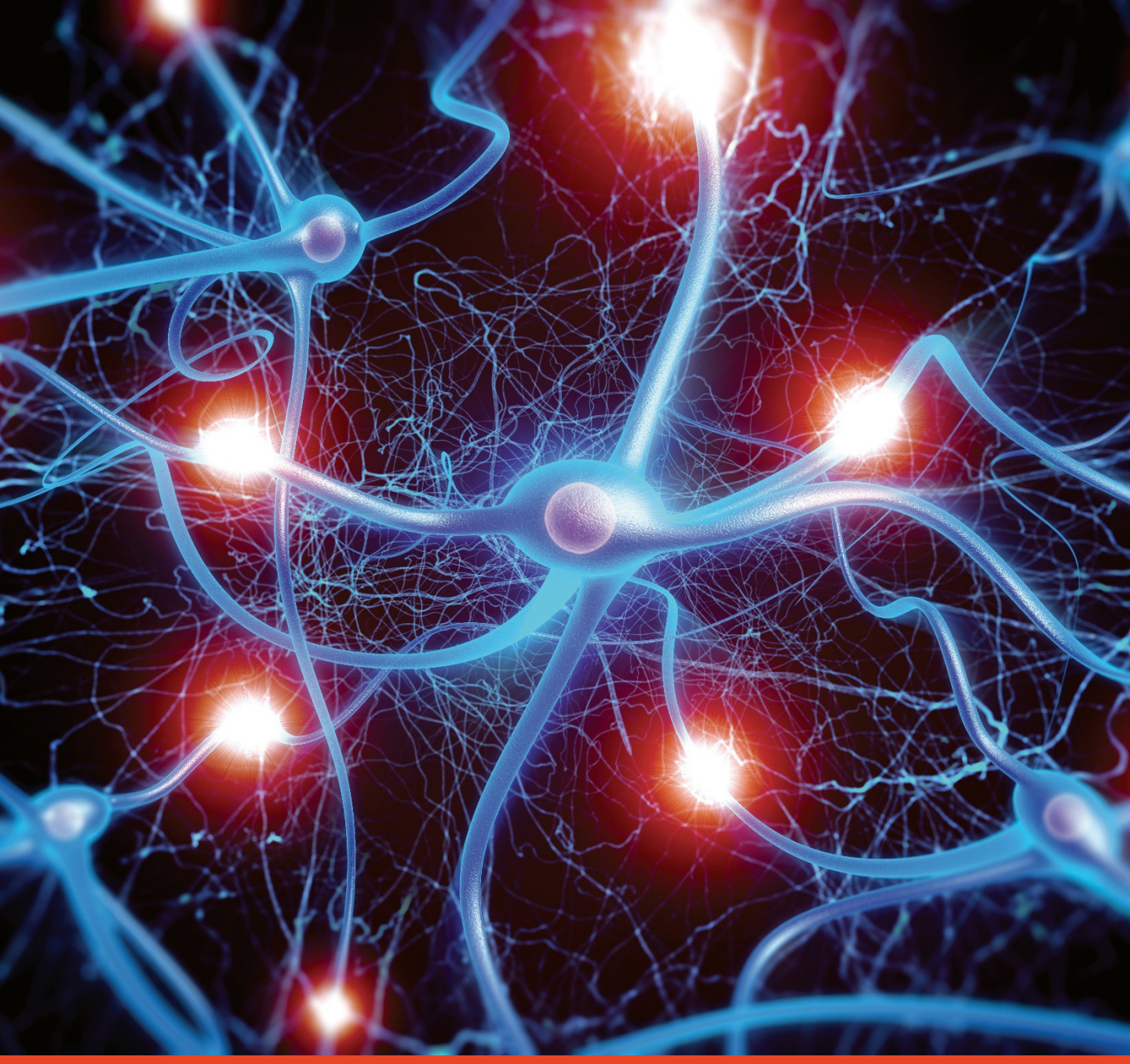

Generating new breakthroughs for treating Motor Neurone Disease

THE UNIVERSITY OF SYDNEY


FACVLTY
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MEDICINE

Contents

Generating new breakthroughs for treating Motor Neurone Disease

Innovative and translational research at the University of Sydney can make a real difference to the lives of Australians impacted by neurological disorders such as Motor Neurone Disease

40% of health-related disability in Australia stems from brain disease

Thousands left disabled by Multiple Sclerosis and Motor Neuron Disease.

$2.37 billion - annual cost to the Australian economy

EACH DAY two patients will pass from MND and a similar amount will be newly diagnosed

400,000+ Australians living with a neurodegenerative illness such as MND, Alzheimer's, Parkinson's and Huntington's

Executive Summary

There are currently approximately 3,000 cases of Motor Neuron Disease (MND) in Australia. The rates of diagnosis for MND and related neurodegenerative disorders continue to rise with little prospect of major treatment breakthroughs.

Neurodegenerative disorders have a devastating impact on individuals, families, and the wider community. They threaten the social and economic participation of hundreds of thousands of Australians and more importantly, cause great suffering. None of these diseases is crueller or more difficult to treat than Motor Neurone Disease (MND).

While the potential for major discoveries and breakthroughs in neuroscience has never been greater, funding remains the major impediment to achieving significant gains in the battle against MND and towards developing effective treatments and ultimately, a cure.

In partnership with community, government and industry, the University of Sydney's Brain and Mind Centre brings together all the University's various disciplines to drive translational research and specialised clinical services that aim to meet this challenge.

Imagine a world in which the most complex health and neurological disorders can be effectively treated or reversed. People will be able to regain their health, independence and contribute towards social and economic outcomes.

This is what Professor Steve Vucic aims to achieve with his work. Currently Professor Vucic is exploring a novel approach which looks to uncover neurophysiological causes to MND and how he plans to build on this research to potentially create a roadmap to a cure in 5-years.

Novel Motor Neurone Disease research

Professor Vucic and his team are planning to use a novel method for assessing cortical excitability in human MND patients, called threshold tracking transcranial magnetic stimulation (TMS).

TMS is a non-invasive form of brain stimulation in which a changing magnetic field is used to cause electric current at a specific area of the brain through electromagnetic induction. An electric pulse generator, or stimulator, is connected to a magnetic coil, which in turn is connected to the scalp. The stimulator generates a changing electric current within the coil which induces a magnetic field; this field then causes a second inductance of inverted electric charge within the brain itself which can be measured.

Professor Vucic aims to assess inhibitory and excitatory nerves in all patients with TMS (see diagram below). The studies will be performed initially and then every 6 months for 4 years, and measure by:

- a validated questionnaire assessing motor and respiratory function
- muscle strength will be graded from 0 (paralysed) to 5 (normal power), including respiratory muscle strength
- neurophysiological assessment using well-established tools to measure nerve function.

Possibilities

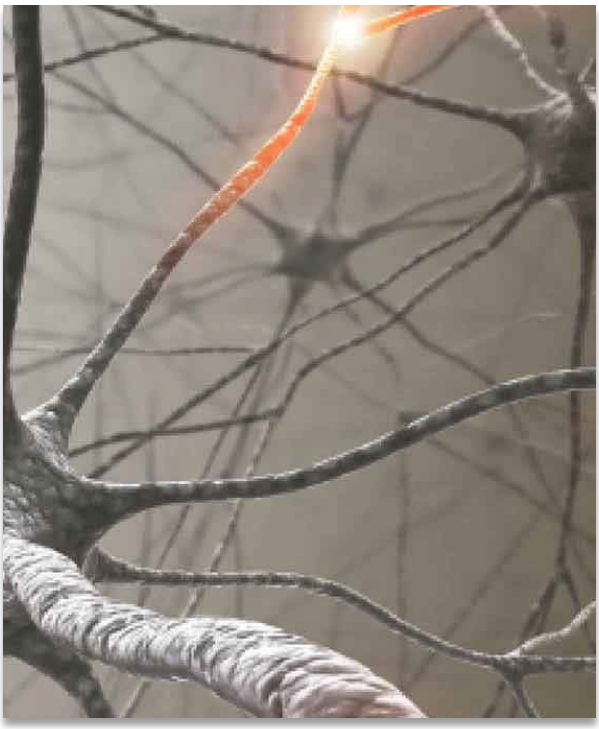
This research could show a loss of inhibitory neurons and excessive activity of excitatory neurons and is critical for understanding the causes of MND. It is envisaged that new mechanisms of disease will be discovered leading to development of effective treatments.

Proving a loss of inhibitory neurons and excessive activity of excitatory neurons, is of tremendous importance.

1. It may lead to discovery of treatment targets in MND, vital for development of therapies.
2. Could lead to new clinical trials using repurposed medicines (i.e medicines that are in use for other neurological conditions).
3. Provides a novel measure for disease activity, which is vital for monitoring disease progression and responses to therapies.

Roadmap to a Cure: The future of MND Research

Professor Vucic envisions a world where Motor Neurone Disease has a cure. He sees the answer laying in a combination of both neurophysiological and molecular approaches to the disease.



By exploring the cortical hyperexcitability in MND patients Professor Vucic envisions a 5 year long revolutionary project involving 120 MND patients that would combine clinical, neurophysiological and molecular approaches.

Such a comprehensive approach has never been undertaken previously. By approaching the solution to MND via a multifaceted approach Professor Vucic aims to uncover root causes and treatments for his patients and all Australians.

Neurophysiological Approach

As seen in his current novel approach to MND, a sophisticated clinical assessment will be undertaken to stage the disease and enable assessment of inhibitory and excitatory neurons via TMS.

Molecular Approach

Concurrently, Professor Vucic plans to grow neuronal cells from patient skin cells so as to determine the molecular mechanisms that caused hyperexcitability. The latter part of this project is vital as it will identify molecular mechanisms causing cortical hyperexcitability and lead to new treatments.

Research leader profile: Professor Steve Vucic

"Hopefully in my lifetime, we will be able to find a cure for MND. It is something I have dedicated my medical career to. There is nothing worse than motor neurone disease. It is the most terrible of all diseases."

- Professor Steve Vucic

Professor Steve Vucic, MBBS (Hons I), PhD, FRACP
Professor Medicine, Westmead Clinical School
Member of the Brain and Mind Centre
Member of the Charles Perkins Centre

About the research leader

Professor Ostoja (Steve) Vucic is a senior staff specialist in neurology at Westmead Hospital, clinical academic and translational researcher at the University of Sydney, whose pioneering research in the field of neuroscience has uncovered novel pathophysiological processes in neurodegenerative diseases, including amyotrophic lateral sclerosis (ALS), frontotemporal dementia and progressive forms of multiple sclerosis.

Professor Vucic has significantly enhanced the understanding of the pathophysiological processes underlying ALS, with the key discoveries relating to the identification of "cortical hyperexcitability" an initial and driving mechanism in ALS.

Professor Vucic is an internationally recognized specialist in the management of a variety of neurological disease.

Professor Vucic has gained an international reputation for his research in neurodegenerative diseases underscored by awards of numerous national and international standing, including:

- the highly prestigious Gottschalk Medal by the Australian Academy of Science (2016) for outstanding research in biomedical sciences;
- and, the Eric Susman Award (2017) by the Royal Australasian College of Physicians for outstanding achievement in research in any branch of internal medicine.

Professor Vucic has published 235 manuscripts in peer reviewed journals, including Lancet, Lancet Neurology, Brain, Nature Genetics, JAMA Neurology.

Supporting future Australian MND researchers

Early Career Researchers (ECRs) are the dedicated individuals performing the day-to-day work required to generate significant health research outcomes. Unfortunately, job security for these researchers is poor, due to ever-dwindling and risk-averse government support. Many researchers are lost to overseas opportunities in what can only be described as a "brain drain", whereas others simply accept defeat and change careers into an area where they might be less suited.

In Australia this year, grants application success rates were below 10% in a profession where regular successful grant funding is crucial for an academic career to advance. Once researchers escape the "early career trap", job security and career progression often follows.

Bridging the funding gap

Philanthropy is vital to bridging this funding gap. The loss of ECRs in the talent stream significantly limits scientific research progress.

Research operates in cycles of years, meaning that translation into widely-available clinical treatments can sometimes take an entire generation. Securing, long-term sources of funding help to ensure that:

- We attract and retain the best minds and that their essential work is allowed to progress to the point of yielding significant research outcomes;
- Clinical and laboratory researchers can shape their research agenda based on the greatest need and the most immediate impact, rather than on available funding;
- Mid- to long-term research projects can be designed and undertaken, which yield more detailed and meaningful data;
- Research can be completed earlier as consistent progress is made, rather than piecemeal efforts dictated by sporadic funding availability;
- The team can be responsive to changes in strategic direction that may arise with new discoveries; and
- Vital research capacity can be built, and the next generation of leading scientists are supported in their early careers.

Network of excellence in research

The University of Sydney

The University is committed to delivering outcomes that have a significant impact on improving the health and well-being of all Australians. With a truly collaborative and multidisciplinary approach, in partnership with industry, community and government, The University is well-positioned to unlock research discoveries that will translate into better outcomes for people impacted by debilitating diseases.

Brain and Mind Centre

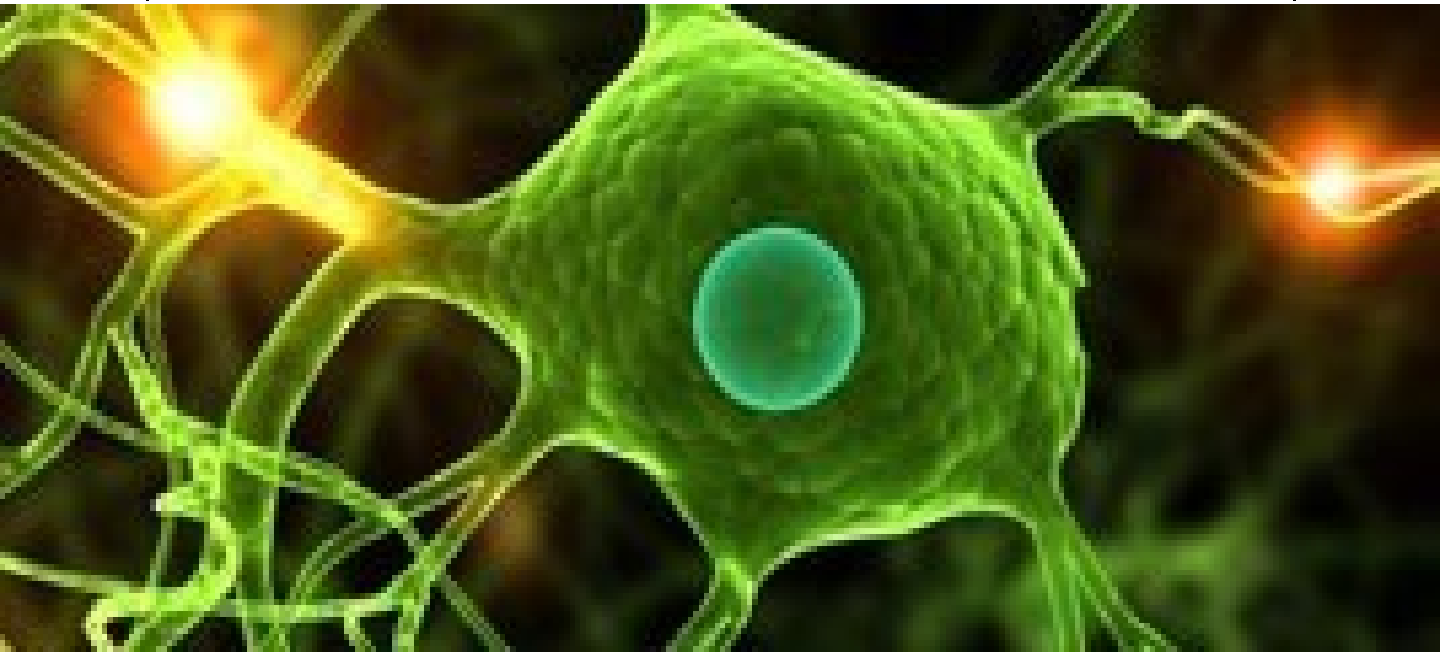
The Brain and Mind Centre (BMC) is the central hub for mental health and neuroscience at the University of Sydney. With a strong focus on translational research and world-class clinical services, the Centre brings together patients, carers, students, scientists, research leaders and clinicians, all with a common goal of driving generational change for disorders of the brain and mind.

Brain and Mind Centre Westmead

BMC Westmead based in the Westmead Institute for Medical Research, brings together researchers and clinicians across Westmead Hospital and the Children's Hospital at Westmead to combine efforts in the battle against disorders of the brain and mind across key developmental and degenerative milestones in life, including childhood, youth and ageing.

Sydney Health Partners Network

Sydney Health Partners is one of the first of four Advanced Health Research and Translation Centres in Australia, recognised by the National Health and Medical Research Council in 2015. It is comprised of the Sydney, Northern Sydney and Western Sydney Local Health Districts; the Sydney Children's Hospitals Network (Westmead); the University of Sydney; and nine affiliated independent medical research institutes.



Thank you

Philanthropy is a catalyst for change, it enables researchers to achieve significant breakthroughs and discoveries, particularly in the field of medicine and health.

Thank you for taking the time to learn more about Professor Steve Vucic and his revolutionary work in uncovering the causes and potential cures to Motor Neurone Disease.

Many people see MND and similar Neurological Diseases as incurable, Professor Vucic and the teams at University of Sydney Brain and Mind Centre believe that this is not the case. Support is required to innovate and build capacity for ground-breaking research to improve patient outcomes.

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