brainWAVES

The Newsletter of the Brain Foundation

Summer 2021/22

The stories inside these pages are guaranteed to fill you with gratitude and hope as we showcase the awardees of our Research Grants for 2021. To read about our talented and dedicated researchers who are working hard to find better treatments and cures for a broad range of brain disorders, diseases and injuries will simply make you feel proud, knowing our Australian researchers are leading the way in so many fields.

The entire team here at the Brain Foundation and its division, Migraine & Headache Australia, are absolutely thrilled that our medical research grants, which were cancelled last year because of Covid, have been reinstated.

If you donated or helped raise funds in any way over the past 12 months for the Brain Foundation or its division; Migraine & Headache Australia, these are the researchers who are putting your dollars hard to work, finding better treatments and cures.

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

OVER **$9,000,000** HAS BEEN GIFTED TO OVER **470 RESEARCH PROJECTS** IN THE LAST **50 YEARS**

OVER **50 YEARS** OF RESEARCH

• MAKING A DIFFERENCE SINCE 1970 •

$5,000,000 IN **GRANTS GIVEN** FROM 2010 TO 2019 WE CAN'T WAIT TO SEE WHAT THE COMING DECADES HAVE IN STORE

Migraine & Headache Awareness Week 2021

Migraine & Headache Awareness Week 20-24 September

Every year we host Migraine & Headache Awareness Week to support people living with migraine or headache disorders. From September 20-24, we invited people to participate in webinars featuring Australia's leading headache specialists and a patient panel. The event doubled in size from last year with over 4,700 people joining us for the presentations.

"Our goal is to support Australians living with migraine or other headache disorders," says Carl Cincinnato, the host of Migraine & Headache Awareness Week. "These disorders can take a heavy toll on the individual without the right support or information. This annual event brings together patients and carers with leading Australian neurologists and specialists in the field to help find answers that can help them turn the corner."

Learning about new treatments and management strategies empowers people to take control of this disease, helping with challenges such as:

- **Ineffective treatments.** 50% of participants said that they had tried three or more treatments that didn't work.
- **Stigma.** Friends, family or colleagues often don't realise how serious migraine can be - it's more than 'just a headache'
- **Feeling trapped or isolated.** A migraine or headache attack can disrupt plans at any time, making it hard for people to live life freely.

These are just a few things that people might experience, but the reality is that migraine and many other headache disorders are different for each individual. We hope that everyone who attended found the information helpful. 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.

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

New drug approved for spinal muscular atrophy

A new drug has been subsidised on the PBS for spinal muscular atrophy (SMA), which could be life changing for children with SMA and their families. SMA is a rare genetic nerve disorder affecting movement. Not all types of SMA are life-threatening, but sadly, it is still the leading genetic cause of death for infants.

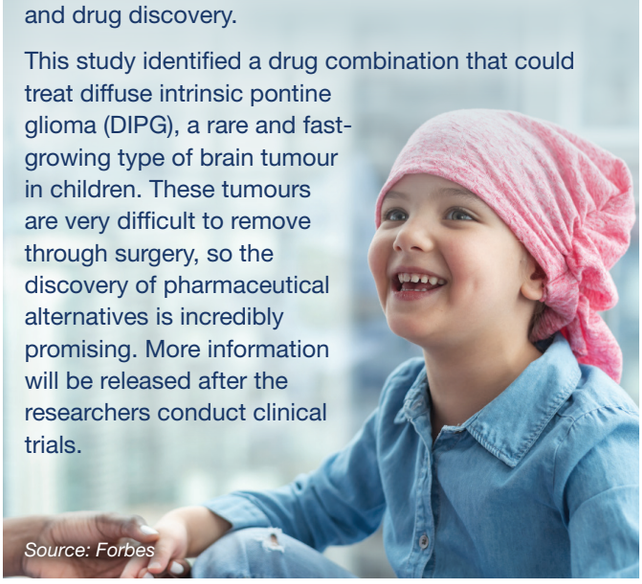
The new drug, EVRYSDI (risdiplam), helps people produce a protein which is critical for maintaining healthy motor neurons. There is already a similar injectable treatment available (nusinersen), but EVRYSDI can be taken at home. While there is no cure, both of these drugs have revolutionised SMA treatment and helped patients reach previously unattainable movement milestones. We look forward to seeing what future research will bring.

Source: BioPharmaDispatch

Scientists use AI to improve treatments for childhood brain cancer

Artificial intelligence (AI) has been used to create a drug regime for children with an aggressive form of brain cancer, which hasn't seen survival rates improve for over 50 years. It's an exciting breakthrough, which could lead to future uses for AI in cancer treatment and drug discovery.

This study identified a drug combination that could treat diffuse intrinsic pontine glioma (DIPG), a rare and fast-growing type of brain tumour in children. These tumours are very difficult to remove through surgery, so the discovery of pharmaceutical alternatives is incredibly promising. More information will be released after the researchers conduct clinical trials.



Source: Forbes

AI algorithm developed to improve brain stimulation devices

The Mayo Clinic and Google have been working on an algorithm to improve deep brain stimulation (DBS) treatments. DBS devices emit electrical impulses into targeted areas of the brain to regulate abnormal brain activity. For example, they are used to ease motor symptoms and tremors in Parkinson's disease.

However, mapping brain network interactions is a complex task, so the researchers used AI to interpret electrical impulses and responses in the brain. This created 'profile curves' of brain activity, which can be applied to improve the efficacy of DBS devices. An algorithm like this will help identify which parts of the brain need to be stimulated to address symptoms. It's an exciting technology that can improve the treatment of epilepsy, movement disorders and psychiatric illnesses.

Source: Parkinson's News Today

Eye conditions linked to dementia

New research has found that certain eye conditions increase a person's risk of developing dementia. Previously, there was a correlation between eye conditions and dementia - but these are also associated with other commonly accepted risk factors like high blood pressure, heart disease, and stroke.

The research revealed an independent link between eye disease and dementia. People with age-related macular degeneration had a 26% increased risk of developing dementia, followed by cataracts (11%) and diabetes-related eye disease (61%). Glaucoma was not linked to increased risk. Understanding the risk factors for dementia will help researchers develop diagnostic tests and preventive measures in the future.

Source: The Guardian

Fundraisers

The Veronicas

What is PSP?

Progressive Supranuclear Palsy is a brain disorder that causes problems with movement, walking, balance and eye movement. It is similar to Parkinson's Disease, but symptoms progress more rapidly. Currently, there is no cure for PSP. You can read more at brainfoundation.org.au/disorders/

The Veronicas on Celebrity Apprentice

Thank you to Lisa and Jess, aka 'The Veronicas', for choosing to support us on Celebrity Apprentice earlier this year. Despite the challenges faced throughout the show, Lisa and Jess have been outspoken about what really matters - supporting people who are affected by brain diseases, disorders, and injuries. Their mother has Progressive Supranuclear Palsy (PSP), a rare brain disorder. The money raised will help so many by funding medical research across Australia.

Books for Betty

Danielle has created a reading challenge to raise money in memory of her grandmother, Betty, who passed away from complications caused by PSP in 2017. Reading was something they both loved, and days at the local library were a major bonding experience for them. But as her PSP symptoms progressed, Betty gradually stopped reading physical books. This challenge is Danielle's way of honouring her grandmother's memory and supporting research into the condition that took her life. Congratulations on your fundraising so far and good luck with your reading.

Bridge to Brisbane

Congratulations to Steve and Amelia, who completed the Bridge to Brisbane run in November. After hundreds of kilometres of training (270km to be exact!), they said "it's exciting to work towards more than just a time goal or a personal best". Like many others, their life has been affected by brain injury after Steve's mother had encephalitis. She now lives with the lifelong impacts of that injury. Thank you both for your hard work and support - we hope that further research can help to prevent and treat these conditions.

Steve & Amelia during one of their training sessions

Shaw House Fun Run

For the past nine years, Shaw House at Caulfield Grammar School has been walking in support of the Brain Foundation. Victoria's lockdown prevented a "traditional" fun run, but that didn't stop them from finding another way to support a cause close to their hearts. On Saturday 18th September, students and their families donned their runners for a run/walk with loved ones – within their 5km radius. Despite being physically apart, their fundraising efforts are a testament to the closeness of their community. They have raised almost $23,000 over the past nine years, and a further $3,000 this year. Thank you for your support!

Caulfield Grammar's fun-runners

Tamworth Christmas Fair

After a difficult 2020, we are so excited to welcome back the Tamworth Christmas Fair! On November 21st, shoppers flocked to the Tamworth Racecourse to enjoy music, food, and local products. We are so thankful to the organisers who have been supporting us for many years through this wonderful regional event. If you missed it, you can follow their Facebook page to stay in the loop for next year's date. facebook.com/BFTCF/

The proceeds from the Tamworth Fair will fund Susanna Park's research into nerve damage after chemotherapy (p.11)

Migraine & Headache Australia Updates

Migraine & Headache Awareness Week 2021

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

- Self-Care & Trigger Management - Dr Bronwyn Jenkins
- New Preventive Treatments - Dr Richard Stark
- COVID-19, Vaccinations & Headache: Symptoms, Interactions & Other Concerns - Professor Tissa Wijeratne
- Patient Panel – Living With A Headache Disorder - hosted by Stephanie Dalzell (ABC Health Reporter), joined by Gabriella Kelly-Davies, Sarah Orwell and Sarah Allely
- Atmospheric Pressure & Headache: The Highs & Lows - Dr Michael Eller

Speakers from top left: Dr Bronwyn Jenkins, Dr Richard Stark, Professor Tissa Wijeratne, Stephanie Dalzell, and Dr Michael Eller.

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

Event feedback from participants

"I wish I had discovered Migraine and Headache Australia 20 years ago. It had never even occurred to me, living in a remote area, that there might be doctors who specialise in headaches! Found the webinar series very informative."

- Anonymous

"Loved the experts, they were very helpful. But the thing I got the most out of was the patient panel. So helpful hearing their ideas of what helps and also just not feeling so alone."

- Aimee

"These sessions are truly invaluable for migraine sufferers like myself."

- Nova

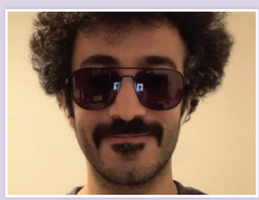
Shades for Migraine Winners

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 so much to everyone who posted a photo, and congratulations to our winners!

We chose three creative entries (one each from Facebook, Instagram, and Twitter) to win a Muse 2 brain sensing headband bundle. These headbands have sensors that provide real-time feedback on your mind, heart, breath and body activity, to help improve meditation.

If you didn't get a chance to participate this time round, we'll be providing more opportunities to raise awareness in the future - hopefully with exciting prizes up for grabs again.





Our winning entries: Karen's whippets are looking stylish in their sunnies, Maria shows us that 'road trips and triptans go hand in hand', and Faraidoon spread the word with his straight-talking self portrait. Well done everyone!

Government Funding for Migraine Education

In last year's summer newsletter, we announced that the government had included migraine education in the 2020-21 budget. We are excited to confirm that we are receiving $300,000 of this funding, which will go towards educating health practitioners and patients. This will make a huge difference in our ability to raise awareness for migraine, and is a significant commitment from the government to support the migraine community.

However, this funding is specifically for education, and education would not be possible without research. If you find our resources valuable, please consider donating so that we can continue to fund further research into this complex disease.

New Treatment Updates:

Ajovy added to the PBS

It has been a huge year for people living with chronic migraine, with two calcitonin gene-related peptide antibodies (CGRPs) being added to the PBS. CGRPs are the newest class of preventive migraine medication, developed specifically for migraine. Studies have found that they are generally more effective and have fewer side effects than older treatments borrowed from other conditions.

Ajovy™ (Teva Pharmaceuticals) was added to the PBS on the 1st of August, shortly after Emgality® (Eli Lilly Australia) was added in June. This will allow people to access potentially life-changing medications for a fraction of the cost.

The criteria to access these medications at PBS pricing is as follows:

- Diagnosed with chronic migraine (15 headache days per month, for more than 3 months)
- Three other medications have failed/not worked
- You need a new prescription from a neurologist

If you aren't eligible under the PBS criteria, you can also ask your doctor about accessing Ajovy™ privately through the Momentum program.

Dehydration & Headache:

A Common Trigger Explained

If you experience frequent headache or migraine attacks, you have probably started to notice that you have a few 'triggers'. This could be a lack of sleep, stress, or dietary changes - including dehydration. Thankfully, some of these triggers can be avoided, which can help you manage your headache disorder.

Some key points about dehydration and headache:

- Dehydration is a trigger for 17% of people with migraine.
- 8 in 10 Australians don't drink enough water (the recommended daily intake is 2.6L for men, and 2.1L for women).
- You can be dehydrated even when you don't feel thirsty.
- You can prevent dehydration by tracking your water intake and making sure you drink water while exercising or working outside.
- Dehydration is more than just not drinking enough water – you lose essential minerals (electrolytes), which is why electrolyte solutions are used to rehydrate quickly.

If you think that dehydration plays a role in your headache, you can read the full article on our website at headacheaustralia.org.au/dehydration-headache/

We would like to thank our major sponsor, Hydralyte, for their support during Migraine & Headache Awareness Week.

New CGRP approval

Vypeti is another CGRP monoclonal antibody that uses a different method of administration. It is administered intravenously (IV) once every three months or four times per year. Vyepti was approved in late June of this year, and hopefully we will hear more about it's PBS recommendation status in the future. Currently, it is available privately. You can ask your doctor about an access program.

You can find more information on all CGRPs via the New Treatment Updates page on our website.

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

2021 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 events of 2020 were an unprecedented challenge, and for the first time ever we weren't able to fund research grants. Thankfully, the world is slowly returning to normal, and we are pleased to announce our research grants re-opened in 2021.

The applications we received were a fantastic insight into the talent, dedication, and curiosity of Australian researchers. We would like to thank the members of our Scientific Committee for volunteering their time and expertise to assess these applications. It's certainly not an easy task, with over 150 applications this year.

The effects of the pandemic are still lingering - we are still working to bring our funding back to regular levels as well, so that we can give out more grants each year. Despite these obstacles, the recipients of our 2021 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 & OTHER NEURODEGENERATIVE DISEASES

Understanding why some people develop delirium after surgery

Chief Investigator:
A/Prof Hannah Keage,
University of
South Australia

Co-Investigators:
Dr Daniel Davis
Dr Daniel Feuerriegel
A/Prof Marta Garrido

Delirium is a medical emergency, associated with increased hospitalisation, institutionalisation, mortality, cognitive decline, and dementia in older adults. Delirium is characterised by acute and fluctuating impairments in cognition and arousal. It can occur at any age but is most common in late-life. Delirium affects at least one in four older adults in hospital.

With thanks to the Brain Foundation, we will run a study that aims to identify patterns of neural activity associated with risk for delirium in older adults. Brain activity will be collected pre-surgery, and will be used to differentiate those who develop delirium after a surgery from those who do not. We aim to determine these patterns for each delirium subtype.

Findings will fundamentally transform our understanding of the neurobiology of delirium. Results can also be taken forward to develop a delirium risk prediction tool, enabling better prognosis, the targeting of interventions, and the improvement of clinical care. Delirium is preventable in a third of cases with multicomponent interventions, but we need a way to index risk prospectively.

It has been estimated that 11% of dementia cases in Australia are attributable to delirium. The total costs of delirium are enormous: AUD$8.8 billion in Australia in the 2016/2017 financial year. It is often a very distressing condition for patients, families, and their clinical teams. The social, economic, and personal impacts of delirium are huge, yet research efforts have been relatively modest and disproportionate to these impacts. We hope to start to address these gaps.

▼ CONCUSSION & TRAUMATIC BRAIN INJURY

Detecting concussion in the brain

Chief Investigator:
Dr Remika Mito,
The Florey Institute

Co-Investigators:
Dr Mangor Pedersen
Prof. Graeme Jackson

Imagine being a clinician and trying to treat a brain disorder without being able to see the site and extent of actual brain damage. This is essentially the current situation with concussion.

Sports-related concussion is a growing public health concern in Australia and overseas. The detection and management of concussion is very important, as mismanagement can lead to persistent or long-term problems. On a standard brain scan (magnetic resonance imaging or MRI), there are no visible abnormalities that can be detected after a concussion. Recently, a specialised type of brain imaging tool, known as diffusion MRI, has been shown to detect subtle changes in the brain's white matter (the brain's connections or 'wires') following a concussion.

Our research group has developed world-leading diffusion MRI technologies, which are able to detect very specific changes to the brain's wiring. We have promising new findings that show subtle but distinctive changes in the brain following a sports-related concussion, using these advanced technologies. However, for these technologies to be useful in clinical practice, they must be able to detect the signs of concussion in an individual.

The major expected outcome of this project is a tool that can detect concussion in patients. This tool should also be able to track brain changes over time, and be associated with clinical symptomatology, returning to normal as the person recovers. Having such a device could hugely improve the short-term management of concussion, and could help to predict individual outcomes.

▼ EPILEPSY

Modelling cortical dysplasia in epilepsy patients

Chief Investigator:
Dr Hannah Leeson,
University of Queensland

Co-Investigator:
A/Prof Lata Vadlamudi

One of the most common causes of epilepsy is cortical dysplasia, where the outer layers of the brain are malformed during development. Cortical dysplasia epilepsies are often resistant to drug treatments and are hugely detrimental to the quality of life in both adults and infants. The exact causes of cortical dysplasia remain an enigma, and neurologists can struggle to find the best treatment options. An accurate and clinically relevant model for cortical dysplasias is desperately needed. The answer lies with stem cells, which can be generated from a sample of the patient's blood and used in the lab to make 3D brain organoids, or mini-brains. These mini-brains contain the same genetic make-up as the patient they are derived from, and mimic brain development in the dish.

Dr Leeson will generate patient-specific stem cell-derived mini-brains and measure electrical signals to investigate to what extent this model can reflect the abnormal brain structures and seizure activity of cortical dysplasia patients. For each patient, the lab data will be directly compared with detailed clinical observations, including brain imaging and drug response profiles. This will reveal the translational relevance of this model and provide unprecedented new insights into the cellular and molecular processes that underlie cortical dysplasia epilepsy. Establishing a patient-specific model for cortical dysplasias will allow testing of drug treatments, revolutionising the frontiers of personalised medicine and assisting neurologists to make informed and personalised decisions regarding anti-seizure drug selection for epilepsy patients and drastically improving patient outcomes.

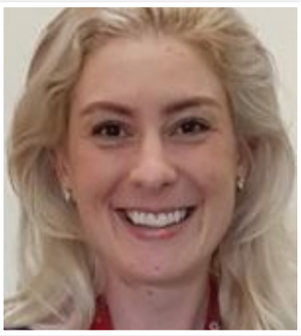
WHAT IS CONCUSSION?

Concussion is a mild brain injury caused by some kind of trauma to the head. Contrary to popular belief, you don't need to lose consciousness to have a concussion. Even a mild concussion can be dangerous if it is not properly treated, and it is important to seek medical attention whenever a concussion is suspected.

2021 Research Grant Awards

▼ MIGRAINE & HEADACHE

Headache in Australia – epidemiological study



Chief Investigator:
Dr Emma Foster,
Monash University

Co-Investigators:
A/Prof Alessandro Zagami
Dr Elspeth Hutton
Dr Zhibin Chen
A/Prof Zanfina Ademi

Migraine and medication overuse headache (MOH) are the second leading cause of years lived with disability worldwide. Unfortunately, robust Australian migraine and MOH data are completely lacking. These are desperately needed to determine the actual extent of what is likely a major Australian public health issue.

Our research team includes senior headache neurologists Professor Alessandro Zagami (inaugural President of the Australia and New Zealand Headache Society), Dr Elspeth Hutton (Head of Alfred Health Headache Unit, VIC), and Dr Emma Foster; medical psychologist and consumer advocate Professor Claire Wakefield; senior biostatistician Dr Zhibin Chen; senior health economist and epidemiologist Associate Professor Zanfina Ademi; and senior research coordinator Ms Christine Cormack.

The 2021 Brain Foundation Research Award will support a survey of 19,445 Australian households to assess the magnitude, impact, and current gaps in treatment and healthcare services for people living with migraine and MOH. This is the most significant assessment of migraine and MOH in Australia to date, and will help close the largest knowledge gap in Australian headache medicine.

The outcomes from this research are critical for informing guidelines regarding diagnosis, directing future healthcare priorities, incentivising investment in new therapies, improving equitable access to existing and new treatments, and shaping healthcare pathways that will bring impactful change to individuals, their families, and our communities.

The researchers sincerely thank the Brain Foundation for their support.

▼ MND, ALS & OTHER NEURODEGENERATIVE DISEASES

A novel approach to improving delay to diagnosis in ALS

Chief Investigator:
Dr Emma Devenney,
Brain and Mind Centre

Co-Investigators:
Dr Jashelle Caga
Dr Sicong Tu

We now know that MND can extend beyond impairments in the motor system to involve changes in the systems responsible for thinking (cognition) which can impact how people respond to everyday life events and social interactions (behaviour). These systems may become dysfunctional early in MND and can occur before the onset of physical symptoms. Therefore, they are important targets for the development of markers of early disease.

As yet however this has not been translated to clinically useful markers. This is in part due to the constraints of traditional cognitive and behavioural measures that were initially developed for FTD rather than MND, which are often insensitive to subtle changes, show population variability and are confounded by reporter reliability. These motor, cognitive and behavioural systems work together to help us complete complex tasks. Although these domains have been studied extensively in isolation the synergistic impact of their decline is unknown despite mounting evidence of MND as a disorder of integrated cognitive, behavioural and motor dysfunction.

With all of these issues in mind, this project will develop objective tests, using neurophysiological methods and advanced statistical modelling, to accurately identify and define the emergence of cognitive and behavioural dysfunction in MND. This project will also identify the earliest brain changes that can cause these symptoms. This project will address the critical need to improve the diagnostic process in MND and develop markers to track progression and therapeutic effect that will improve timely access to support and care and appropriate access to pharmaceutical therapies.

Does a familial gene variant drive neurodegeneration in multiple sclerosis?

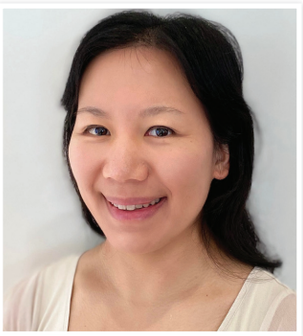
Chief Investigator:
Dr Jessica Fletcher,
University of Tasmania

Co-Investigators:
A/Prof Kaylene Young
Dr Jac Charlesworth

Multiple Sclerosis (MS) is a complex disease, involving the immune system and brain, with no clear cause and no known cure. It typically results in fatigue, weakness, and difficulty in walking –symptoms which start early in adulthood as MS is most frequently diagnosed when people are in their 20 to 40s, starting their careers and raising young families. Numerous factors, including a person's environment, lifestyle and genetics, influence whether they will develop MS. However, many genetic risk factors identified have no clear biological role in MS. Our team has studied a family with an unusually high incidence of MS within first-degree relatives, meaning that the genetic factors outweigh the environmental and lifestyle risks that contribute to developing MS. Using this approach, we have identified that a gene called NLRX1 is changed in the family members with MS but not any of their unaffected relatives.

Our project will look at the consequences of this change in NLRX1 using cells from the family members with MS, that we can grow in the lab and transform into different kinds of brain cells. We will determine if the MS-family version of NLRX1 causes brain cells to act differently than they usually would, and if this is likely to contribute to the symptoms of MS. We expect that from this project we will identify new ways we can prevent brain cell dysfunction and ultimately use these treatments to prevent the symptoms of MS from developing.

Advanced MRI to monitor disease activity in multiple sclerosis patients after suspending therapy



Chief Investigator:
Dr Vivien Li,
Royal Melbourne Hospital,
Victoria

Co-Investigator:
Dr Scott Kolbe
A/Prof Elaine Lui

Multiple sclerosis (MS) is an autoimmune disorder producing inflammation in the brain and spinal cord. MS usually begins with a relapsing-remitting phase, with flare-ups of symptoms or 'relapses' followed by recovery. Many treatments are available that reduce the chances of relapse, but each has possible risks. Patients might need to stop or switch treatments for reasons including side effects, pregnancy or if transitioning to progressive MS, where few treatments have proven to be effective. Furthermore, recent research found patients on certain therapies do not develop a protective immune response following COVID-19 vaccination, meaning they and their doctors could decide to pause therapy to be vaccinated. Balancing potential risks of more relapses or worsening disease without treatment versus problems of continuing therapy can be difficult. This research will study how inflammation in the brain is affected by stopping or pausing treatment using new MRI technologies.

Patients will have brain scans using a 7-Tesla MRI which has over twice the magnetic strength as scanners available in hospitals, providing better images and more information about disease activity. This will be compared to routine hospital scans to see if smaller and subtler changes of MS activity can be identified, potentially giving clinicians and patients more information to make treatment decisions. Also, in patients with stable symptoms and free of relapses for many years, a powerful scanner can detect very low levels of inflammation not seen on regular MRIs to help distinguish between people who could safely stop treatment versus those still requiring immunotherapy.

WHAT DOES NOVEL MEAN?

Novel is used to describe something new or original. It is a fresh idea which has not been previously reported, to the knowledge of the investigators.

WHAT IS MULTIPLE SCLEROSIS (MS)?

MS is a chronic neurological condition that causes attacks to the central nervous system. It is a lifelong condition, but it is not terminal. MS is the most common acquired chronic neurological disease affecting young adults.

2021 Research Grant Awards

▼ NEUROMUSCULAR DISEASES

Newborn screening as an intervention for spinal muscular atrophy: the long-term outcomes of the Australian pilot program

Chief Investigator:
Dr Didu Sanduni Kariyawasam, University of New South Wales

Co-Investigators:
A/Prof Michelle Farrar
Dr Arlene D'Silva
Prof. Veronica Wiley

Spinal muscular atrophy (SMA) affects thirty newborns in Australia annually. Known as a progressive peripheral nerve disease, it causes irreversible muscle weakness and wasting. In its severest and most common form, untreated SMA is life-limiting. The therapeutic landscape for SMA is being transformed by disease modifying treatments. In clinical trials, these agents show greatest utility when given prior to disease onset. Subsequently, there is an urgency to diagnose children before symptoms develop. Newborn screening (NBS) for SMA provides a framework for early identification of affected children.

Whilst prior studies concentrated on the screening methodologies, clinical processes and short-term outcomes of NBS for SMA programs, long-term outcomes for screen positive infants and families are unknown. Furthermore, the efficacy of early diagnosis and management in children outside clinical trials remains uncertain, making real-world data imperative to understand health outcomes for individuals who fall outside the inclusion criteria of these trials. As NBS for SMA coupled with disease modifying agents shifts SMA presentations into milder forms, it is essential to understand new health burdens incurred by affected individuals and their caregivers.

An NBS for SMA pilot commenced in NSW/ACT in 2018. This study compares long-term outcomes from two cohorts (pre and post NBS) across the rapidly changing diagnostic and therapeutic landscape, enabling us to assess whether a drive towards a precision medicine approach through NBS for SMA is clinically impactful. The results of this study will contribute to the decision-making criteria for routine national adoption of NBS for SMA, forming an integral part of the submission to effect policy change.

Measuring nerve damage after chemotherapy treatment

Chief Investigator:
A/Prof Susanna Park, University of Sydney

Co-Investigators:
Dr Hannah Timmins
Ms Tiffany Li

Significant advances in cancer diagnosis and treatment mean that there are now an estimated 32 million cancer survivors worldwide, with > 1 million in Australia. Chemotherapy-induced nerve damage or peripheral neuropathy (CIPN) is a major side effect of cancer treatment, leading to early cessation of treatment and long-lasting disability. Despite successful treatment, up to 40% of cancer survivors may be left with long-term disability and reduced quality of life due to CIPN following treatment with neurotoxic chemotherapies. Patients with CIPN have significant functional disability, pain, loss of sensation and increased falls risk, significantly contributing to the health burden of cancer survival. Despite this high burden, there remain no methods to identify which patients are at-risk, no objective assessment tools and no treatment or preventative approaches to stop long-lasting toxicity. Critically there remains a lack of mechanistic understanding of how chemotherapy produces nerve damage. Multiple mechanisms are involved but the final common pathway is a type of nerve damage termed axonal degeneration. Developing sensitive markers of axonal degeneration will provide early identification of patients with CIPN as well as highlighting key mechanisms. This project will measure the trajectory of nerve degeneration in patients with CIPN through innovative methods of assessing nerve dysfunction, including specialised nerve testing methods and analysis of protein markers of axon degeneration in blood. Ultimately, this will enable development of neuroprotective strategies to prevent nerve damage following chemotherapy. Further, this information will be valuable towards understanding how to measure and monitor progression of axonal degeneration across multiple disorders.

DID YOU KNOW?

When you move a muscle, the messages travel from upper motor neurons in your brain to the lower motor neurons leading to your body parts. A typical muscle is powered by anywhere between 50 and 200 (or more) lower motor neurons!

▼ OTHER (SYRINGOMYELIA)

Spinal fluid circulation in the abnormal spinal cord

Chief Investigator:
Dr Shinuo Liu,
Macquarie Neurosurgery

Co-Investigators:
Dr Sarah Hemley
Prof. Marcus Stoodley
Prof. Lynne Bilston

The brain and spinal cord are bathed in a liquid called cerebrospinal fluid (CSF). CSF has many vital roles, one of which is to help maintain a constant biochemical environment for precise function of brain and spinal cord cells. Central to this, is its ability to flow into and out of the central nervous system. Although many advances in this field have been made by our group and others, there is still only a rudimentary understanding of how CSF circulates and enters the spinal cord.

Conditions like spinal cord injury and syringomyelia are related to abnormalities in CSF flow. In syringomyelia, there is an abnormal collection of fluid within the spinal cord that damages the nerve fibres, leading to pain, paralysis, and sometimes, death. It is the endpoint of various conditions such as abnormal displacement of brain into the spine and spinal cord injuries. Treatment of syringomyelia is often unsatisfactory, due to an incomplete understanding of how it forms.

This project will examine CSF flow in syringomyelia models in rodents to further our understanding of how fluid abnormally collects in the spinal cord. In this study, we will employ world first imaging techniques recently developed by our laboratory that allow assessment of fluid flow in the live animal. “Glow-in-the-dark” fluorescent tracers will be injected into the CSF spaces, and their redistribution into the spinal cord will be studied. We will employ a previously validated model of syringomyelia, as well as a new model where abnormal traction is placed on the spinal cord.

Updates from our researchers

You’ve seen the exciting projects that we are funding in our 2021 grants, but what about past research? In the following section we are highlighting the research of previous grant recipients, Dr Michelle Farrar (Neuromuscular Disease - 2018) and Dr Claire Shepherd (Neuro-trauma - 2019).

Dr Farrar established a biobank of tissue samples from children with peripheral nerve disorders, such as spinal muscular atrophy (SMA). This kind of research infrastructure is a rich scientific resource which supports research into all stages of a disease, from diagnosis to potential treatments.

Dr Shepherd’s work is focused on the consequences of repetitive brain injuries (such as concussion), and how this could lead to a progressive neurodegenerative disorder called chronic traumatic encephalopathy (CTE). Concussion and CTE have been in the media frequently in recent years, but there’s still a lot we don’t know. This research will help identify the links between head injuries and future disease, which will be important for people who play contact sports and many other people.

More research reports will be included in future issues of Brainwaves to keep you up to date on the latest research.

BRAIN ANEURYSM SUPPORT AUSTRALIA

This site is for all who are survivors, sufferers, know someone suffering, or supporting someone with an Aneurysm, to share their story and support.

facebook.com/basa.com.au/

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!

Establishing an Australian paediatric peripheral neuropathy biobank

RESEARCH TEAM:

Chief Investigator:

Associate Professor Michelle Farrar

Paediatric Neurologist, Sydney Children's Hospital Randwick. School of Women's and Children's Health, University of New South Wales

Co-investigator:

Dr Arlene D'Silva (pictured below)

Post-Doctoral Research Fellow, Sydney Children's Hospital Randwick. School of Women's and Children's Health, University of New South Wales

Research

Spinal muscular atrophy (SMA) is a rare genetic disease characterized by progressive loss of motor neurons in the brain stem and the spinal cord. This condition affects a child's ability to crawl, walk, sit up, and control head movements. Severe SMA can damage the muscles used for breathing and swallowing. With an occurrence of 1:10,000 newborns, SMA is the number one genetic cause of death for infants. The therapeutic landscape for SMA transformed since the therapy, nusinersen in 2018. Nusinersen resulted in improvements in survival, reduction in morbidity and achievement of functional motor skills across the spectrum in treated patients. There is sufficient data to highlight the importance of early diagnosis and initiation of treatment with the most beneficial response to treatment to date, in these disorders, seen in patients treated prior to the commencement of symptoms.

The nusinersen clinical trials in SMA have established that not all patients have the same response to therapy. The current dose of nusinersen is standard across all patients at 12mg/5 mls. It is not understood how long therapy is required for and lifelong therapy may be essential for some children. Parents of children with SMA are interested in understanding how well the children will respond to treatment, and if having higher dosing improves the response to treatment. Furthermore, we are interested in understanding how the disease develops over time. Our study hopes to answer these questions by using laboratory-based experiments to test for specific proteins and genetic signatures in biological specimens obtained from the children with SMA.

For us to achieve the above, it is imperative to establish specific research infrastructures to ensure collection and management of high-quality specimens and data. We therefore performed a study to address these issues by establishing an Australian biobank for children with SMA. The main aim is to use these biological specimens to gain information about the disease pathway and answer the questions regarding response to treatment and dosage. This information will enable us to improve our understanding and knowledge of SMA and guide clinicians to eventually improve the outcomes for children with SMA.

Outcome

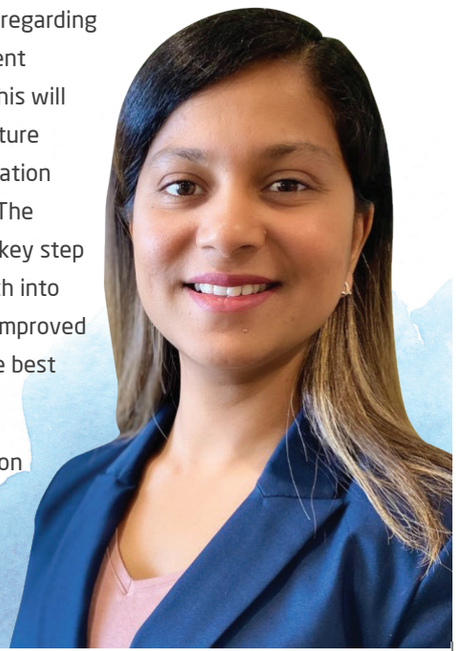
The Brain Foundation Research Grant has greatly enabled us to establish a biobank of 300 biological samples from patients affected with SMA at Sydney Children's Hospital, Randwick in a period of 12 months. These specimens (cerebrospinal fluids and serum) were analysed to complete proof of concept studies utilising high throughput protein and gene sequencing technologies.

Preliminary findings identified a panel of biomarkers involved in various molecular and biological processes of SMA. These are involved in protease binding, lyase activity, cysteine-type endopeptidase inhibitor activity, neutrophil degranulation and amyloid fiber formation. Some of these protein species have been previously identified in other research as possible biomarkers for neuropathies, including amyotrophic lateral sclerosis.

Using gene technologies, we identified genetic signatures as a response to nusinersen treatment and the potential of these miRNAs to monitor disease progression and response to therapeutic intervention. With new SMA therapeutics on the horizon, our findings indicate the potential clinical application of these genetic signatures as promising non-invasive biomarkers for this disease.

We will promote ongoing collection of biological data and utilise banked samples to carry out molecular work to expand scientific knowledge regarding pathophysiology and treatment responses. Taken together, this will provide a rich resource for future studies and enhance collaboration for SMA research nationally. The present project represents a key step essential to translate research into clinical practice and to drive improved clinical outcomes and achieve best care for children with SMA.

We thank the Brain foundation for the generous support of our research.



Understanding the impact of head injury on brain health

RESEARCH TEAM:

Chief Investigator:

Dr Claire Shepherd

Sydney Brain Bank Director,
Neuroscience Research Australia

Co-investigator:

Associate Professor Andrew Gardner

The Hunter Medical Research Institute

Research

There is considerable scientific and community interest in the consequences of repetitive traumatic brain injury (TBI) and global public concern that even mild head injury may lead to a progressive neurodegenerative disorder known as chronic traumatic encephalopathy (CTE) in later life.

CTE can only be recognised by microscopic examination of brain tissue after death and is characterised by the abnormal accumulation of a protein known as tau that deposits in irregular patterns in the brain of some individuals. Current research suggests that these tau changes arise following head injury and can spread to other brain regions in a progressive manner, akin to neurodegenerative disorders like Alzheimer's disease.

However, our understanding of the clinical consequences of CTE is still in its infancy. We do not yet understand how much pathology is required to cause clinical disease and if these changes are progressive.

CTE has been commonly reported in individuals who participate in contact sports such as American football, where up to 87% of players were found to have this neuropathology at post-mortem. Research also suggests that CTE is more common in individuals who suffer from neurodegenerative disorders where falling is common, such as Parkinson's disease and Progressive Supranuclear Palsy, although the strength of this finding has not been tested.

Outcome

The generosity of the Brain Foundation has facilitated this research project investigating CTE in a large number of well-characterised cases collected through the Sydney Brain Bank. Brain donors are recruited through longitudinal, prospective brain donor programs with an interest in ageing and neurodegeneration. Donors participate in on-going health and lifestyle assessments during life so we are uniquely placed to examine the relationship between CTE pathology and clinical outcome. A large number of our cases also have a history of head injury (over 130 cases) or frequent falls (177), which will allow us to assess the relationship between these factors and CTE.

Over 2800 tissue sections have been cut and stained from 633 cases for the purpose of this project. We have assessed the presence and severity of CTE using the most recently published (2021) research diagnostic criteria and are now in the process of analysing the data.

This work represents one of the largest studies of CTE pathology in a clinically, well-characterised brain bank population. It will allow us to directly test the reliability and reproducibility of the most recently published clinical and pathological research diagnostic criteria and will determine the relationship between CTE, head injury and clinical disease. This work is of significant concern to the public as well as to athletes participating in contact sports.

Everything you need to know about brain donation

MORE THAN 1 IN 10 AUSTRALIANS ARE REGISTERED ORGAN DONORS, BUT DID YOU KNOW YOU CAN **DONATE** YOUR **BRAIN** FOR **RESEARCH**?

Brain donation programs are an essential part of research, but they face a number of complex challenges. They have often struggled to secure funding, and not many people know that they exist. We spoke to Associate Professor Greg Sutherland and Ali Sweeney from the NSW Brain Tissue Resource Centre (NSW BTRC) to explain everything you need to know about brain donation.

What is brain donation?

Brain donation is when a person and their family decide to donate their brain for medical research after their death. It's a fundamental part of advancing our understanding of diseases affecting the brain.

The brain is a notoriously complex organ, and studying tissue allows researchers to:

- Confirm a suspected diagnosis, and use this information to improve existing diagnostic criteria.
- Investigate things that don't show up in imaging technology like magnetic resonance imaging (MRIs).
- Compare brain tissue between people with and without neurological diseases to determine why only some people get diseases like dementia and stroke

It goes without saying that brain donation and organ donation are very different. Registering as a brain donor is also an ongoing process, rather than the one-time sign up for organ donation.

How do you become a brain donor?

Many brain banks are associated with clinicians or specific diseases. Once someone receives a diagnosis (i.e. of frontotemporal dementia), their doctor might speak to them about becoming a brain donor. However, the process is different for brain banks who collect healthy brain tissue, or 'control' tissue.

The NSW BTRC recruits donors through the 'Using Our Brains' program. People register their interest online and complete an eligibility questionnaire, and if they are eligible, they will be sent a consent package. This involves some paperwork for the person and their next of kin, providing information such as:

- General medical history
- Mental health
- Lifestyle - exercise, alcohol/tobacco consumption, diet, if they live alone or with others, etc.
- End of life plan (organised with next of kin)

This information is updated annually through a survey.

> *"I describe it as a long-term relationship - there's a lot of communication between us and the donors."*

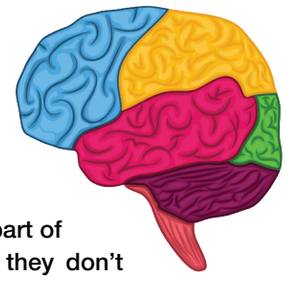
Ali Sweeney, Donor Relationship Manager for the 'Using Our Brains' program.

But why do they need so much information?

A/Prof Sutherland explains it succinctly: "Brain tissue is most important if you know a lot about what happened to that person before they died. The brain doesn't exist without a body, and a body doesn't exist without a unique genetic make-up and lifetime full of experiences."

Studying the brain alone, without a detailed life history, can leave a lot of questions unanswered, because researchers normally don't have access to the rest of the person's body. This is also why brain donation programs can rarely accept donations at the end of someone's life.

Why is brain banking important?



Brain banks are an important part of research infrastructure. While they don't always do the research themselves, they are an important part of allowing research to be done.

Brain tissue is still an unparalleled resource for so many conditions, despite advances in imaging technologies. Researchers are able to investigate diseases at macroscopic, microscopic, and molecular levels, presenting diverse opportunities for research. On top of this, many diseases are just so uniquely human, so animal models aren't as effective as they are in other fields.

This is particularly true in dementia research. Brain tissue has been pivotal for research into Alzheimer's disease, recently helping scientists identify new targets for treatment. With over one million Australians expected to have dementia by 2056, it's undeniable that we need to continue supporting this research.

A/Prof Sutherland also sees an opportunity for this to evolve into a wider system of biobanking. A broader 'brain and body biolibrary' could support medical researchers in all disciplines, and eventually become a collaborative international resource. Brains don't exist without bodies, and we are just at the start of understanding how neurological and peripheral diseases share common mechanisms.

> *"That's my grand design for the type of stuff we could be doing: different tissue goes out to different things, and we're always working on these synergies, known and unknown."*

Associate Professor Greg Sutherland, Director of the NSW BTRC

You can read the full article about brain banking on our website at:
brainfoundation.org.au/everything-you-need-to-know-about-brain-donation/

Healthy Brain Games

Word scramble

Solving word scrambles and anagrams are great skills to practice to keep your memory sharp. Once you've found all the correct words, use the highlighted letters to answer the question at the end.

Hint: we've underlined the first letter of each word for you

ULANNERO

MIPDONAE

RYEG TAREMT

NOGXEY

REDOAICNTO

NILENARG

BRECRELA

MCAO

What part of the brain controls your 'fight or flight' response?

_____

Sudoku

MEDIUM

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

Solutions are on the back page.

Get Involved

Companies giving back

We would like to thank the AMP Foundation for their generous donation to the Brain Foundation. An employee initially contacted us to make an individual donation, but we were excited to hear that the company was matching the donation.

If you are thinking about making a donation to the Brain Foundation, why not consider asking your employer if they can match your donation? There are many ways to donate through your workplace. They could match your one-off donation, but you can also support us through a workplace giving program. This means that your donation is taken out of your pay cheque and you receive the tax benefit straight away, rather than waiting until the end of the financial year. It's a win-win for you, your employer, and the researchers we fund. Ask your employer if you have a workplace giving program (such as **Good2Give**), and please contact our office if you have any further questions.

IN MEMORIAM

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

Ian Dunstall	Krystal Alexander
Aleksander Varga	Leanne Giddings
Peter Gordon Bennett	Peter Lister

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

Thank you to our sponsors

We would like to thank the Griffith Hack team, who have provided us with pro bono legal work. Their advice and assistance to help us protect our trade marks has been indispensable over the past year.

GRIFFITH HACK

abbvie Lundbeck Hydralyte Lilly teva

Migraine & Headache Awareness Week was proudly supported by Hydralyte, Lundbeck, Teva Pharmaceuticals, Lilly, Abbvie and the Brain Foundation this year. It was a fantastic event, and with the help of our sponsors we were able to reach more people than ever before. Thank you!

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 to all our amazing fundraisers for your hard work!

Healthy Brain Solutions

Word scramble

Neuronal
Dopamine
Grey matter
Oxygen
Co-ordinate
Learning
Cerebral
Coma
Amygdala

Sudoku

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

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