlling movement (specific to working muscles). Therefore, the overarching aim of this thesis was to investigate how regular exercise modulates both use-dependent and experimentally induced plasticity.

I first had to optimise the parameters of transcranial magnetic stimulation (TMS) (e.g., stimulation intensity and frequency) to be used for the region of the human cortex dedicated to lower limb muscles. This study successfully identified the optimal methods for activating interneuron circuits that are important for neuroplasticity. These findings were necessary for the subsequent investigation of how regular physical activity (endurance cycling) influences neuroplasticity induced by skill training involving the upper (non-exercised) and lower (exercised) limb muscles. Endurance-trained participants showed enhanced motor cortex plasticity following skill training. Importantly, this effect was not exclusive to muscle groups directly involved in the exercise.

Finally, this thesis aimed to determine if regular endurance training enhanced TMS-induced plasticity following a single exercise session. Endurance-trained participants demonstrated improved neuroplasticity following acute exercise compared with sedentary participants. Together, these studies provide novel evidence showing that regular endurance training promotes both use-dependent and experimentally induced motor cortex plasticity.

Vitamin D in Neuroinflammatory Disorders

RESEARCH TEAM:

Chief Investigator:

Associate Professor Susanna Park, PhD
Brain and Mind Centre, Discipline of Physiology, Faculty of Medicine and Health, University of Sydney, Camperdown

Co-investigators:

Professor Bruce Taylor
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Professor Rebecca Mason
Discipline of Physiology, University of Sydney, Camperdown

Professor Con Yiannikas
Royal North Shore Hospital, St Leonards

Associate Professor Vasant Hirani
School of Life and Environmental Sciences, University of Sydney, Camperdown

Research

Vitamin D is important in modulating the immune system – and reduced vitamin D levels are linked to autoimmune conditions such as multiple sclerosis (MS) and type 1 diabetes. Vitamin D is also known as 'vitamin sunlight' and production of vitamin D requires sun exposure - so sunlight exposure and the distance from the equator known as latitude are important in determining vitamin D levels. Accordingly, the prevalence of autoimmune conditions are also associated with latitude. This means that in Australia, MS is seven times more common in Tasmania (higher latitude) than in Queensland (lower latitude). Importantly, in patients with MS, vitamin D levels are also associated with disease activity and disability, suggesting that they may provide markers of disease burden.

However these factors have never been investigated in patients with immune-mediated peripheral neuropathies, related autoimmune disorders which affect the peripheral nervous system – leading to progressive difficulties with walking and sensation. These disorders [called chronic inflammatory demyelinating polyneuropathy (CIDP) and multifocal motor neuropathy (MMN)] are costly in terms of healthcare costs and burden on patients. The most common treatment for immune-mediated neuropathies is the human blood product intravenous immunoglobulin, which accounts for 50% of Australian Government spending on blood products – more than $579 million per year in 2018. Our project aimed to examine the links between vitamin D and latitude in autoimmune neuropathies, in order to better understand the risk factors underlying their development and the need to develop better markers of disease activity to direct appropriate treatment.

Outcome

To determine rates of immune-mediated peripheral neuropathies at different latitudes– we identified all patients with CIDP and MMN in North Queensland (Townsville and Cairns regions – lower latitude) and compared to Tasmania (higher latitude). We used multiple methods to identify patients including survey of neurologists, search of hospital databases and search of statewide data collections.
We identified that there was no difference across regions by latitude (CIDP TAS: 4.7 per 100,000; Nth QLD: 5.3 per 100,000 population). However there was a trend towards a younger age of disease onset in Tasmania at higher latitude. The prevalence of MMN was high compared to international cohorts in both regions (TAS: 1.2 per 100,000; North QLD: 1.5 per 100,000 population). In addition, we measured vitamin D levels in a cohort of immune-mediated neuropathy patients to compare with their functional ability. While the relationship between disability and vitamin D is complex, we found that vitamin D levels were significantly associated with overall disability status in CIDP patients with reduced functional status. This project has underscored the need for national registry of immune-mediated neuropathies to be established in order to facilitate future research to ensure appropriate treatment of patients and to identify markers of disease activity.

Healthy brain

How does the brain work?

In our last BRAINwaves newsletter we covered the basics of how the brain works. We explained how neurons work and the difference between white and grey matter. If you didn't catch the last issue, you can find everything on our website at www.brainfoundation.org.au/healthy-brain/.

This time, we're getting into more detail about the different parts of the brain and what they do. There are three main parts of the brain: the cerebrum, the cerebellum, and the brainstem.

Learning about the function of these regions in the brain can help you understand how the brain works together as a whole, and will hopefully demystify some of the scientific jargon you might see in medical articles.

Cerebrum

The cerebrum is the largest part of the brain and it performs higher levels of thinking and action. This includes speech, judgement, emotions, learning, reasoning, and interpreting touch, vision & hearing. It is made up of four lobes which each perform a different job.

The frontal lobe: This is at the front and top of the brain. It is responsible for tasks that are essential in higher level thinking and behaviour, such as planning, judgement, decision making, impulse control, and attention.

The parietal lobe: The parietal lobe is behind the frontal lobe. It takes in sensory information (including pain and temperature) and spatial information, which help you understand your position in your environment.

The temporal lobe: This is at the lower front of the brain. It is important for visual memory, emotion, and language.

T**he occipital lobe:** This lobe is at the back of the brain, and it processes visual input from the eyes.

Cerebellum

The cerebellum might look small, but it actually contains as many as 80% of all neurons in the brain! It is located under the cerebrum, and is responsible for coordinating muscle movements, maintaining posture, and balance.

These are complex functions involving special sensors that detect shifts in balance and movement. These sensors (alongside other parts of the brain) help you do everything from standing upright to learning complex motor skills like riding a bike.

New studies are also exploring the cerebellum's role in thought, emotions, and social behaviour. This might reveal some involvement in psychiatric and neurological disorders.

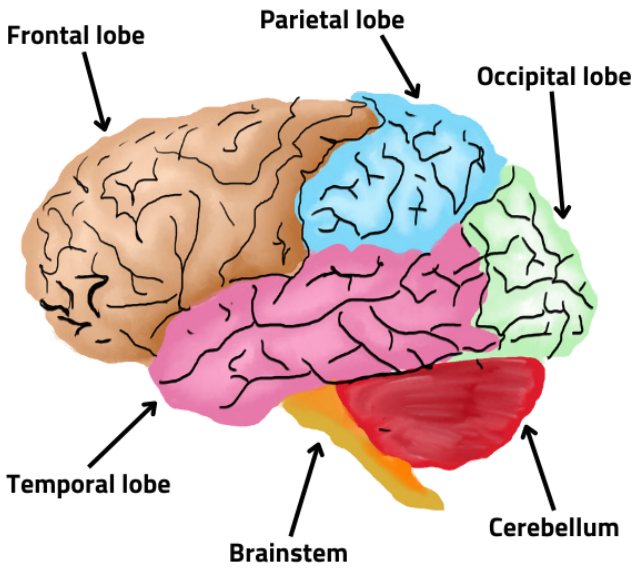
Brainstem

The brainstem is at the bottom of the brain and connects the cerebrum & cerebellum to the spinal cord. It controls many vital automatic functions, such as breathing, circulation, and sleeping. It is composed of:

The midbrain: This is a complex part of the brainstem, and it facilitates many functions. Some of these include hearing, movement, and calculating responses to changes in your environment.

The pons: The pons is the origin of four cranial nerves. It is responsible for many facial movements and functions, such as chewing, blinking, focusing your eyes, tear production, and facial expressions.

The medulla: This is where the brain meets the spinal cord. The medulla is critical for survival, as it regulates your heart rhythm and breathing. It also controls reflex activities such as coughing or sneezing.



Parts of the brain & brain disease

Now that we've explained how these parts of the brain work, we can start to think about how brain diseases, disorders, and injuries can affect them.

Some brain diseases can occur in any part of the brain, such as stroke. Other conditions only affect a specific region, which is reflected in the symptoms. And in other cases, it might be more complex. For example, dystonia is not a single disease but a syndrome - a set of symptoms that cannot be attributed to a single cause but share common elements.

As a general guideline, these are some of the symptoms you might expect to see depending on what brain region is affected. Keep in mind that this is a very simple overview - brain diseases can affect people differently or develop in unexpected ways.

Cerebrum: Huge variety of symptoms, particularly depending on what lobe is affected. Could include motor impairments, problem solving and judgement issues, behavioural changes, and difficulty with speech

Cerebellum: Lack of muscle control and coordination (ataxia), walking & mobility issues, slurred speech, abnormal eye movements

Brainstem: Coma, difficulty breathing, difficulty swallowing, sleep problems, apathy, trouble regulating blood pressure

In our next issue, we'll be covering some of the deeper structures in the brain such as the hippocampus, plus the role of neurotransmitters.

Healthy Brain Games

Sudoku

MEDIUM

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

HARD

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

Solutions are on the back page.

Remembering Tracey Gibbs

We are deeply sad to announce that Tracey Gibb, the ambassador of the Australian Register of Disorders of Consciousness, passed away earlier this year. She had been Locked-in from a rare stroke caused by a tumour on her brainstem since the age of 19. Thirty years of her life spent unable to move a muscle apart from a small movement of her chin and blinking one eye.

Tracey was a disability activist. She gave lectures at conferences, raised awareness about disability at schools and workplaces, and worked for Maven, part of Scope Global which delivers inclusive international education, training and skills development. Tracey won the International Day of People Living with Disabilities Award, and the Stroke Foundation's Courage Award.

She was an inspiration. She was courageous, strong, kind-hearted, patient, generous, feisty and funny. Her Facebook page lists her likes as 'music, cooking, dancing, socialising, chocolate, horror movies and drinking JB'!

Tracey was immensely proud of playing a part in the first International LiS Webinar which was held on 13th June 2022. The LiS Webinar will now be a regular annual event. Her legacy of good work lives on. She will be remembered with love and affection and will be greatly missed.

IN MEMORIAM

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

Ernest (Ernie) Jackson

Carol Clare

Anna Chiu Lan Fung

Tracey Gibbs

Melissa Leaudais

Scan the QR code to donate towards brain research today, or visit brainfoundation.org.au/donation

What can you do to fundraise?

Well, there is no one answer to that question. With the help of fundraising platforms **My Cause**, **Go Fundraise** and even **Facebook**, you can do just about anything you like.

These sites can direct you to a community event such as a fun run or a swim. You could also hold your own fundraising event, such as a trivia night. You can speak to our office to get a trivia pack and any information you want to give to friends. If you're using Facebook, you can make a fundraiser through a news feed post at any time - simply select 'Raise Money' then search for Brain Foundation in the list of charities.

If you use any of the platforms mentioned above, all donations and receipts are taken care of for you. Easy!

THANK YOU FOR YOUR SUPPORT IN 2022!

MERRY CHRISTMAS AND BEST WISHES FOR THE NEW YEAR.

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.

Healthy Brain Solutions

Sudoku Medium

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

Sudoku Hard

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