

Moving Forward

Despite the global pandemic, research is continuing around the world looking at all aspects of MND, from the underlying biology of the disease through to developing better ways of caring for MND patients. Six years on from the huge injection of funds and resources provided by the Ice Bucket Challenge, we are now seeing significant numbers of new potential therapies entering into the clinical trial pathway.

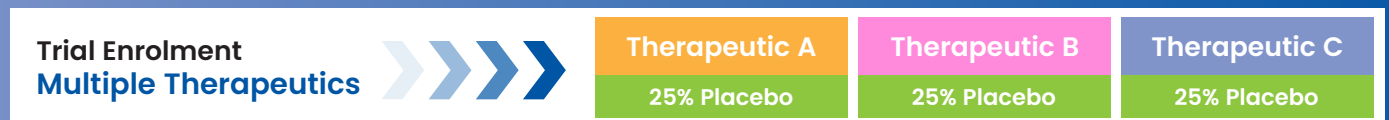
Currently there are over 80 potential new treatments in clinical trial – more than ever before. These treatments range from ground-breaking new approaches at the Phase 1 stage to more developed treatments in Phase 2 and Phase 3. In just the last few months we have heard about a positive Phase 2 results for AMX0035, a combination of Tauroursodeoxycholic Acid (TUDCA) and Sodium Phenylbutyrate (PB). A phase 3 antisense gene therapy trial targeting SOD1 (Tofersen) is currently underway following positive Phase 2 results. Other antisense treatments targeting C9ORF72 and FUS have also entered Phase 1 trials and will be closely watched. Phase 3 trials for Tofersen and NurOwn (a stem cell therapy) are due to complete this year, and we are very much hoping to see some positive outcomes in 2021 from these studies (although the initial data from the NurOwn trial is not encouraging unfortunately). The IAMALS ALS Signal Dashboard is a fantastic resource to keep abreast of the trials currently underway – <https://iamals.org/get-help/als-signal-clinical-research-dashboard>

A big advance in MND clinical trials has been the adoption of “Platform Trials”. Originally developed in the cancer field, this approach allows multiple treatments to be trialled in parallel using the same infrastructure. A number of advantages are achieved through such an approach including: testing multiple treatments simultaneously; use of ‘shared’ control groups; the ability to expand to incorporate promising new treatments as they become available, even while the trial is underway; and use of broader inclusion criteria. Such an approach greatly speeds up the trial process as well as reducing the numbers of patients in placebo arms. Platform trials are currently running in the US, Europe and the UK.

Traditional Clinical Trial Model



Platform Trial Model



An aligned protocol allows for a shared placebo group and facilitates the addition of new therapeutics as they become available

We also had fantastic news about significant funding for Dr David Berlowitz to undertake a clinical trial to improve the delivery of non-invasive ventilation (NIV) to MND patients. This study is funded with \$3.5M from the Medical Research Future Fund and will look at how customising the delivery of NIV to patients can improve the uptake of this treatment and improve both patient survival and quality-of-life. NIV has already been demonstrated as the most effective method of improving survival in MND and improving accessibility and uptake of this approach will see significant benefits across the MND community. MND Research Australia has funded Dr Berlowitz’s earlier stage research and it is great to see the impact of his work being taken to the next level. Two other projects, which received MNDRA funding in their early stages, have also been in the news recently.

An early feasibility study of the Stentrode brain implant has successfully shown that it can aid people living with paralysis, such as those with MND, to continue to maintain communication. MND Research Australia funded early research into development of this device through the Grant McKenzie MND Research Grant in 2018. The feasibility study saw this paperclip-sized implant inserted into a blood vessel in the brain of two people living with MND. The Stentrode enables signals from the brain to be directly transmitted to a device which allows people to complete tasks such as emails, text messaging and online banking.

Walter and Eliza Hall Institute researchers Associate Professor Seth Masters and Dr Alan Yu have identified an immune pathway that may play a key role in the neuroinflammation seen in MND and present a novel target for developing new treatments. They found that by blocking an immune sensor called STING, they could dramatically prevent inflammation from MND patient cells, paving the way for a new class of drugs to be developed for people with neurodegenerative disorders, such as MND. The research was supported by MND Research Australia via the Superball XI MND Research Grant (Masters) and the Betty Laidlaw MND Research Grant (Peter Crouch who is a co-author).

Executive Director Research Report

Unfortunately, six-months on from the last Advance, we are still wrestling with COVID-19. We have been very fortunate in Australia to avoid the very high case numbers seen in Europe and the Americas but this does not mean it has not had a significant impact.

Lockdowns and business restrictions have significantly impacted incomes and financial resources right across the Australian community and our MND community has not been spared. Australia has experienced its first recession for many years. In addition to our community members experiencing their own hardships, fundraising events have been either cancelled or moved online. Despite this, our fantastic team of fundraisers and donors, through hard work and amazing generosity, have again managed to raise almost \$3M for MND Research.

These funds have supported 26 grants to be awarded for 2021 including the Betty and John Laidlaw MND Research Prize, three postdoctoral fellowships and 14 Innovator Grants. A new initiative for 2021 was the offering of the Linda Rynalski Bridge-funding Grants. Eight of these were awarded to enable researchers to complete their 2020 projects that had been disrupted by COVID-19. Please keep reading for further details of the 2021 grants.

A new team was established for MND Research Australia (MNDRA) during 2019 - 2020. Our team consisting of myself, the Executive Director, Research, Professor David Burke, Chair of the Research Committee, and Laura Birks, Research Coordinator, are now well bedded in and through great teamwork we have managed to adapt well to the challenges 2020 has thrown at us.

Many of you will have seen that we have changed our name from the MND Research Institute of Australia (MNDRIA) to MND Research Australia (MNDRA) which we feel better reflects our role as the National MND Research Organisation and further highlights our symbiotic relationship with MND Australia.

With me being new to the MND research community, one of my early goals was to get to know the Australian and International MND Community. To this end I undertook several visits to MNDRA-funded researchers, in Sydney, Brisbane and Melbourne, as well as attending two prominent International research meetings that took place in Australia in 2019.

One really significant event in Australian MND Research in 2020 was the hosting of the inaugural National MND Research Summit jointly hosted by MND Research Australia and Fight MND. This took place over two days in a virtual format and was facilitated with the help of the PWC Impact Assembly team. For the summit we brought together people with lived experience of MND, medical and allied health practitioners, researchers, care providers, pharmaceutical industry representatives and funding bodies. The critical aims were to ensure people with lived MND experience are at the heart of our research decision making and that we work together across the whole community to ensure we get the best possible outcomes. A more comprehensive report is included later in this bulletin.

On a much sadder note we unfortunately also said goodbye to David Healey. Since developing MND, Dave made significant contributions to MND research through his attendance as a patient fellow at the Perth Symposium and also as a member of the MND Australia Research Development Committee. Vale Dave.

Dr Gethin Thomas, Executive Director Research, MND Australia

**MND Research Australia's
Dr Gethin Thomas and
Laura Birks meeting with
members of the Research
Committee at the annual
Grants Allocation Meeting**

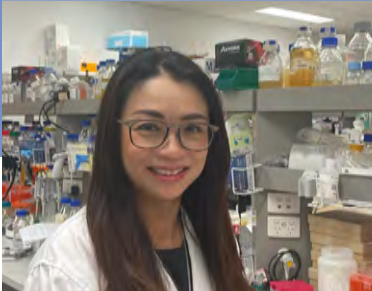


MND Research Australia Grants in 2021

Despite the considerable impact of COVID-19, our supporters have made incredible efforts to ensure MNDRA can continue to fund top quality MND research.

MNDRA has continued to build Australian MND research capacity with the 2021 grant funding round bringing MNDRA's contribution to over \$40M since the first grant was awarded in 1987.

For 2021, MNDRA allocated almost \$3M across 26 projects, made up of the Betty and John Laidlaw MND Research Prize, three postdoctoral fellowships, 14 Innovator Grants and 8 Bridge-funding grants.



In memory of both Betty and John Laidlaw who passed away in the last 12 months, we awarded the **Betty and John Laidlaw MND Research Prize**. This \$200,000 2-year grant was awarded to Associate Professor Yazi Ke from Macquarie University for her project "Novel therapeutic strategies targeting TDP-43 in Motor Neuron Disease". This project will examine how a new protein that their group has discovered may contribute to the role of TDP-43 in MND.



The **Bill Gole MND Postdoctoral Fellowship for 2021 – 2023** has been awarded to Dr Thomas Shaw at the University of Queensland. His project is titled "Ultra-High Field MRI of Spinal Cord Tissue in Motor Neurone Diseases" and will look at how they can use MRI to differentiate between different forms of MND and provide insights into the mechanisms accounting for the irreversible progression of MND.



The **Beryl Bayley MND Postdoctoral Fellowship for 2021 – 2023** has been awarded to Dr Emily McCann based at Macquarie University. Her project is titled "Investigating the role of complex genomic variation in MND" and will use advanced genomics approaches to identify previously unknown genetic changes underlying MND and provide clues to how MND develops and progresses.



An additional fellowship was able to be offered this year. Supported from the estate of Marisa Aguis who passed away from MND, this award will support Dr Nicholas Geraghty from the University of Wollongong. The 3-year **Marisa Aguis MND Postdoctoral Fellowship** is titled "High-throughput flow cytometry drug screen to discover new treatments for MND". He will use a cell model in which TDP-43 forms toxic aggregates, similar to those seen in diseased neurons, in a high-throughput drug screen of thousands of chemicals to find potential drugs to treat MND patients.



For 2021, the top-ranked Innovator Grant was awarded the **Charcot Research Grant funded by the NTI MND Research Grant**. This award went to Dr Shyuan Ngo at the University of Queensland. Her project is titled "MND in space and time: deciphering the spatio-temporal landscape of cell-autonomous and non-cell-autonomous drivers of motor neuron death in MND". This project will use cutting-edge genomics and stem cell technology to identify gene activity changes in 3-dimensions within organoids grown from human stem cells.

Innovator Grants for 2021

A further 13 Innovator Grants were also awarded, ranging from ascertaining which basic biological processes are disrupted in MND through to the use of novel imaging approaches to measure disease, identifying and investigating new genetic changes and development of biosensors and using artificial intelligence to improve the effectiveness of non-invasive ventilation.

Judy Mitchell MND Research Grant

Dr Victor Anggono, University of Queensland

Molecular mechanisms underlying the cytoplasmic aggregation of the RNA binding protein, SFPQ, in ALS

Mavis Gallienne and Graham Lang MND Victoria Research Grant

Prof David Berlowitz, University of Melbourne

REPAIR MND: REduced PATient – ventilator asynchrony with Artificial Intelligence assisted Respiration in MND

Peter Stearne Familial MND Research Grant

Prof Ian Blair, Macquarie University

Genome-wide detection of short tandem repeats that are expanded in ALS

Robert Turnbull MND Research Grant

Dr Christopher Bye, The Florey Institute of Neuroscience and Mental Health

Next generation pre-clinical modelling for MND

Jack and Joan Thompson MND Research Grant

Dr Mouna Haidar, The Florey Institute of Neuroscience and Mental Health

Will reducing abnormal cortical activity in MND have a therapeutic effect?

Col Bambrick MND Research Grant

Dr Robert Henderson, University of Queensland

A Novel PET Imaging Marker of Astrocytes and Glutamate Reuptake in Brain and Spinal Cord in Amyotrophic Lateral Sclerosis

Dr Angela Worthington MND Research Grant

Dr Colin Mahoney, University of Sydney

Establishing the role of high definition-density EEG in the diagnosis and monitoring of Motor Neuron Disease

Run MND NSW Research Grant

Prof Pamela McCombe, University of Queensland

Revisiting excitotoxicity in ALS: how does this occur?

Dr Paul Brock MND NSW Research Grant

Dr David McKenzie, University of Sydney

Development of an amperometric biosensor for the detection of TARDNA binding protein 43 (TDP-43) in Motor Neuron Diseases (MND)

Jenny Simko MND Research Grant

Dr Nirma Perera, The Florey Institute of Neuroscience and Mental Health

Autophagy in Neuroglia: a hidden player in abnormal MND proteostasis

MonSTAR MND Research Grant

Dr Frederik Steyn, University of Queensland

N-acetyltransferase 1, a modifier of disease outcome in patients with Motor Neurone Disease (MND)

Superball XIII MND Research Grant

A/Prof Bradley Turner, The Florey Institute of Neuroscience and Mental Health

Defining upper motor neuron markers using translational RNA profiling

Fat Rabbit MND Research Grant

Dr Adam Walker, University of Queensland

Defining the involvement of ubiquitin-2 in MND

MNDRA Linda Rynalski Bridge-funding Grants

A number of research projects we funded in 2020 were disrupted by COVID-19. To ensure the researchers could complete these projects we offered Bridge-Funding Grants for 2021. These were funded by a donation in the name of Linda Rynalski who passed away from MND. With this amazing donation we were able to fund eight Linda Rynalski Bridge-Funding Grants to a total of \$230,000.

Professor Julie Atkin, Macquarie University

Novel mechanisms of neurodegeneration induced by dysfunctional actin dynamics in MND

Dr Richard Gordon, University of Queensland

Targeting inflammasome-driven neuropathology and motor neuron death in MND using a clinically approved cancer drug

Dr Albert Lee, Macquarie University

Clearance of TDP-43 by PROteolysis TArgeting Chimera (PROTAC) dual targeting to treat amyotrophic lateral sclerosis (ALS)

Dr Fiona McKay, University of Sydney

Natural Killer cells in amyotrophic lateral sclerosis

Dr Marco Morsch, Macquarie University

The unexplored posttranslational modification (SUMOylation) of TDP-43 affects aggregate formation and localisation

Dr Mary-Louise Rogers, Flinders University

Urinary Neopterin as a candidate biomarker that can be used to test disease progress in clinical trials for Motor Neurone Disease

Dr Kara Vine, University of Wollongong

Non-invasive drug delivery across the blood brain barrier: Improving the bioavailability of drugs for MND

Dr Trent Woodruff, University of Queensland

Transcriptomic and Functional Evaluation of Immune-Activated Monocytes in MND

Dr Emma Devenney

2017–2019 Beryl Bayley Fellowship Summary

Emma Devenney (front left) with her team at the University of Sydney's Brain and Mind Centre



As well as motor function, we now know that MND can also have an impact on cognitive functioning, behaviour and mental health, collectively known as neuropsychiatric symptoms. As a research community, we are becoming increasingly aware of the effect this can have on relationships, decision-making and quality of life for people living with MND and their family members and carers. In parallel, one of the most important discoveries of the recent decade has been the discovery of the C9orf72 expansion as the most common cause of inherited MND. Our previous research has shown that patients with MND who carry this expansion are more likely to experience neuropsychiatric symptoms. The C9orf72 expansion can be identified in family members prior to the onset of disease and can ensure we are particularly alert for the earliest clinical signs.

With all of this in mind, the Beryl Bayley fellowship has provided me with a fantastic opportunity to make a difference to the care and management of people living with MND.

This fellowship focuses on the clinical aspects of the disease and combines this with cutting edge neuroimaging and physiological techniques to investigate neuropsychiatric features and identify early and pre-symptomatic features in MND patients and C9orf72 carriers. The project is conducted at the Forefront MND and FTD research clinic and group (pictured above) at the University of Sydney Brain and Mind Centre, where a diverse group of experienced researchers have provided support and advice to ensure the successful completion of this project.

To date, I have identified that, in some families, MND, the C9orf72 expansion and neuropsychiatric disorders, including Schizophrenia and Autism Spectrum Disorders, can co-exist. This has implications for genetic counselling and family planning and suggests shared risk factors across conditions. I have also identified specific early characteristics that identify people who may be more vulnerable to these psychiatric symptoms and, with early identification, we can ensure these individuals receive timely and appropriate care. Another project has mapped the brain regions responsible for these symptoms that includes regions in frontal and deep grey matter of the brain (see figure below) to help us understand how these symptoms are generated. This has taught us that a network of regions are responsible for these symptoms and that these regions are similar across many neurodegenerative and neuropsychiatric disorders.

Due to the successful and anticipated outcomes of this fellowship I am now moving towards developing a system for clinicians and patients that incorporates the findings from this project and addresses the unmet needs of overlapping psychiatric and neurodegenerative conditions. This system will allow for early detection of and management of these complex symptoms associated with MND and will continue to develop biomarkers of early disease.



Neuroimaging analysis mapping the brain regions responsible for psychiatric symptoms

The Australian Summit for MND Research: A collective impact approach to tackling MND

Australian National MND Research Summit
Tuesday 17 & Wednesday 18 November



ENGAGE - CHALLENGE - COLLABORATE

Significant increases in research funding over the last 5 years have seen an exciting surge in momentum in the MND research sector. Globally, and particularly within Australia, this influx in funding has drastically changed the research landscape, allowing researchers to undertake clinical research as well as large-scale collaborative projects.

It is essential that our research funds are committed into critical and high impact areas of research that address key questions in MND and are, importantly, patient focused. This ensures every dollar invested has the biggest impact on those living with MND. With the aim to maximise our resources and ensure we are serving the MND Community's needs, MNDRA and FightMND came together to host the inaugural Australian Summit for MND Research. To facilitate and to jointly design and run this virtual event, we engaged the PwC "Impact Assembly" team, a social venture that partners with the NFP sector.

The Summit was designed to 'mobilise a collective approach to research that enables better outcomes for people living with MND'. The aims of this Summit were to:

- Define how the lived experience voice is prominent and plays a leading role at all stages of research and how people living with MND and their loved ones would like to participate in research and other engagement/leadership opportunities
- Ensure research efforts best serve the needs of the MND community
- Plan how we can work together to maximise the impact of our investments effectively and efficiently

To bring about the Summit, a Summit Planning Committee was assembled, bringing together representatives from all key sectors of the MND research community. The first summit meeting was held at the International Symposium in Perth last December. Following strong enthusiasm to take the event forward, a "Discovery Session" was held with 15 members of the Planning Committee with the scope of "Creating the conditions for a successful summit which will be used to co-design an integrated MND research strategy to improve outcomes for people living with MND". Critical inputs came from PLEx (People with Lived Experience), underlining the importance of emphasising the patient voice. Outcomes from the Discovery Session included identification of the key features of an integrated strategy and the core aims and deliverables of the Summit.

For the final planning stages, a dedicated 7-person "Design Team" worked closely with the PwC team. A key input into the Summit was a survey of the MND patient and carers community ascertaining their priorities and insights in research needs.

The Summit took place over 2-days on the 17th and 18th of November in a virtual online format involving over 50 key members of the Australian MND community, including people with lived experience, researchers, clinical and allied health practitioners, funding bodies, as well as representatives from the State Associations and the pharmaceutical industry. We will be bringing you the outcomes from the Summit and the plans moving forward over the coming weeks.

MNDRA Research Committee

We have had a few changes on the MNDRA Research Committee in 2020.

Longstanding members Professor Naomi Wray from the University of Queensland and Professor Dominic Thyagarajan from Monash Health stepped down at the end of 2019. Their contributions identifying the best projects to fund and guiding MNDRA's research agenda have been extremely valuable.

We welcome five new members to the committee: Dr Anne Hogden is a speech therapist and Senior Lecturer at the Australian Institute of Health Service Management, University of Tasmania; Associate Professor Michelle Farrar is a Paediatric Neurologist and Director of the Nerve and Muscle Clinic at the Sydney Children's Hospital, Randwick and holds an academic position at UNSW; Dr Mary-Louise Rogers is a Senior Research Fellow and Head of the Motor Neurone Disease and Neurotrophic Research Laboratory at Flinders University; Dr Allan McRae is an ARC Future Fellow and leads the Systems Genomics theme in the Program in Complex Trait Genomics at the University of Queensland; Associate Professor Rebekah Ahmed is a Staff Specialist Neurologist and Director of the Memory and Cognition Clinic at the Royal Prince Alfred Hospital, Sydney and also holds an academic position at the University of Sydney.

MND Research Australia 'State of Play' research seminars

Throughout November and December, MND Research Australia will be hosting a series of virtual research seminars titled 'State of Play'. If you missed them, each seminar will be available on the MND Australia Facebook page ([Facebook.com/mndaustralia/videos](https://www.facebook.com/mndaustralia/videos)). The seminars cover four topics:

What can mice models and stem-cells teach us about MND?

Tuesday 24 November, 7pm AEDT

Novel Therapies and Healthcare Decision-Making

Tuesday 1 December, 7pm AEDT

How is the progression of MND measured?

Tuesday 8 December, 7pm AEDT

What do brain activity and metabolism have to do with MND?

Tuesday 15 December, 7pm AEDT



The work of MNDRA, the research committee and researchers would not be possible without our donors, supporters and volunteers who enable MNDRA to support world-class high quality MND research. MNDRA is making a significant difference by supporting ground-breaking research and increasing capacity for MND research in Australia. Many new therapies currently in clinical trial have been supported by MNDRA during their vital early development stages. As always, every dollar of each donation goes to research as we strive for the goal of a World Without MND!

MND Research Australia relies on the generous support of donors to maintain its important MND research grants program. Please fill in the form below or visit mndresearch.org.au

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I would like to make a donation to MND Research Australia of:

- \$20 \$100 \$200
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For information on becoming a monthly donor please visit; mndresearch.org.au/donate

Return this form in the reply paid envelope provided or:

- Donate online at www.mndaustralia.org.au/donate-research
- Call us on 02 8287 4989
- Post to: MND Research Australia
PO Box 117, Deakin West, ACT 2600

Governance

MND Australia is the principal member of MND Research Australia. The governance and operations of both organisations are the responsibility of MND Australia.

Directors

The board of MND Australia consists of an independent elected President and a nominated representative from each member MND Association board, the chair of the MND Research Australia Research Committee and up to three independent directors.

Research Committee

The MND Research Australia Research Committee reviews research grant applications and determines the distribution of funds within the set policies and criteria for scientific assessment.

Research Committee Members:

- Chair Professor David Burke AC, NSW
- A/Prof Rebekah Ahmed, NSW
- Professor Samar Aoun, WA
- Professor Ian Blair, NSW
- Professor Tracey Dickson, TAS
- A/Prof Michelle Farrar, NSW
- Professor Simon Foote, ACT
- Professor Glenda Halliday, NSW
- Dr Anne Hogden, TAS
- Professor Matthew Kiernan, AM, NSW
- Dr Susan Mathers, VIC
- Professor Pamela McCombe, QLD
- Dr Allan McRae, QLD
- Dr Shyuan Ngo, QLD
- Dr Mary-Louise Rogers, SA
- Professor Dominic Rowe AM, NSW
- Associate Professor Bradley Turner, VIC
- Professor Steve Vucic, NSW

Bequests

Your Will can provide an important way of making a gift that can have lasting influence on MND research and give hope for the future.

If you would like to consider the MND Research Australia in your Will by providing a Bequest from your Estate, please contact your solicitor.

For more details on how your bequest can help MND research

Contact Dr Gethin Thomas, Executive Director Research:

Phone: 02 8287 4989

Email: research@mndaustralia.org.au

Donations

Research funded by the MND Research Australia is dependent on donations. To contribute to this vital work, please send your gift to:

**MND Research Australia
PO Box 117, Deakin West, ACT 2600**

Donations can be made by cheque (payable to MND Research Australia).

Visa or MasterCard donations can be made by phone (02 8287 4989) or online at: www.mndaustralia.org.au/donate-research

All donations of \$2 and over are tax deductible.
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