FIGHT MND.

Researcher.
DR FREDERIK STEYN

IMPACT Project.
POINT OF CARE ASSESSMENT OF VENOUS ACID-BASE BALANCE AND CREATININE AS MARKERS FOR DISEASE PROGRESSION IN MND


Dr Frederik Steyn

Where do you work?

The University of Queensland. My position is with the School of Biomedical Sciences (Lecturer, Anatomy and Pathology, Medicine) and my research is conducted between the Centre for Clinical Research and The School of Biomedical Sciences.

What is your research experience and background?

I received a Master's Degree in Anatomy in 2002, and a PhD in Anatomy, Structural Biology and Neuroendocrinology in 2007. I then relocated to Australia commencing postdoctoral research at the University of Queensland, studying the hypothalamic integration of energy homeostasis, growth and reproduction, with a focus on the impact of obesity and metabolic syndrome on overall health. During this time I developed an interest in understanding the metabolic changes that occur in preclinical models of MND, and how this might be relevant to disease progression. I completed a series of experiments that improved our understanding of the release and impact of growth factors that promote the reinnervation of muscle. Subsequently, I expanded my research program to include clinically-focussed studies, to better capture the heterogeneity of MND. In 2015, I co-founded the first Australian project to comprehensively assess the metabolic impact of MND on disease progression in patients. These studies were the foundation for a much larger research program that includes preclinical and clinical studies aimed to improve our understanding of the impact of MND on the body, and how this relates to disease heterogeneity and progression.

What led you to pursue your investigations into MND?

I moved to Australia in 2008 to support my parents in Brisbane. My mother had been diagnosed with early-onset frontotemporal dementia (FTD). She had a rapid progressing form of disease, and I took on the role as care-giver. She passed away within a year of my arrival. This was a very challenging experience, and following my mother's passing I was motivated to reposition my career focus to improve knowledge that could contribute to the treatment of neurodegenerative disease. I found it easier to focus on neurodegenerative diseases other than FTD as I was still coming to terms with my mother's death. It was difficult to process emotions around the impact of FTD, both on the individual but also on their families. We never completely recovered. I gravitated towards MND. During this time, I also met research collaborator and wife, Dr Shyuan Ngo. Shu was conducting studies in MND and we combined her interests in neuroscience research and my expertise in the field of metabolism to create a combined MND/Metabolism research program. As I became more involved in studies in MND I had opportunities to meet and spend time with people living with MND;

this included the late Dr Ian Davis. I spent two weeks travelling from Brisbane to Sydney with Ian, during which I learnt more about the impact of MND on the individual, and their community. Since, my motivation to develop treatments for MND is largely motivated through the friendships I have developed within the MND community, and the people directly impacted by MND. I am inspired by their refusal to allow MND to change who they are, and their commitment to create a better world for future patients with MND. I am inspired by the families of those living with MND, and the strength of the MND community.

Can you describe the research your team is currently focusing on?

My team conducts preclinical and clinical studies in MND, with a specific focus on factors that impact disease progression. My research is based around three C's: Care, Cure and Community. Under the umbrella of Care, I conduct preclinical (i.e. animal model) and clinical (i.e. patient studies) studies that focus on factors that impact the progression of disease and quality of life; this includes studies on metabolism and appetite. I am also developing novel approaches to improve our capacity to monitor the progression of disease (biomarkers). My focus is on causes and markers of weight loss, and factors that can improve detection of respiratory insufficiency and the progressive worsening of disability. Under the umbrella of "Cure", I am testing drugs that target multiple components of disease, with the hope that these compounds will offer therapeutic benefits across a wider spectrum of patients and across multiple disease subtypes. A key component of my work involves the MND "Community"; I am committed to connecting with as many patients as possible. This is through regular engagement with MND organisations to share research insights, the development of patient-focussed seminars and symposia, and involvement in events that raise awareness for MND. I am also developing strategies to allow inclusion of more people with MND in research; In 2020 this will include the provision of support for people across Queensland to attend research studies in Brisbane. Queensland is a very large state, and many patients with MND are isolated. I'm aware that research, while providing critical information to improve our understanding of MND, can offer hope. Through engagement with the community I get to say thank you for the support we receive to conduct our studies, and found that discussions with people living with MND also highlight critical areas for improved research focus.

What excites you about the new tests you are developing?

Developing this blood analysis technology will free up valuable time for people living with MND. I am most excited by the fact that this test could provide measures that will better direct the individual to seek support when needed. There is the added benefit that this method will also help people that are far from specialists centres that conduct respiratory tests. I am hopeful that these measures will direct patients to a respiratory physiologist at the most appropriate time for introducing effective breathing support. This will greatly improve their quality of life, and there is potential to slow the progression of MND. If this technology allows one patient to spend more quality of time with their families then I will consider this project a success.

What difference will this grant make to your work?

We have completed pilot studies at the Royal Brisbane & Women's Hospital to show the utility of point of care testing of blood gas markers in MND, however these results are not likely to change clinical practise. Measures are collected from a relatively small cohort of patients within a single MND research clinic. To expand the utility of this method, and to convince an international body of researchers and clinicians to use the technology, this grant will allow the conduct of a much larger and multi-site study. The study will be conducted across Australian and European sites, and will incorporate new and evolving questionaries that are being developed to inform our understanding of respiratory failure in MND. Ultimately, this should fast-track the development of measures that promise to improve clinical care for people with MND.

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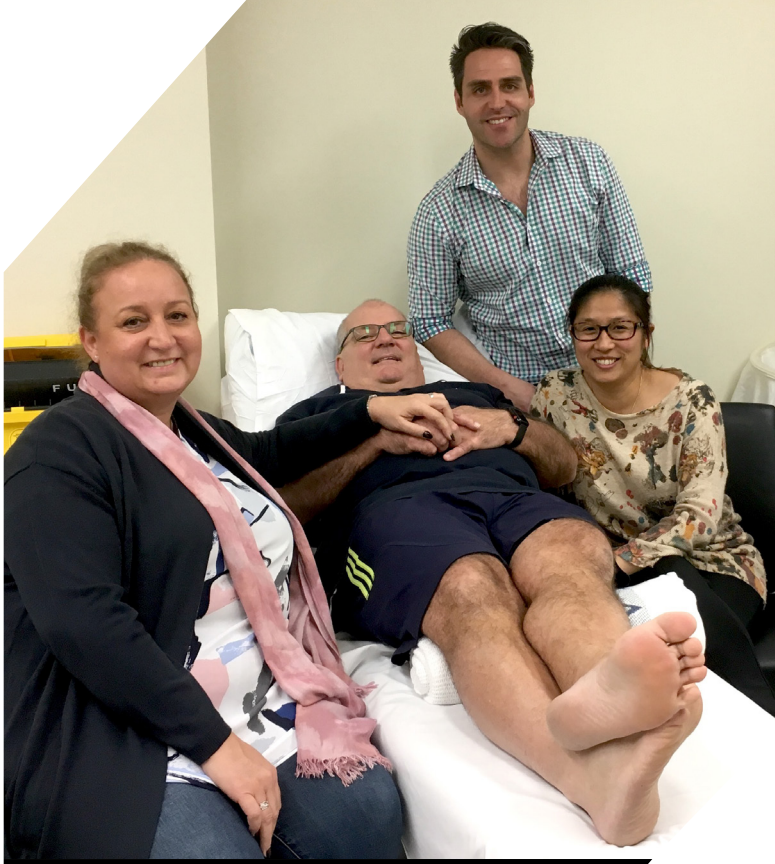

A typical day for Dr Frederik Steyn, Dr Shyuan Ngo and study participants in the research clinic.

This project will test the use of a portal blood analysis device that can measure components of blood-gas exchange in less than a minute – it is expected that these measures will provide critical information on the health of a person's lungs, in the context of MND. This is important as impaired breathing in MND is a leading cause for loss of quality of life, and most patients die as a consequence of respiratory failure. Early and effective intervention to improve oxygen supply improves quality of life and delays death. During research visits with patients', discussions often centre around their frustration with having to complete routine breathing tests. Patients noted that these tests were exhausting, and felt that they were not always needed. Patients felt that the time spent at the hospital could be better invested. Many patients missed critical breathing exams, and mentioned that their results from these exams could vary greatly relative to how they felt on the day, based on who conducted the test, and their ability to use equipment needed for lung function testing (for example, patients with bulbar symptoms could not reliably conducts tests). This is of concern, as improper testing and the resulting delayed intervention could significantly impact quality of life.

These discussions motivated me to look for alternative methods to monitor breathing in patients with MND. I tested a number of approaches, and ultimately settled on the device tested in this project as the technology offers a reliable measure that doesn't increase patient burden. I was also motivated to develop a technology that provides immediate feedback to clinicians (i.e. results are generated immediately), as this will ensure that information can be used to inform immediate care – in this case, results will hopefully identify patients with immediate needs for specialists breathing assessments.

OBJECTIVES:

- To validate that specific biomarkers measured during on-the-spot blood tests reliably detect symptoms of MND, including insufficient breathing and weakening of muscles required for breathing, as well as the onset and progression of MND.
- To assess blood gas exchange biomarkers in MND patients and compare them with clinical measures of respiratory function and progression of MND.
- Adoption of these biomarkers for detecting the onset and progression of MND within 2 years.