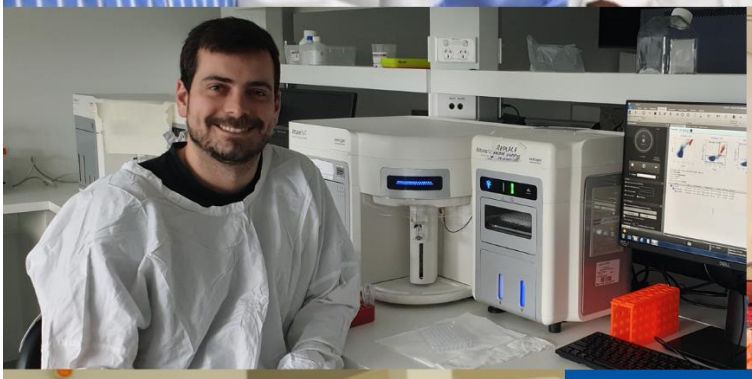

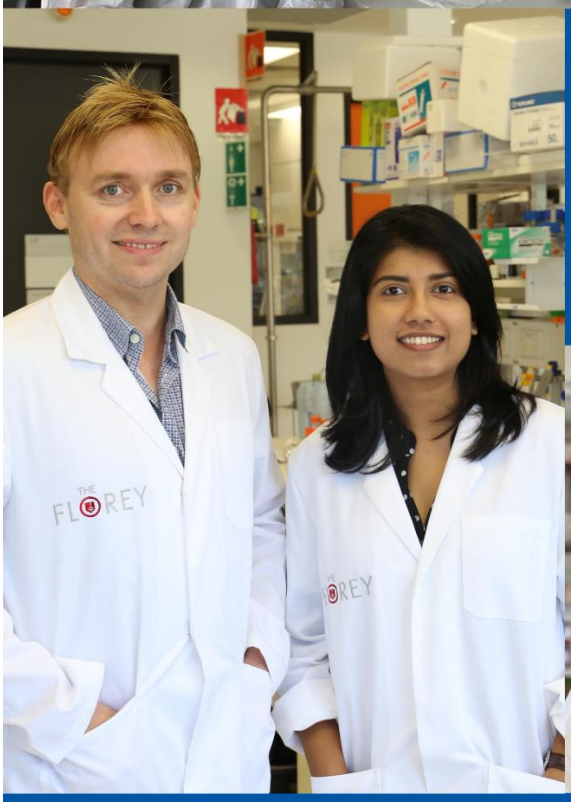

mnd Research Australia

2021 Funded Research

What types of research does MND Research Australia fund?

In 2021, MNDRA awarded five different types of research grants to 26 talented researchers around Australia.

The Betty and John Laidlaw MND Research Prize aims to reward an outstanding *mid-career researcher with a demonstrated background of excellence in neuroscience research. The Prize is a grant of up to $200,000 for an innovative and collaborative two-year project to advance the understanding, treatment and care of classical MND.

The three MND Postdoctoral research Fellowships awarded in 2021 span three-years and aim to encourage young researchers to focus their interest on ALS/MND. Funds of $300,000 are provided to cover the salary of a full time research fellow. Postdoctoral scientists with a track record in areas of neuroscience related to MND and no more than three years postdoctoral research experience were invited to apply.

MNDRA Innovator Grants provide funding for research that is innovative and has a clear relationship to the causes, treatments or cures of MND or the support of people living with MND. Innovator Grants support research for one year commencing in the calendar year 2021, and were awarded to 14 Australian researchers. The prestigious Charcot Prize is awarded to the highest ranked Innovator Grant.

The MNDRA Linda Rynalski Bridge Funding Grants provided additional funding to eight MNDRA funded researchers whose 2020 projects were disrupted by COVID-19. These grants ensured that researchers could see their projects through to completion.

The MNDRA PhD Scholarship Top-up Grants are awarded as an incentive to an outstanding PhD student. The grant provides a $5,000 per annum stipend for a PhD candidate. PhD students who have been awarded a full PhD scholarship for biomedical or public health research in motor neurone disease are encouraged to apply. In 2021, two of these top-up grants were awarded.

mnd Research Australia

MNDRA Betty and John Laidlaw MND Research Prize 2021-2022

BETTY AND JOHN LAIDLAW MND RESEARCH PRIZE 2021	
Lead investigator	Associate Professor Yazi Ke
Institution	Macquarie University
Title	Novel therapeutic strategies targeting TDP-43 in Motor Neuron Disease
Our research team has discovered a new, previously unidentified protein complex that appears to be involved in Motor Neurone Disease (MND). This protein complex contributes to disease processes such as nerve cell death. This proposal has three main aims: firstly, to understand how different components of this protein complex contribute to its function; secondly, to study this protein complex in an established MND mouse model to understand its disease-relevance; and, finally, to harness the knowledge of this protein complex in the development of two highly feasible therapeutic approaches in a pre-clinical setting. This project could identify new therapies for MND.	

The Betty Laidlaw MND Research Prize was first awarded in 2015 and has been funded every year since. Betty Laidlaw lived with primary lateral sclerosis for over 30 before her death in early 2020. Her husband, John Laidlaw, was her primary carer. John died in late 2019, after which time the award was renamed to the Betty and John MND Research Prize, to acknowledge the incredible generosity of both John and Betty, who supported the Betty Laidlaw MND Research Prize from the time of its inception in 2016.

Previous recipients of this award

2020: Dr Shyuan Ngo, University of Queensland

2019: Dr Marco Morsch, Macquarie University

2018: Associate Professor Justin Yerbury, University of Wollongong

2017: Dr Catherine Blizzard, University of Tasmania

2016: Dr Peter Crouch, University of Melbourne

MNDRA Postdoctoral Fellowships 2021-2023

Bill Gole MND Postdoctoral Fellowship (2021 – 2023)	
Lead investigator	Dr Thomas Shaw
Institution	University of Queensland
Title	Ultra-High Field MRI of Spinal Cord Tissue in Motor Neurone Diseases
Characterising differences in MND sub-types including ALS and PLS is important for understanding the disease. This project aims to distinguish these sub-types, which have separate patterns of brain and spine pathology. To achieve this, I will use Magnetic Resonance Imaging to measure tissue properties of brain and spine over time in MND patients, comparing these with clinical outcomes of disease. The project will generate significant outcomes by - for the first time - relating pathology in the brain and spinal cord to MND sub-types over time. This will increase understanding of mechanisms accounting for the irreversible progression of MND.	

Beryl Bayley MND Postdoctoral Fellowship (2021 – 2023)	
Lead investigator	Dr Emily McCann
Institution	Macquarie University
Title	Investigating the role of complex genomic variation in MND
Gene mutations are the only known cause of MND, however almost 90% of patients have an unidentified genetic cause of MND. Little is also known about why the clinical presentation of MND varies substantially between patients. In this project, I will use innovative bioinformatic strategies to search through the genomes of MND patients to find complex genomic changes that play a role in the cause, onset and progression of MND. Once identified, these MND-relevant genomic changes will provide clues to how MND develops and progresses, to help patients and clinicians make informed decisions about treatment and family management strategies.	

Marisa Aguis MND Postdoctoral Fellowship (2021 – 2023)	
Lead investigator	Dr Nicholas Geraghty
Institution	University of Wollongong
Title	High-throughput flow cytometry drug screen to discover new treatments for MND
Motor Neurone Disease (MND) arises due to proteins misfolding inside motor neurone cells, leading to toxicity, cell death and loss of motor function. TDP-43 is an important protein known to misfold, leading to its clumping or “aggregating”, which causes cell death and leads to MND. This project uses a cell model in which TDP-43 forms toxic aggregates, in a high-throughput drug screen of thousands of chemicals to find potential drugs to treat MND patients. A small number of “hits” have already been identified and will be screened in animal models of MND, to identify a therapeutic to treat MND patients.	

MNDRA Innovator Grants 2021

Charcot Award, funded by the NTI MND Research Grant	
Lead investigator	Dr Shyuan Ngo
Institution	University of Queensland
Title	MND in space and time: deciphering the spatio-temporal landscape of cell-autonomous and non-cell-autonomous drivers of motor neuron death in MND
Motor neurons are usually supported by a number of different cells that sustain their function and survival. In MND, it is proposed that these support cells become toxic and contribute to the death of neurons, although we do not know how this occurs. Using mini 3D spinal cords that we have generated from MND patient skin cells, we will study how neurons and their support cells interact over time. This will allow us to generate the first "cell-to-cell communication network maps" that will give us insights into how we can manipulate this communication to save neurons from death.	

Judy Mitchell MND Research Grant	
Lead investigator	Dr Victor Anggono
Institution	University of Queensland
Title	Molecular mechanisms underlying the cytoplasmic aggregation of the RNA binding protein, SFPQ, in ALS
The mislocalisation and aggregation of RNA binding proteins are pathological hallmarks of amyotrophic lateral sclerosis (ALS). However, the molecular mechanisms underlying these aberrant processes are poorly understood. This project aims to define the molecular basis of zinc-induced cytoplasmic aggregation of an ALS-associated RNA binding protein, SFPQ. Using a combination of biochemistry, and structural and cell biology, this project will examine how two human SFPQ variants that are exclusively found in familial ALS subjects affect neuronal functions. The outcomes of this study will provide a novel conceptual framework for understanding the cytoplasmic aggregation of RNA binding proteins in ALS.	

Robert Turnbull MND Research Grant	
Lead investigator	Dr Christopher Bye
Institution	The Florey Institute of Neuroscience and Mental Health
Title	Next generation pre-clinical modelling for MND
Using a small skin sample from a person with MND, we can now grow motor neurons identical to those inside of that person's body. This is an important breakthrough because we can use these motor neurons to find and test drugs to treat MND in that person. In this project, we have developed a new approach to grow these motor neurons inside a "living brain" to more accurately test potential treatments. We aim to show that this "living brain" model can accelerate the selection of drugs for clinical trials for people with MND.	

Mavis Gallienne and Graham Lang MND Victoria Research Grant	
Lead investigator	Professor David Berlowitz
Institution	University of Melbourne
Title	REPAIR MND: REduced PAtient – ventilator asynchrony with Artificial Intelligence assisted Respiration in MND
Non-invasive ventilation (NIV), overnight breathing support with a machine and mask, is the most effective way to increase survival in MND. NIV only works if you use it and our team has shown that careful coordination of the breathing machine to the patient can convert NIV non-users into users. The coordination process is however very labour intensive and therefore challenging to translate into clinical practice. This project will build an Artificial Intelligence-based decision support tool (REPAIR MND) that will increase clinicians' capacity to optimize NIV and usage; 20% more people with better usage is 20% more people surviving longer.	

Peter Stearne Familial MND Research Grant	
Lead investigator	Professor Ian Blair
Institution	Macquarie University
Title	Genome-wide detection of short tandem repeats that are expanded in ALS
DNA mutations are responsible for familial MND and genetic factors contribute about half the risk of developing sporadic MND. However, the genetic causes of MND are unknown in one third of MND families and most genetic risk factors are unknown. Rare expansions of DNA repeat sequences cause many other neurodegenerative diseases. Until recently we had little capacity to screen MND patients for these repeated sequences. Excitingly, this is about to change: drawing on latest technologies and bioinformatics tools, this project will screen Australian MND patients in combination with international datasets to make fresh inroads to solving the genetic basis of MND.	

Jack and Joan Thompson MND Research Grant	
Lead investigator	Dr Mouna Haidar
Institution	The Florey Institute of Neuroscience and Mental Health
Title	Will reducing abnormal cortical activity in MND have a therapeutic effect?
Nerve cells in the motor regions (or motor neurons) of the brain carry signals to the spinal cord which in turn ommunicate with muscles to control movement. These brain motor neurons are overactive early in MND and eventually die, losing their ability to initiate and control muscle movement. We will evaluate a novel genetic approach targeted to brain motor neurons to reduce their overactivity in a mouse model of MND. Our approach uses "chemogenetic technology" to selectively reduce the overactivity of brain motor neurons. This study will encourage future use of our novel approach for the potential treatment of MND.	

Col Bambrick MND Research Grant	
Lead investigator	Dr Robert Henderson
Institution	University of Queensland
Title	A Novel PET Imaging Marker of Astrocytes and Glutamate Reuptake in Brain and Spinal Cord in ALS
Damage to motor nerves through activation ("excitotoxicity") is long-recognised as a potential avenue to target new therapeutics in MND. To date, there has been no reliable method to image excitotoxic injury in vivo. This novel project will test a new PET imaging method to identify key alterations in the main transporter of glutamate, the principal excitatory neurotransmitter, into glial cells in the brain and spinal cord of patients with MND. The ultimate objective is that this method will help to predict progression in individual MND patients and aid in the selection of new therapies for clinical trials.	

Dr Angela Worthington MND Research Grant	
Lead investigator	Dr Colin Mahoney
Institution	University of Sydney
Title	Establishing the role of high definition-density EEG in the diagnosis and monitoring of MND
There continues to be significant challenges in diagnosing and successfully treating those with motor neuron disease. We increasingly recognise that MND is a multi-systems disease, affecting structures beyond the motor systems, often in advance of weakness. It is crucial to develop sensitive tools to detect pathological changes across other brain regions. We will use high-density electroencephalography (EEG), to assess abnormal brain wave changes relating to both cognitive and motor processes, potentially in advance of motor weakness. The detection of early brain changes using this innovative technology may reduce diagnostic delay, and improve precision in prognosis and enrolment in clinical trials.	

Run MND NSW Research Grant	
Lead investigator	Professor Pam McCombe
Institution	University of Queensland
Title	Revisiting excitotoxicity in ALS: how does this occur?
In MND, some of the damage to motor neurones comes about because of over-excitation. This appears to be an early event in disease. This study will examine how this occurs. We have developed novel techniques to measure amino acids that can cause over-excitation and will determine whether these are elevated in the blood of MND patients. In addition, our preliminary studies have discovered a novel molecule that helps reduce over-excitation. We will use genetic techniques to see whether variation on this molecule is associated with the clinical course of MND. This would be evidence of its involvement in MND pathogenesis.	

Dr Paul Brock MND NSW Research Grant	
Lead investigator	Dr David McKenzie
Institution	University of Sydney
Title	Development of an amperometric biosensor for the detection of TARDNA binding protein 43 (TDP-43) in MND
The underlying causes of amyotrophic lateral sclerosis (ALS, a subtype of MND) are not yet completely understood. This complicates timely and accurate diagnosis and the development of new efficient treatments. The hallmark of ALS is a protein named TDP-43 that accumulates in degenerating motor neurons of around 95% of people with ALS. We will develop a biosensor, a device that is able to detect TDP-43 in liquids, to study in future why and how this happens and if it can be reversed. In future, our biosensor can also be modified to detect other molecules relevant for ALS or other MNDs.	

Jenny Simko MND Research Grant	
Lead investigator	Dr Nirma Perera
Institution	The Florey Institute of Neuroscience and Mental Health
Title	Autophagy in Neuroglia: a hidden player in abnormal MND proteostasis
MND is characterised by accumulation of toxic protein deposits in motor neurons and surrounding neuronal supporting glial cells. Autophagy is the only pathway in our cells that can purge large protein deposits. Therapeutic rescue of autophagy to clear culprit protein aggregates may have therapeutic potential. Many studies so far have focused on exploring neuronal autophagy while glia autophagy remain unexplored. Using the powerful combination of an autophagy reporter mouse model, stem cell derived glia and post-mortem tissue, we will analyse autophagy in glia for the first time, providing new insights leading to therapeutic modulation of intricate autophagy pathway in MND.	

MonSTaR MND Research Grant	
Lead investigator	Dr Frederik Steyn
Institution	University of Queensland
Title	Targeting NAT1 to improve metabolism and slow disease progression in MND
Through working with people with ALS we have made new discoveries on a mechanism that could contribute to more rapidly progressing disease, and impairments in metabolism that are associated with rapidly progressing disease. NAT1 is an ancient protein that controls how our mitochondria respond to metabolic stress. We have found that NAT1 is linked to metabolic imbalance and faster disease progression in people with ALS. We will now conduct a world first study to understand how NAT1 modifies the body's response to ALS. This will help reveal how we might target NAT1 to improve outcomes in ALS.	

Superball XIII MND Research Grant	
Lead investigator	Associate Professor Bradley Turner
Institution	The Florey Institute of Neuroscience and Mental Health
Title	Defining upper motor neuron markers using translational RNA profiling
The mechanisms that cause the death of motor neurons in MND are still not completely understood. In this project, we will employ cutting-edge genetic engineering technology in cells to identify genes that control the pathology formed by a key MND-related protein. Importantly, unique inherited mutations in this core pathological protein also cause MND in some Australian/New Zealand families. We will analyse the mechanisms of disease related to this protein, and compare our results to human pathology. Overall, these studies will define, in an unbiased high-throughput manner, the early pathological mechanisms involved in MND.	

Fat Rabbit MND Research Grant	
Lead investigator	Dr Adam Walker
Institution	University of Queensland
Title	Defining the involvement of ubiquilin-2 in MND
The mislocalisation and aggregation of RNA binding proteins are pathological hallmarks of amyotrophic lateral sclerosis (ALS). However, the molecular mechanisms underlying these aberrant processes are poorly understood. This project aims to define the molecular basis of zinc-induced cytoplasmic aggregation of an ALS-associated RNA binding protein, SFPQ. Using a combination of biochemistry, and structural and cell biology, this project will examine how two human SFPQ variants that are exclusively found in familial ALS subjects affect neuronal functions. The outcomes of this study will provide a novel conceptual framework for understanding the cytoplasmic aggregation of RNA binding proteins in ALS.	

MNDRA Linda Rynalski Bridge Funding Grants 2021

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 ALS
Dr Nicole Fewings 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
Associate Professor Mary-Louise Rodgers 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

MNDRA PhD Scholarship Top-Up Grants 2021-2023

MNDRA PhD Scholarship Top-Up Grant 2021-23	
Lead investigator	Natalie Grima
Institution	Macquarie University
Title	Investigating novel genomic and transcriptomic features of sporadic MND
MND is marked by substantial heterogeneity and it is therefore likely that personalised therapeutic strategies will be required. However, for the 90% of patients classified as having sporadic MND, the biological factors affecting development and progression remain largely unresolved. This project aims to identify novel risk and protective factors associated with sporadic MND, providing new targets for diagnosis, research and treatment. It will employ cutting-edge genomic and transcriptomic strategies to an extensive and unique collection of patient samples to look for complex genetic variants and gene expression changes associated with disease onset and/or variable development of the hallmark TDP-43 pathology.	

MNDRA PhD Scholarship Top-Up Grant 2021-23	
Lead investigator	Dr Anna Ridgers
Institution	Austin Health
Title	Virtual Ventilation: An evaluation of the utility of ventilator-recorded data to titrate ventilator settings in comparison to non-invasive ventilation polysomnography
Home ventilation with non-invasive ventilation (NIV) is used to support breathing in respiratory (breathing) failure due to muscle weakness in motor neuron disease. Patients require different ventilator settings to optimally support breathing and improve symptoms and survival. Settings are based on daytime assessment, with subsequent overnight laboratory sleep study and face to face appointments. This is important for successful NIV but can be burdensome for patients and their carers. Newer generations of NIV record information that clinicians can review remotely. This study aims to assess whether remotely recorded ventilator data could be used to optimise ventilator settings without having to rely upon a hospital sleep study, providing the scientific foundation for remote, patient centred models of care.	

MND Research Australia is forever grateful for the support of its donors, for making all of this research possible.

mnd Research Australia