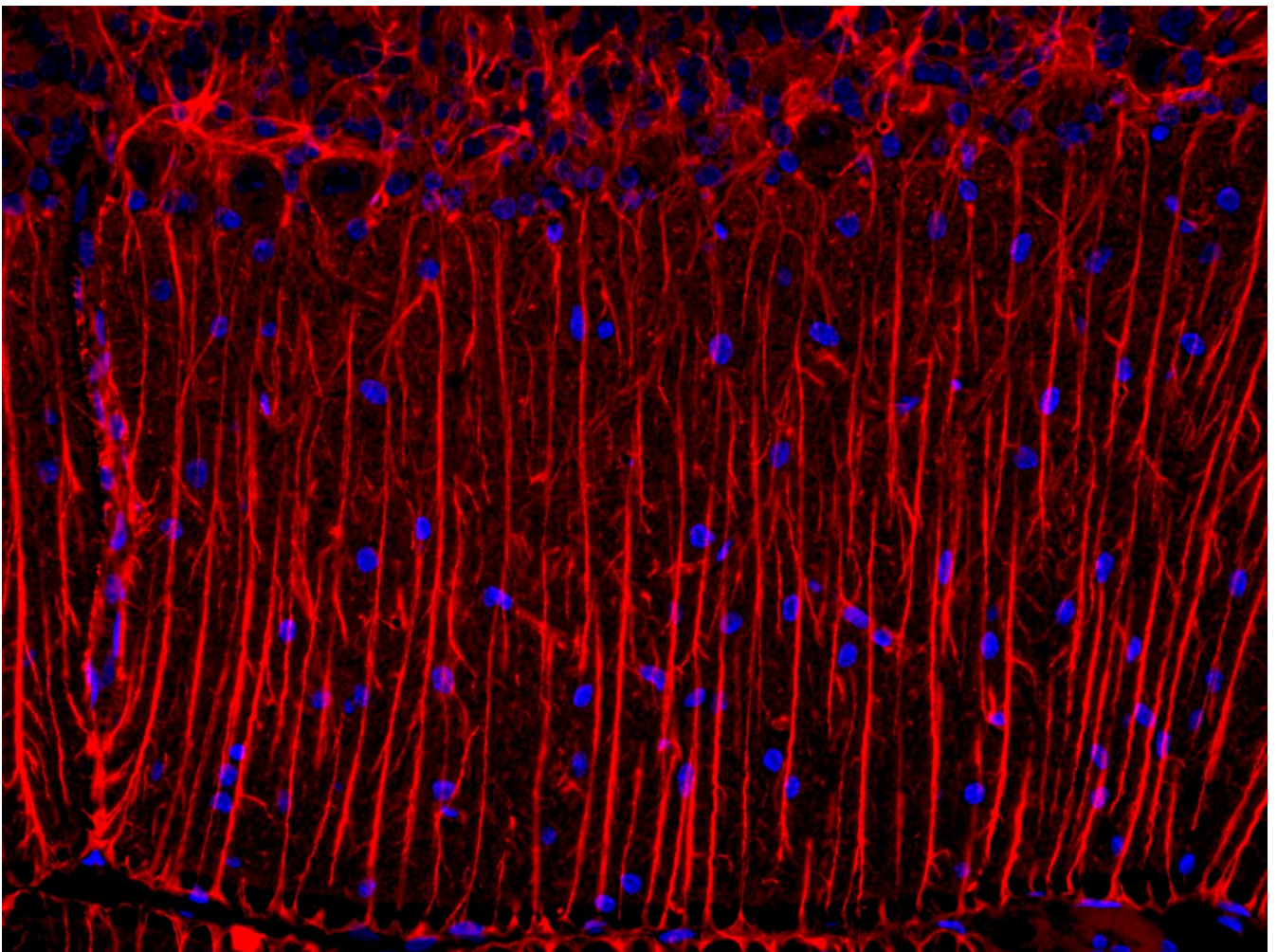


Nerve Research Foundation



Annual Report 2018

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Cover image – Glial cells (cells which support the nerve cells) in the cerebellum, an area of the brain responsible for coordinating voluntary movements such as posture, balance, coordination and speech (T.Kaplinovsky).

President's and Directors' Report

In 2018 the Nerve Research Foundation made important contributions to Research at the University of Sydney by supporting research projects into Multiple Sclerosis, Peripheral Neuropathy and Pain Management using photobiomodulation. Foundation funds supplemented salaries and provided infrastructure funding for scientists in the purchase of expensive equipment for research. Seed funding from the NRF facilitated grant application to major funding bodies with outstanding success.

Once again we express our gratitude to our benefactors who have continued to support the work of the Foundation and in particular the Sydney Executive Business Association who have generously supported our work over many years. The Goodridge Foundation made a most generous donation to assist research and foster novel therapies for Multiple Sclerosis.

We especially thank all members of the NRF Council who gave their precious time to attend meetings, review documents and provide wise counsel.

Highlights and Updates

Dr. Tim (Chenyu) Wang was appointed the Inaugural NRF Fellow at the Brain and Mind Centre supported by funds raised by the NRF to assist research into Multiple Sclerosis and to accelerate the development of the Imaging Neuroanalytics Platform. Dr Wang also received the Peter Bancroft Prize for his outstanding PhD thesis entitled "Improving the specificity of quantitative neuroimaging biomarkers for monitoring disease progression and understanding disease mechanisms in multiple sclerosis with diffusion magnetic resonance imaging." Moreover, Dr Wang was awarded a Multiple Sclerosis Research Association Fellowship of \$180,000 to support his research.

Professor Michael Barnett, Dr. Tim (Chenyu) Wang and the Sydney Neuroimaging Analysis Centre won a prestigious Australian government CRC-P grant of \$2,360,061 for their research into the application of Artificial Intelligence to the use of MRI in Multiple Sclerosis and a range of other neurological conditions.

Professor Michael Barnett, Professor Fernando Calamante and Professor Dacheng Tao were awarded an NHMRC/Sydney University equipment grant of \$180,000, which will fund the purchase of an NVIDIA supercomputer for the Brain and Mind Centre's computational neuroscience team. The equipment will facilitate cutting edge artificial intelligence research that has been part-funded by the NRF.

Professor Matthew Kiernan gave three invited major platform presentations at the 15th International Congress on Neuromuscular Diseases, in Vienna, Austria in July 2018; a tribute to his outstanding international reputation in the Neuromuscular field, and communication skills.

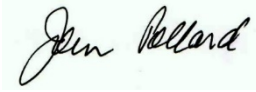
Dr. Justin Garber was awarded a Multiple Sclerosis Research Australia postgraduate scholarship to further his NRF-supported research on "MRI Biomarkers and Mechanisms of Progression in Multiple Sclerosis."

The Goodridge Foundation made a generous donation of \$72,513 to the NRF for research into novel treatment strategies for cognitive and neuropsychological problems in Multiple Sclerosis.

Dr. Heidi Beadnall was awarded a Brain Foundation grant for \$30,000 to further her research "Measuring changes in brain tissue volume over time using magnetic resonance imaging."



Benjamin Chow - President



John Pollard - Co-Director



Patricia Armati - Vice President and Co-Director

Members

Council

- Ms Belinda Jane Hutchinson AM, Chancellor, The University of Sydney
- Dr Michael Spence AC, Vice Chancellor, The University of Sydney
- Professor Arthur Conigrave, Dean, Faculty of Medicine, The University of Sydney
- Mr Benjamin Chow AO, President
- Professor (Hon.) Patricia Armati AM, Vice President and Co-Director
- Professor Emeritus John Pollard AO, Co-Director
- Professor Emeritus Robert Ouvrier AC
- Dr Ruth Kerr OAM
- Mr Tony Carroll KCSG, AM
- Mr David Jacobs
- Mr Roy Melick
- Professor Michael Barnett
- The Hon Alan R Abadee AM RFD QC
- Associate Professor Stephen Reddel
- Professor Matthew Kiernan
- Ms Melissa Bonevska

Scientific Committee

- Professor John Pollard AO
- Professor Patricia Armati AM
- Professor Robert Ouvrier AC
- Professor Matthew Kiernan AM

Honorary Governor

- Ms Rikki O'Neill

Honorary Life Members

- Mr David Jacobs
- Ms Rikki O'Neill
- Dr Ruth Kerr OAM
- Mr Tony Carroll KCSG, AM

Researchers Supported by the Nerve Research Foundation

Academic

- Professor John Pollard AO, BSc (Med) MB BS PhD, FRACP, FRCP
- Professor Patricia Armati AM, BSc, MSc, PhD
- Professor John Prineas AO, MB Bs, FRCP, FRCP (Edin)
- Dr Judy Spies, MB BS PhD, FRACP
- Dr Emily Mathey, BSc (Hons 1), PhD
- Dr Min-Xia Wang MB MD
- Professor Michael Barnett MB BS (Hons 1) FRACP PhD
- Dr Stephen Reddel MB BS FRACP PhD
- Dr John Parratt MB BS MD

Honorary Research Associate

- Dr Roberta Chow AM MBBS PhD, FRACGP, FAMAC, MAppISci (Med Acu)
- Dr Ambrose Chan BDS Hons (Uni Syd), DipClin.Dent (Uni Syd), MScDent (Uni Syd), FRACDS

Research Associates

- Dr Linda Ly PhD

Senior Research Fellows

- Dr Emily Mathey BSc (Hons) PhD
- Dr Claire Goldsbury PhD

Clinical Trials Staff

- Mrs Marinda Taha, Trials Co-ordinator

Technical Staff

- Toan Nguyen
- Neeta Lal BSc Dip. Path
- Ms Hung Jiew Lee, BSc, MSc

Research Staff

- Dr Nidhi Garg
- Dr Thanuja Dharmadasa
 - MNDRIA PhD top-up Grant 2017-2018
 - Top up award from the Yugalbar Foundation (2017-2019)
 - PhD Top up award from Rotary (2017-2019)
- Associate Professor Cindy Lin
- Dr Rebekah Ahmed (Neurologist)
- Dr Michael Lee (Neurophysiologist & Physiotherapist, Postdoctoral Research Fellow)
- Dr Emma Devenney (Neurologist, PhD candidate)
- Dr Susanna Park (Senior Lecturer)
- Dr Tim Howells (Postdoctoral Research Fellow)
- Jashelle Caga (Health Psychologist, PhD Candidate)
- Hannah Timmins (Research Assistant)
- Dr William Huynh (Neurologist, Postdoctoral Researcher).
- Dr Tala Kaplinovsky BSc, BA, PhD (Armati group)
- Margie Zoing (MND CNC)
- Dr Yoshimitsu Shimatani (Neurologist, Japanese visiting researcher)
- Dr Yuichi Noto (Neurologist, Japanese visiting researcher)
- Dr Jose Mattamala Capponi (Neurologist, Chilean visiting researcher)
- Elizabeth Highton-Williamson (Research Assistant)
- Tiffany Li (Research Assistant)
- Nicollette Thornton (Research Assistant)
- Eleanor Ramsey (Research Coordinator)

Higher Degree Candidates

- Ms Jashelle Caga, 2014 – ongoing (PhD Candidate; Co-supervised with Dr Anne Hodgen)
- Dr Nidhi Garg, 2015 – ongoing (PhD Candidate)
- Dr Thanuja Dharmadasa 2017-ongoing (PhD Candidate)
- Jashelle Caga (Health Psychologist, PhD Candidate)

- Dr Nidhi Garg (Neurologist, PhD Candidate)
- Dr Thanuja Dharmadasa (Neurologist, PhD Candidate)
- Dr Dev Nathani (Neurologist, PhD Candidate)
- Hannah Timmins (Neuroscience, PhD Candidate)
- Elizabeth Highton-Williamson (Neuroscience, PhD Candidate)
- GuYu Gu (Physiotherapist, PhD Candidate)

Degrees awarded - PhD

- Dr Ambrose Chan

Administrative Staff

- Dr Tala Kaplinovsky

Strategy, Achievement of Objectives and Financial Performance Against Budget

The Sydney University Nerve Research Foundation, established in 1985, promotes basic research into the mechanisms and effects of disease of the central and peripheral nervous system by scientists, clinicians and postgraduate students. It assists the formation of patient support groups and aims to increase public understanding of diseases of the nervous system.

Achieving Objectives

The NRF achieves the above goals by its members being awarded nationally competitive grants, supporting post graduate students, clinical trials, organizing invited lectures, conference presentations and seminars.

Fundraising Activity

The NRF did not actively fundraise during 2018.

The NRF receives donations and bequests from time to time as well as in response to our Annual Report.

The Nerve Research Foundation does not employ full time administrative staff, this is done by Dr. Tala Kaplinovsky on an 'as needs' basis – which minimizes such costs and allows us to maximize our donations to fulfill our objectives.

Foundation Governance Statement

The Nerve Research Foundation recognises the importance and benefit of reviewing its adoption and alignment with governance principles and provides the following report

Principle 1 – Lay solid foundations for management and oversight

Nature of the entity

The Nerve Research Foundation is a part of the University of Sydney ABN 15211513464 and not separately incorporated under a state or commonwealth Act. The Foundation is required to gain prior approval for its fundraising activities from the appropriate University delegate. The Foundation's activities are not-for-profit and covered by the DGR status of the University of Sydney. The University is exempted from the requirement to hold an Authority to Fundraise and obligations upon holders of such an authority but is still required to comply with the balance of provisions of the Charitable Fundraising Act

Roles of board / council and management

The Foundation operates under the authority of the Senate of the University of Sydney, as approved on 21 March 2011 and has no powers of delegation. The Foundation conducts its affairs pursuant to the Foundation Rules and the relevant policies of the University. The Foundation had its annual fundraising plan approved and was able to meet its objectives.

Principle 2 – Structure of the council to add value

The Council of the Foundation in 2018 consisted of the following members:

Benjamin M T Chow AO

President NRF Council

Civil Engineer, Property Development, Company Director, Government and University Councils, Council Member Sydney Medical School Foundation

Term of Appointment: 2012 – 2018

Special Responsibilities: Fund raising in partnership with outside organisations such as Lions Club, The Sydney Business Executive Club, donations and bequests

Attended all meetings in 2018

Professor Patricia Armati AM

BSc MSc PhD, Vice President and Co-Director and Founder of the NRF

Current Term of Appointment: 2012 – 2018

Special Responsibilities: Oversight of administration of the Foundation and liaison with other Council members and the general public

Attended all meetings in 2018

Professor John Pollard AO

MB BS BSc (Med) PhD FRACP FRCP (Lond), Co-Director and Founder of Nerve Research Foundation

Current Term of Appointment: 2012 – 2018

Attended all meetings in 2018

Matthew Kiernan PhD, DSc, FRACP

Bushell Chair of Neurology, Royal Prince Alfred Hospital
University of Sydney

Current Term of Appointment: 2017 - 2018

Special Responsibilities:

Attended all meetings in 2018

The Hon Alan Richard Abadee AM RFD QC LLB

Retired Judge

Special Responsibilities: Review and advise on legal issues

Current Term of Appointment: 2012 – 2018

Attended all meetings in 2018

Professor Michael Barnett MB BS (Hons I) FRACP PhD

Current Term of Appointment: 2012 – 2018

Attended all meetings in 2018

Associate Professor Stephen Reddel MB BS FRACP PhD

Current Term of Appointment: 2012 – 2018

Attended all meetings in 2018

Professor Emeritus Robert Ouvrier AC BSc (Med) (Hons), MB, BS (Hons), MRACP, FRACP, M.D.

Emeritus Professor

Research in the field of Paediatric Neurology

Current Term of Appointment: 2012 – 2018

Attended all meetings in 2018

Dr Ruth Kerr OAM PhD; B. Leg. Studies; BA; Gr Dip Lib Sc; Cert Tchg
Current Term of Appointment: 2012 – 2018
Attended all meetings in 2018

Stanislaus Anthony Carroll KCSG; AM D.Univ; LLB
Partner – Carroll & O’Dea Lawyers
Current Term of Appointment: 2012 – 2018
Special Responsibilities: Review and advise on legal issues
Attended all meetings in 2018

Mr David Jacobs LLB, LLM
Solicitor; former managing partner of Baker & McKenzie in Australia, former Chairman of Asia Pacific for Baker & McKenzie, former member of the global Executive Committee of Baker & McKenzie, numerous other management roles in Baker & McKenzie
Current Term of Appointment: 2012 – 2018
Special Responsibilities: Review and advise on legal issues
Attended all meetings in 2018

Mr Roy Melick LLB BA LLM
Partner at Baker McKenzie, Sydney. Chairman of the Asia Pacific Structured Real Estate Group, a representative of Baker McKenzie’s Global Real Estate Steering Committee and a founding member of Baker McKenzie’s Hotels, Resorts and Tourism Group.
Special Responsibilities: Review and advise on legal issues
Current Term of Appointment: 2012 – 2018
Attended all meetings in 2018

Ms Melissa Bonevska
Current Term of Appointment: 2017 - 2018
Special Responsibilities: Ex-Officio University (Provost’s nominee)
Attended all meetings in 2018

Council members were elected and/or co-opted at the Foundation’s AGM on 28 February 2012. There is separate nomination sub-committee of Council elected at the Foundations AGM on 4 February 2015 consisting of Matthew Kiernan, Stephen Reddel and Ben Chow. The full Council resolves on nominations for co-opting of members to fill vacancies outside of the process of election at the AGM. There was not a performance evaluation of the Council undertaken in the reporting period.

Principle 3 – Promote ethical and responsible decision-making

Council members have been provided with the University of Sydney Foundation Governance Guide, Foundation Rules, Code of Conduct, Work Health & Safety policy and the External Interests policy. All these policies are available on the University’s Policy Register as are other relevant University policies regarding harassment, grievance procedures and the Delegations of Authority.

Principle 4 – Safeguard integrity in financial reporting

The annual accounts of the Foundation are prepared by the financial staff of the University, signed off by Petrus Swemmer and included in this Annual Report to the Senate. The Foundation is part of the University and therefore does not have its own audit sub-committee. While the Annual Financial Report of the University is audited by the Audit Office of NSW, the Annual Report of the Foundation has not itself been audited.

The Foundation did not undertake any fundraising appeals¹ during 2018.

¹ See s5 Charitable Fundraising Act 1991 (NSW)

Principle 5 – Make timely and balanced disclosure

The Foundation complied with the reporting and disclosure requirements of the Senate. These include an annual budget and this Annual Report.

Members and Council have been made aware of the processes for disclosure pursuant to the Code of Conduct, External Interests policy, which include protected disclosure to the ICAC, to the Ombudsman or the Auditor General.

Principle 6 - Respect the rights of shareholders, members, staff, volunteers, clients, & other stakeholders

The Foundation Council and/or membership consists of members of the community, industry bodies and the University whose input is invited via the Annual General Meeting and Council meetings of the Foundation. The following forums/mechanisms have been held during the year to involve stakeholders in election of the Council, activities of the foundation or other stakeholder participation AGM – March 2019.

Under the Charitable Fundraising Act, the University may be questioned about any appeal on details of the purpose of the appeal such as the appeal target, objectives, distribution of proceeds, and the process to provide answers. During the year the Foundation published information - and outlines those activities in this annual report. There were no specific requests for information responded to by the Foundation office. Other enquiries may have been made to other parts of the University.

Principle 7 - Recognise and manage risk

The Foundation recognises its activities within University premises or other premises require risks such as health and safety, environmental protection, privacy, trade practices, and compliance with the Charitable Fundraising Act to be considered and managed.

Principle 8 – Remunerate fairly and responsibly

No member of a Council is entitled to receive any remuneration for acting in that capacity except reasonable remuneration on a basis which has first been approved in writing by the University Officer (Foundations).

Members of the Foundation Council may be reimbursed for reasonable expenses after written approval of the University Officer (Foundations). Any such instances are recorded in the minutes of the Council.

Research Projects

Peripheral Neuropathy - Neuroinflammation Group at the Brain and Mind Centre

Autoimmunity to the Node of Ranvier in inflammatory diseases of the peripheral nervous system

Emily Mathey, Toan Nguyen, Nidhi Garg, Susanna Park, Matthew Kiernan, John Pollard

Chronic inflammatory demyelinating polyneuropathy (CIDP) is a neuroinflammatory disorder of the peripheral nervous system (PNS). CIDP occurs when the immune system mistakenly mounts an immune response against the peripheral nerve and strips the myelin away from the axon. This process leaves the axon uninsulated and unable to conduct nerve impulses efficiently. However, the immune response in some patients with CIDP is directed towards molecules in and around the node of Ranvier. The node of Ranvier is a gap in the myelin covering of the nerve fibre which seems to be particularly vulnerable to autoimmune attack. We have been screening patient sera for antibody responses to the nodal/paranodal proteins neurofascin 155, neurofascin 186, contactin 1 and gliomedin as well as a panel of gangliosides. We have detected autoantibody responses to some of these molecules in a proportion of patients with CIDP and have monitored these patients with respect to nerve function and clinical phenotypes. The presence of these antibodies is associated with certain clinical phenotypes and a lack of response to IVIg. This clinical heterogeneity in CIDP makes it probable that distinct immunopathological mechanisms underlie different phenotypic subtypes.

We are also testing the pathogenic significance of these antibodies in experimental models to determine whether they damage the nerve and inhibit nerve function. Further characterisation of autoimmune responses to these antigens should give greater insight into the pathogenesis of inflammatory demyelinating neuropathies and may help guide diagnosis, treatment options and prognosis.

Developing New Therapies for Neurodegeneration and Dementia

Professor Matthew Kiernan et al

The forefront multidisciplinary motor neurone disease and frontotemporal dementia (MND/FTD) patient care unit was jointly established at the University of Sydney and Royal Prince Alfred Hospital. This service reviewed more than a thousand new referrals over the past 3 years and currently manages 250 patients per year. All patients have clinical, respiratory and functional assessments, a comprehensive core neuropsychological assessment, in addition to a range of behavioural assessments such as the Cambridge Behavioural Inventory.

Following from these clinical investigations to determine phenotype, recent research studies investigated the behavioural changes that develop with neurodegenerative disease identified that MND patients with apathy had lower overall quality of life (QOL), and hence patient-reported outcomes, particularly those assessing psychosocial functioning will be critical for demonstrating efficacy of interventions designed to improve QOL in patients with behavioural impairments (Caga et al., 2018).

Separate results from our studies that investigated psychiatric symptomatology in patients and their relatives carrying the C9orf72 mutation linked to the development of neurodegeneration, suggested that a psychiatric phenotype that includes schizophrenia, psychosis and autism, exists within C9orf72 kindreds. Further studies delineated the risk of psychiatric disorders in C9orf72 kindreds to aid in clinical decision making, particularly regarding counseling, through genetic-based collaborations between neurology and psychiatry (Devenney et al., 2018).

To further validate the diagnostic application of Transcranial Magnetic Stimulation in MND and related neurodegenerative diseases, a recent study on TMS reproducibility demonstrated that averaged SICl was the most reproducible variable across paired-pulse TMS measures with an excellent reproducibility and that changes in cortical excitability be measured and averaged over a number of interstimulus intervals to minimize variability (Matamala et al., 2018). Using TMS to interrogate cortical function of muscles with differing motor functions showed greater intracortical inhibition and less facilitation for limb muscles. These findings relate to differences in the functional organization of the corticomotoneuronal system innervating different muscle regions and may have significance in relation to areas of cortical vulnerability and the site of onset in MND (Menon et al., 2018).

In terms of understanding functional physiological changes in the nerves of MND patients, our clinical research team established that approximately 99% of functional change in surviving motor neurons in patients with MND was explained by reductions in the expression of all ion channels and these changes were likely a result of failure in supply of ion channel and other membrane proteins from the diseased motor neuron (Howells et al., 2018). This study was published in the highly prestigious Journal of Physiology (UK) and suggests new ways of targeting diseased nerves from a therapeutic perspective.

Studies involving structural imaging of the brain in ALS and frontotemporal dementia (FTD) undertaken using a dedicated 3-Tesla Philips scanner were completed at the University of Sydney Brain and Mind Centre. A full range of grey and white matter tract imaging was achieved in all patients to better determine involvement of brain circuitry in relation to disease involvement. In patients with FTD, our research studies demonstrated that widespread attenuation of sexual drive, intimacy and the display of affection were evident irrespective of dementia subtype. Neuroimaging analyses with VBM revealed an association between changes in sexual behavior and structure changes in multiple brain regions, likely reflecting the degeneration of cortical and subcortical neural circuits implicated in reward, autonomic function, empathy, and emotional processing in these regions (Ahmed et al., 2018a).

Neuromuscular ultrasound studies were performed to improve understanding of nerve function in relation to disease pathophysiology. Our research identified that muscle fasciculation intensity on ultrasound was linked to disease progression and separately to markers of cortical dysfunction, and hence assessing the intensity of patient fasciculations could provide a noninvasive approach to gaining further insight into the disease pathophysiology in MND (Tsugawa et al., 2018). Furthermore, in MND patients, fasciculations were more widespread, greater in number and higher in firing frequency than in peripheral hyperexcitability patients thereby suggesting that a significant proportion of fasciculations in MND may be influenced by changes in central excitability (Noto et al., 2018b) which provides insight into the pathophysiology of symptom generation in MND as well as adding further support to the notion of a dying forward process in the disorder. Separately, the median nerve cross-sectional area (CSA) in the upper arm of MND patients was decreased, whilst the median nerve wrist-upper arm ratio was increased in MND patients and thereby may provide a useful marker to aid in MND diagnosis (Noto et al., 2018a).

A proportion of patients were also incorporated into a functional brain imaging study utilizing PET scanning located at the RPA Hospital. Functional imaging will improve our current understanding of MND as a multisystems disorder affecting other extramotor regions of the brain. It was recently shown that regional thalamic connectivity changes mirror progressive frontotemporal cortical involvement associated with the motor functional decline in MND, and hence longitudinal MRI has potential as a non-invasive surrogate marker of cortical dysfunction in MND (Tu et al., 2018).

Given the evidence for an overlap between frontotemporal dementia (FTD) and MND at a clinical and pathological level, all patients also underwent a battery of cognitive testing to determine the degree of impairment at diagnosis and the rate of deterioration over time. The cognitive profile in patients with a phenotype of MND, primary lateral sclerosis (PLS) resembles ALS-FTD but without prominent behavioural disturbances. In addition, whilst certain TMS parameters were similar across patients with classic ALS / ALS-FTD and PLS, there were also differences between the groups suggesting that although PLS lies on the ALS-FTD spectrum, mechanisms underlying slow disease progression are likely to be distinct in PLS phenotypes (Agarwal et al., 2018). Cognitive assessments were also correlated with baseline respiratory function to determine whether respiratory compromise may result in poor cognition and hence negatively impact survival and quality of life. This may have clinical implication towards revised criteria for the early institution of interventions to improve respiratory parameters such as the use of intermittent non-invasive ventilation.

Increasing evidence from our separate streams of research across disease cohorts suggests that metabolic change, including fluctuations in weight, insulin resistance and cholesterol has an increased incidence across a range of neurodegenerative conditions. A recent study by our team has established a spectrum of changes in lipid metabolism in patients with ALS-FTD, with total cholesterol levels found to potentially impact on survival. These changes were mediated by changes in fat intake, and BMI, and may also be mediated by the neurodegenerative process, offering the potential to modify these factors to slow disease progression and improve survival (Ahmed et al., 2018b).

In summary, the research achievements briefly highlighted above are validation that the clinical service and research teams have flourished since relocating to the Brain and Mind Centre and Royal Prince Alfred Hospital.

Directed references highlighted in this report:

- CAGA, J., HSIEH, S., HIGHTON-WILLIAMSON, E., ZOING, M. C., RAMSEY, E., DEVENNEY, E., AHMED, R. M. & **KIERNAN, M. C.** 2018. Apathy and its impact on patient outcome in amyotrophic lateral sclerosis. *J Neurol*, 265, 187-193.
- DEVENNEY, E. M., AHMED, R. M., HALLIDAY, G., PIGUET, O., **KIERNAN, M. C.** & HODGES, J. R. 2018. Psychiatric disorders in C9orf72 kindreds: Study of 1,414 family members. *Neurology*, 91, e1498-e1507.
- HOWELLS, J., MATAMALA, J. M., PARK, S. B., GARG, N., VUCIC, S., BOSTOCK, H., BURKE, D. & **KIERNAN, M. C.** 2018. In vivo evidence for reduced ion channel expression in motor axons of patients with amyotrophic lateral sclerosis. *J Physiol*, 596, 5379-5396.
- MATAMALA, J. M., HOWELLS, J., DHARMADASA, T., TRINH, T., MA, Y., LERA, L., VUCIC, S., BURKE, D. & **KIERNAN, M. C.** 2018. Inter-session reliability of short-interval intracortical inhibition measured by threshold tracking TMS. *Neurosci Lett*, 674, 18-23.
- MENON, P., **KIERNAN, M. C.** & VUCIC, S. 2018. Cortical excitability varies across different muscles. *J Neurophysiol*, 120, 1397-1403.
- NOTO, Y. I., GARG, N., LI, T., TIMMINS, H. C., PARK, S. B., SHIBUYA, K., SHAHRIZAILA, N., HUYNH, W., MATAMALA, J. M., DHARMADASA, T., YIANNIKAS, C., VUCIC, S. & **KIERNAN, M. C.** 2018a. Comparison of cross-sectional areas and distal-proximal nerve ratios in amyotrophic lateral sclerosis. *Muscle Nerve*.
- NOTO, Y. I., SIMON, N. G., SELBY, A., GARG, N., SHIBUYA, K., SHAHRIZAILA, N., HUYNH, W., MATAMALA, J. M., DHARMADASA, T., PARK, S. B., VUCIC, S. & **KIERNAN, M. C.** 2018b. Ectopic impulse generation in peripheral nerve hyperexcitability syndromes and amyotrophic lateral sclerosis. *Clin Neurophysiol*, 129, 974-980.
- TSUGAWA, J., DHARMADASA, T., MA, Y., HUYNH, W., VUCIC, S. & **KIERNAN, M. C.** 2018. Fasciculation intensity and disease progression in amyotrophic lateral sclerosis. *Clin Neurophysiol*, 129, 2149-2154.
- TU, S., MENKE, R. A. L., TALBOT, K., **KIERNAN, M. C.** & TURNER, M. R. 2018. Regional thalamic MRI as a marker of widespread cortical pathology and progressive frontotemporal involvement in amyotrophic lateral sclerosis. *J Neurol Neurosurg Psychiatry*.

Multiple Sclerosis Research Group

Professor Michael Barnett et al

The MS Research Group maintained a strong focus of biomarker discovery through 2018. Using novel brain imaging techniques, we demonstrated progressive loss of nerve fibres in chronic MS lesions and the impact of these changes have on the brain as a whole. Dr Chenyu Wang, the inaugural NRF Fellow, developed new techniques to quantitate damage to the visual pathways in patients with MS and has been awarded a prestigious MS Research Australia fellowship to continue this work. In collaboration with Professors Dacheng Tao and Tom (Weidong) Cai, the group expanded its research focus to include the application of artificial intelligence / deep learning techniques to MS neuroimaging datasets. We expect this work, which is funded by an Australian government CRC-P grant, to lead to the development of new diagnostic tools and biomarkers for both MS researchers and the diagnostic neuroimaging industry.

Our group also collaborated extensively with local, national and international leaders in the field. This collaborative work yielded publication of the landmark AMS3 study in *Multiple Sclerosis Journal*, which demonstrated the utility of novel digital platforms to support the safety of patients taking complex medicines such as alemtuzumab. Our collaboration with MSBASE, the largest international MS patient registry (>70,000

patients), generated important epidemiological, treatment and imaging publications in 2018. Support from the NRF has also led to the signing of a MOU between MSBASE and the University of Sydney to develop the MSBASE Neuroimaging Repository and analysis platform.

The MS Clinical Trials Unit, managed by Dr Marinda Taha continues to provide patients with access to cutting-edge clinical trials, and in 2018 was the first site in the world to enrol patients in Clene Nanomedicine's remyelinating trial using nanocrystalline gold. Finally, we are continuing with 4 large investigator initiated studies, investigating visual, motor and cognitive function in MS that will complete in 2019. This work is supported by the NRF, industry partners and external philanthropy. We would also like to take this opportunity to express our gratitude to the many patients who have enthusiastically participated in this research.

Team Members

Prof. Michael Barnett, PhD, MBBS, FRACP
Prof. John D Pollard, PhD, MBBS, FRACP
A/Professor Stephen Reddel, PhD, MBBS, FRACP
Dr Todd Hardy, PhD, MBBS, FRACP
Dr Judith Spies, PhD, MBBS, FRACP
Dr Benjamin Trewin, MBBS, FRACP (Neuroimmunology and MS Fellow)
A/Professor Michael Buckland, BSc (Med), MBBS, PhD, FRCPA (MS Brain Bank co-director)
Dr Tony Harding (MS Brain Bank Manager)
A/Prof. Alexander Klistorner, PhD.
Dr. Chenyu Wang, PhD
Dr Marinda Taha PhD (MS Clinical Trials Manager)
Annmaree O'Connell (MS CNC and clinical researcher)
Dr Keri Diamond (Neuropsychologist)
Ms Caitlin Dawes (Clinical Psychologist and Neuropsychology Registrar)
Dr. Hao Xiong, PhD (BMC postdoctoral researcher)
Mr. Kain Kyle, MS (physicist)
Dr. Kaushik Ram, PhD (postdoctoral researcher)
Dr. Linda Ly, PhD (postdoctoral researcher)
Dr. Justin Garber, MBBS, FRACP (PhD candidate)
Dr. Joshua Barton, MBBS, FRACP (PhD candidate)
Dr. Heidi Beadnall, MBBS, FRACP (PhD candidate)
Dr Mahtab Ghadiri, MBBS, FRACP (PhD candidate)
Dr Grace Lu, MBBS (Honours student)

Pain Management

Photobiomodulation (PBM)

A Chan, R Chow, T Kaplinovsky, P Armati

This project explores the use of a-thermal low level application of photobiomodulation (PBM) delivered by contribution laser devices – both with anaesthetic applications in dentistry as well as pain management in nerve injury. The research contributed to the award of a PhD for Dr. Ambrose Chan with a title of “Quantitative Optimization, Standardization and Individualization of Photobiomodulation Delivery in Dentistry: Photobiomodulation Pre-emptive Dental Anaesthesia Delivered by Neodymium: Yttrium Aluminium Garnet (Nd:YAG) Photons.”

The work has also been presented at multiple meetings, including a multidisciplinary meeting of dentistry and clinical streams entitled “Photobiomodulation Therapy (PBMT): New Frontiers in Neurological Disorders & Practical Applications in Dentistry & Primary Care Settings in Medicine & Allied Health.” This meeting was held at the Brain and Mind Centre, University of Sydney, in June 2018.

Molecular Heterogeneity in Diffuse Gliomas

RPA Department of Neuropathology, Brain & Mind Centre, University of Sydney

Michael Buckland, Grace Wei, Maggie Lee, Kim Kaufman, John Turchini

Nerve Research Foundation 2018 Annual Report

Gliomas are the most common brain tumours of adults and children. They are devastating tumours that are resistant to surgery and chemoradiotherapy, and most are fatal. Unlike more common cancers, we still have no idea of how or why gliomas occur in some individuals. In the last 5 years great progress has been made in defining some of the common genetic lesions associated with glioma growth and progression. An important unanswered question is whether these genetic lesions are present throughout a tumour, or restricted to a subset of tumour cells, and if their distribution changes with treatment or tumour progression.

We have been examining a large number of brain tumour samples in order to define the extent of this 'molecular heterogeneity' We have used a variety of techniques to quantify the level of various mutations, as well as visualising the distribution of mutations in individual cells within a tumour. Support from the Nerve Research Foundation has allowed us to apply state of the art deep sequencing techniques to comprehensively examine a panel of over 50 genetic mutations in each sample. We have completed our deep sequencing analysis on over 100 such tumours now. Our results indicate that molecular heterogeneity is very rare in primary untreated gliomas, but is not uncommon in recurrent tumours after chemotherapy. This phenomenon of 'hypermutation' after chemotherapy in a subset of tumours indicates that treatment of these recurrent tumours may need to be different to that of recurrent tumours not exhibiting hypermutation. Evidence from other cancers suggests that these hypermutated tumours may be amenable to new forms of immunotherapy.

This work was presented at the 19th International Congress of Neuropathology (ICN) in Tokyo Japan, 23 - 27 September 2018. This was an invited (plenary) presentation, entitled "Molecular heterogeneity in diffuse gliomas." The work is currently being prepared for publication.

Publications - Researchers Associated with the NRF

Garg, N., Park, S., Howells, J., Noto, Y., Vucic, S., Yiannikas, C., Tomlinson, S., Huynh, W., Simon, N., Mathey, E., Spies, J., Pollard, J., Kiernan, M., et al (2018). Anti-MAG neuropathy: Role of IgM antibodies, the paranodal junction and juxtaparanodal potassium channels. *Clinical Neurophysiology*, 129(10), 2162-2169.

Kieseier, B., Mathey, E., Sommer, C., Hartung, H. (2018). Immune-mediated neuropathies. *Nature Reviews Disease Primers*, 4(1), 31.

Garg, N., Park, S., Yiannikas, K., Vucic, S., Howells, J., Noto, Y., Mathey, E., Pollard, J., Kiernan, M. (2018). Neurofascin-155 IgG4 Neuropathy: Pathophysiological insights, spectrum of clinical severity and response to treatment. *Muscle and Nerve*, 57(5), 848-851.

Ng, D., Chan, A., Papadopoulou, K., Dalci, O., Petocz, P., Darendeller, M. A., (2018). The effect of low-level laser therapy on orthodontically induced root resorption: a pilot double blind randomized controlled trial. *European Journal of Orthodontics*, 40, 317-325.

Tsugawa J, Dharmadasa T, Ma Y, Huynh W, Vucic S, Kiernan MC (2018); Fasciculation intensity and disease progression in amyotrophic lateral sclerosis; *Clin Neurophysiol*. 2018 Oct;129(10):2149-2154. doi: 10.1016/j.clinph.2018.07.015.

Garg N, Park SB, Howells J, Noto YI, Vucic S, Yiannikas C, Tomlinson SE, Huynh W, Simon NG, Mathey EK, Spies J, Pollard JD, Krishnan AV, Kiernan MC (2018); Anti-MAG neuropathy: Role of IgM antibodies, the paranodal junction and juxtaparanodal potassium channels; *Clin Neurophysiol*. 2018 Oct; 129(10):2162-2169. doi: 10.1016/j.clinph.2018.07.021.

Ahmed RM, Goldberg ZL, Kaizik C, Kiernan MC, Hodges JR, Piguet O, Irish M (2018); Neural correlates of changes in sexual function in frontotemporal dementia: implications for reward and physiological functioning. *J Neurol*. 2018 Aug 28. doi: 10.1007/s00415-018-9024-3

Howells J, Matamala JM, Park SB, Garg N, Vucic S, Bostock H, Burke D, Kiernan MC (2018); In vivo evidence for reduced ion channel expression in motor axons of patients with amyotrophic lateral sclerosis; *J Physiol*. 2018 Sep 2. doi: 10.1113/JP276624

Arnold R, Pianta TJ, Pussell BA, Endre Z, Kiernan MC, Krishnan AV (2018); Potassium control in chronic kidney disease: Implications for neuromuscular function; *Intern Med J*. 2018 Sep 19. doi: 10.1111/imj.14114

Arnold R, Pianta TJ, Pussell BA, Endre Z, Kiernan MC, Krishnan AV. (2018); Potassium control in chronic kidney disease: Implications for neuromuscular function; *Intern Med J*. 2018 Sep 19. doi: 10.1111/imj.14114

Vincent A, Pettingill P, Pettingill R, Lang B, Birch R, Waters P, Irani SR, Buckley C, Watanabe O, Arimura K, Kiernan MC (2018); Association of Leucine-Rich Glioma Inactivated Protein 1, Contactin-Associated Protein 2, and Contactin 2

Antibodies With Clinical Features and Patient-Reported Pain in Acquired Neuromyotonia.; *JAMA Neurol.* 2018 Sep 17. doi: 10.1001/jamaneurol.2018.2681.

Devenney EM, Ahmed RM, Halliday G, Piguet O, Kiernan MC, Hodges JR (2018); Psychiatric disorders in C9orf72 kindreds: Study of 1,414 family members; *Neurology.* 2018 Sep 26. pii: 10.1212/WNL.0000000000006344. doi: 10.1212/WNL.0000000000006344

Baker MR, Dharmadasa T, Jaiser SR, Kiernan MC (2018); Amyotrophic lateral sclerosis - Time for beta testing?; *Clin Neurophysiol. Jul; 129(7):1455-1456.* doi: 10.1016/j.clinph.2018.04.613.

Tu S, Menke RAL, Talbot K, Kiernan MC, Turner MR (2018); Regional thalamic MRI as a marker of widespread cortical pathology and progressive frontotemporal involvement in amyotrophic lateral sclerosis; *J Neurol Neurosurg Psychiatry.* 2018 Jul 26. pii: jnnp-2018-318625. doi: 10.1136/jnnp-2018-318625.

Noto YI, Garg N, Li T, Timmins HC, Park SB, Shibuya K, Shahrizaila N, Huynh W, Matamala JM, Dharmadasa T, Yiannikas C, Vucic S, Kiernan MC (2018); Comparison of cross-sectional area and distal-proximal nerve ratios in amyotrophic lateral sclerosis; *Muscle Nerve.* 2018 Jul 17. doi: 10.1002/mus.26301.

Menon P, Kiernan MC, Vucic S (2018); Cortical excitability varies across different motor regions; *J Neurophysiol.* 2018 Jul 5. doi: 10.1152/jn.00148.2018

Kandula T, Farrar MA, Cohn RJ, Mizrahi D, Carey K, Johnston K, Kiernan MC, Krishnan AV, Park (2018); Chemotherapy-Induced Peripheral Neuropathy in Long-term Survivors of Childhood Cancer: Clinical, Neurophysiological, Functional, and Patient-Reported Outcomes; *JAMA Neurol.* 2018 May 14. doi: 10.1001/jamaneurol.2018.0963

Borire AA, Issar T, Kwai NC, Visser LH, Simon NG, Poynten AM, Kiernan MC, Krishnan AV (2018); Correlation between markers of peripheral nerve function and structure in type 1 diabetes; *Diabetes Metab Res Rev.* 2018 Jun 1:e3028. doi: 10.1002/dmrr.3028.

Agarwal S, Koch G, Hillis AE, Huynh W, Ward NS, Vucic S, Kiernan MC (2018); Interrogating cortical function with transcranial magnetic stimulation: insights from neurodegenerative disease and stroke; *J Neurol Neurosurg Psychiatry.* 2018 Jun 4. pii: jnnp-2017-317371. doi: 10.1136/jnnp-2017-317371

Agarwal S, Highton-Williamson E, Caga J, Matamala JM, Dharmadasa T, Howells J, Zoing MC, Shibuya K, Geevasinga N, Vucic S, Hodges JR, Ahmed RM, Kiernan MC (2018); Primary lateral sclerosis and the amyotrophic lateral sclerosis-frontotemporal dementia spectrum; *J Neurol.* 2018 Jun 4. doi: 10.1007/s00415-018-8917-5

Makker PGS, Matamala JM, Park SB, Lees JG, Kiernan MC, Burke D, Moalem-Taylor G, Howells J (2018); A unified model of the excitability of mouse sensory and motor axons; *J Peripher Nerv Syst.* 2018 Jun 19. doi: 10.1111/jns.12278.

Garg N, Park SB, Kiernan MC (2018); Inflammatory neuropathies: all shapes and sizes; *J Neurol Neurosurg Psychiatry.* pii: jnnp-2018-318513. doi: 10.1136/jnnp-2018-318513.

Ahmed RM, Dupuis L, Kiernan MC (2018); Paradox of amyotrophic lateral sclerosis and energy metabolism; *J Neurol Neurosurg Psychiatry.* 2018 May 7. pii: jnnp-2018-318428. doi: 10.1136/jnnp-2018-318428.

Dharmadasa T, Huynh W, Tsugawa J, Shimatani Y, Ma Y, Kiernan MC (2018); Implications of structural and functional brain changes in amyotrophic lateral sclerosis; *Expert Rev Neurother.* 2018 May; 18(5):407-419. doi: 10.1080/14737175.2018.1464912

Henderson RD, Garton FC, Kiernan MC, Turner MR, Eisen A (2018); Human cerebral evolution and the clinical syndrome of amyotrophic lateral sclerosis; *J Neurol Neurosurg Psychiatry.* 2018 Apr 17. pii: jnnp-2017-317245. doi: 10.1136/jnnp-2017-317245.

Van den Bos MAJ, Menon P, Howells J, Geevasinga N, Kiernan MC, Vucic S (2018); Physiological Processes Underlying Short Interval Intracortical Facilitation in the Human Motor Cortex; *Front Neurosci.* 2018 Apr 11; 12:240. doi: 10.3389/fnins.2018.00240.

Matamala JM, Howells J, Dharmadasa T, Huynh W, Park SB, Burke D, Kiernan MC (2018); Excitability of sensory axons in amyotrophic lateral sclerosis; *Clin Neurophysiol.* 2018 Apr 2. pii: S1388-2457(18)30268-2. doi: 10.1016/j.clinph.2018.03.014.

Van Hummel A, Chan G, van der Hoven J, Morsch M, Ippati S, Suh L, Bi M, Asih PR, Lee WS, Butler TA, Przybyla M, Halliday GM, Piguet O, Kiernan MC, Chung RS, Ittner LM, Ke YD (2018); Selective Spatiotemporal Vulnerability of Central Nervous System Neurons to Pathologic TAR DNA-Binding Protein 43 in Aged Transgenic Mice; *Am J Pathol.* 2018 Mar 22. pii: S0002-9440(17)31124-0. doi: 10.1016/j.ajpath.2018.03.002

Noto YI, Simon NG, Selby A, Garg N, Shibuya K, Shahrizaila N, Huynh W, Matamala JM, Dharmadasa T, Park SB, Vucic S, Kiernan MC (2018); Ectopic impulse generation in peripheral nerve hyperexcitability syndromes and amyotrophic lateral sclerosis; *Clin Neurophysiol.* 2018 May; 129(5):974-980. doi: 10.1016/j.clinph.2018.01.061.

Issar T, Arnold R, Kwai NCG, Pussell BA, Endre ZH, Poynten AM, Kiernan MC, Krishnan AV (2018); The utility of the Total Neuropathy Score as an instrument to assess neuropathy severity in chronic kidney disease: A validation study; *Clin Neurophysiol.* 2018 May; 129(5):889-894. doi: 10.1016/j.clinph.2018.02.120.

- Dharmadasa T, Kiernan MC (2018); Riluzole, disease stage and survival in ALS; *Lancet Neurol.* 2018 May; 17(5):385-386. doi: 10.1016/S1474-4422(18)30091-7.
- Sheean RK, McKay FC, Cretney E, Bye CR, Perera ND, Tomas D, Weston RA, Scheller KJ, Djouma E, Menon P, Schibeci SD, Marmash N, Yerbury JJ, Nutt SL, Booth DR, Stewart GJ, Kiernan MC, Vucic S, Turner BJ. (2018); Association of Regulatory T-Cell Expansion With Progression of Amyotrophic Lateral Sclerosis: A Study of Humans and a Transgenic Mouse Model: *JAMA Neurol.* 2018 Mar 5. doi: 10.1001/jamaneurol.2018.0035.
- Ahmed RM, Dupuis L, Kiernan MC (2018); Paradox of amyotrophic lateral sclerosis and energy metabolism: *J Neurol Neurosurg Psychiatry.* 2018 May 7. pii: jnnp-2018-318428. doi: 10.1136/jnnp-2018-318428.
- Matamala JM, Howells J, Dharmadasa T, Trinh T, Ma Y, Lera L, Vucic S, Burke D, Kiernan MC (2018); Inter-session reliability of short-interval intracortical inhibition measured by threshold tracking TMS: *Neurosci Lett.* 2018 Mar 1. pii: S0304-3940(18)30154-X. doi: 10.1016/j.neulet.2018.02.065
- Howells J, Bostock H, Park SB, Kiernan MC, Burke D (2018); Tracking small sensory nerve action potentials in human axonal excitability studies: *J Neurosci Methods.* 2018 Mar 15; 298:45-53. doi: 10.1016/j.jneumeth.2018.02.003.
- Bueno APA, Pinaya WHL, Moura LM, Bertoux M, Radakovic R, Kiernan MC, Teixeira AL, de Souza LC, Hornberger M, Sato JR (2018); Structural and functional papez circuit integrity in amyotrophic lateral sclerosis: *Brain Imaging Behav.* 2018 Jan 27. doi: 10.1007/s11682-018-9825-0.
- Kiernan MC (2018); Motor neuron disease in 2017: Progress towards therapy in motor neuron disease: *Nat Rev Neurol.* 2018 Feb; 14 (2):65-66. doi: 10.1038/nrneurol.2017.186.
- Park SB, Kiernan MC (2018); Oxaliplatin and neuropathy: A role for sodium channels: *Clin Neurophysiol.* 2018 Mar; 129 (3):670-671. doi: 10.1016/j.clinph.2017.12.028.
- Ahmed RM, Highton-Williamson E, Caga J, Thornton N, Ramsey E, Zoing M, Kim WS, Halliday GM, Piguet O, Hodges JR, Farooqi IS, Kiernan MC (2018); Lipid Metabolism and Survival Across the Frontotemporal Dementia-Amyotrophic Lateral Sclerosis Spectrum: Relationships to Eating Behavior and Cognition. *J Alzheimers Dis.* 2018; 61(2):773-783. doi: 10.3233/JAD-170660.
- Ting Shen, Yuyi You, Sukanya Arunachalam, Ariadna Fontes, Sidong Liu, Vivek Gupta, John Parratt, Chenyu Wang, Michael Barnett, Joshua Barton, Nitin Chitranshi, Ling Zhu, Clare L. Fraser, Stuart L. Graham, Alexander Klistorner and Con Yiannikas "Differing Structural and Functional Patterns of Optic Nerve Damage in Multiple Sclerosis and Neuromyelitis Optica Spectrum Disorder." *Ophthalmology*, 2018; 1–9.
- Alexander Klistorner, Chenyu Wang, Con Yiannikas, John Parratt, Joshua Barton, Yuyi You, Stuart L. Graham, and Michael H. Barnett. "Diffusivity in the Core of Chronic Multiple Sclerosis Lesions." *PLoS ONE* 13, no. 4 (2018): 1–20.
- Alexander Klistorner, Chenyu Wang, Con Yiannikas, John Parratt, Michael Dwyer, Joshua Barton, Stuart L. Graham, Yuyi You, Sidong Liu, and Michael H. Barnett. "Evidence of Progressive Tissue Loss in the Core of Chronic MS Lesions: A Longitudinal DTI Study." *NeuroImage: Clinical* 17, no. October 2017 (2018): 1028–35.
- Chenyu Wang, Alexander Klistorner, Linda Ly, and Michael H. Barnett. "White Matter Tract-Specific Quantitative Analysis in Multiple Sclerosis: Comparison of Optic Radiation Reconstruction Techniques." *PLoS ONE* 13, no. 1 (2018): 1–19.
- Grace Lu, Heidi N. Beadnall, Joshua Barton, Todd A. Hardy, Chenyu Wang, and Michael H. Barnett. "The Evolution of 'No Evidence of Disease Activity' in Multiple Sclerosis." *Multiple Sclerosis and Related Disorders* 20, no. October 2017 (2018): 231–38.
- Stephen W. Reddel, Michael H. Barnett, Sean Riminton, Tej Dugal, Katherine Buzzard, Chenyu Wang, Fiona Fitzgerald, Heidi N. Beadnall, Diane Erickson, David Gahan, Daniel Wang, Toby Ackland and Richard Thompson. "Successful Implementation of an Automated Electronic Support System for Patient Safety Monitoring: The Alemtuzumab in Multiple Sclerosis Safety Systems (AMS3) Study." *Multiple Sclerosis Journal* (2018), 135245851878367.
- Ebrahimkhani S, Vafae F, Hallal S, Wei H, Lee MYT, Young PE, Satgunaseelan L, Beadnall H, Barnett MH, Shivalingam B, Suter CM, Buckland ME, Kaufman KL. Deep sequencing of circulating exosomal microRNA allows non-invasive glioblastoma diagnosis. *NPJ Precis Oncol.* 2018 Dec 12;2:28. doi: 10.1038/s41698-018-0071-0. eCollection 2018. PubMed PMID: 30564636; PubMed Central PMCID: PMC6290767.
- Triplett JD, Yiannikas C, Barnett MH, Parratt J, Barton J, Graham SL, You Y, Klistorner A. Pathophysiological basis of low contrast visual acuity loss in multiple sclerosis. *Ann Clin Transl Neurol.* 2018 Oct 24;5(12):1505-1512. doi: 10.1002/acn3.659. eCollection 2018 Dec. PubMed PMID: 30564617; PubMed Central PMCID: PMC6292188.

Min M, Spelman T, Lugaresi A, Boz C, Spitaleri D, Pucci E, Grand'Maison F, Granella F, Izquierdo G, Butzkueven H, Sanchez-Menoyo JL, Barnett M, Girard M, Trojano M, Grammond P, Duquette P, Sola P, Alroughani R, Hupperts R, Vucic S, Kalincik T, Van Pesch V, Lechner-Scott J. Silent lesions on MRI imaging - Shifting goal posts for treatment decisions in multiple sclerosis. *Mult Scler*. 2018 Oct;24(12):1569-1577. doi: 10.1177/1352458518798147. Epub 2018 Sep 20. PubMed PMID: 30234431.

Kalincik T, Jokubaitis V, Spelman T, Horakova D, Havrdova E, Trojano M, Lechner-Scott J, Lugaresi A, Prat A, Girard M, Duquette P, Grammond P, Solaro C, Grand'Maison F, Hupperts R, Prevost J, Sola P, Ferraro D, Terzi M, Butler E, Slee M, Kermodé A, Fabis-Pedrini M, McCombe P, Barnett M, Shaw C, Hodgkinson S, Butzkueven H; MSBase Study Group. Cladribine versus fingolimod, natalizumab and interferon β for multiple sclerosis. *Mult Scler*. 2018 Oct;24(12):1617-1626.

Garber JY, Barnett MH. We should focus more on finding therapeutic targets for the non-inflammatory damage in MS - Yes. *Mult Scler*. 2018 Sep;24(10):1272-1274. doi: 10.1177/1352458518770970. Epub 2018 Apr 16. PubMed PMID: 29656673.

Chaseling GK, Filingeri D, Barnett M, Hoang P, Davis SL, Jay O. Cold Water Ingestion Improves Exercise Tolerance of Heat-Sensitive People with MS. *Med Sci Sports Exerc*. 2018 Apr;50(4):643-648. doi: 10.1249/MSS.0000000000001496. PubMed PMID: 29140896.

Fragoso YD, Spelman T, Boz C, Alroughani R, Lugaresi A, Vucic S, Butzkueven H, Terzi M, Havrdova E, Horakova D, Granella F, Olascoaga J, Sánchez-Menoyo JL, Pucci E, Barnett M, Brooks JBB, Haartsen J; Lymphopenia and Efficacy of Fingolimod MSBase sub-study Investigators. Lymphocyte count in peripheral blood is not associated with the level of clinical response to treatment with fingolimod. *Mult Scler Relat Disord*. 2018 Jan;19:105-108.

Ramanathan S, Mohammad S, Tantsis E, Nguyen TK, Merheb V, Fung VSC, White OB, Broadley S, Lechner-Scott J, Vucic S, Henderson APD, Barnett MH, Reddel SW, Brilot F, Dale RC; Australasian and New Zealand MOG Study Group. Clinical course, therapeutic responses and outcomes in relapsing MOG antibody-associated demyelination. *J Neurol Neurosurg Psychiatry*. 2018 Feb;89(2):127-137. doi: 10.1136/jnnp-2017-316880. Epub 2017 Nov 15. PubMed PMID: 29142145; PubMed Central PMCID: PMC5800335.

Moore JJ, Massey JC, Ford CD, et al. Prospective phase II clinical trial of autologous haematopoietic stem cell transplant for treatment refractory multiple sclerosis. *J Neurol Neurosurg Psychiatry* Published Online First: 11 December 2018. doi:10.1136/jnnp-2018-319446

Zhang C, Song Y, Liu S, Lill, S, Wang, C, Tang Z, You Y, Gao Y, Klistorner A, Barnett M, Cai W. "MS-GAN: GAN-Based Semantic Segmentation of Multiple Sclerosis Lesions in Brain Magnetic Resonance Imaging," 2018 Digital Image Computing: Techniques and Applications (DICTA), Canberra, Australia, 2018, pp. 1-8.

doi: 10.1109/DICTA.2018.8615771

URL: <http://ieeexplore.ieee.org/stamp/stamp.jsp?tp=&arnumber=8615771&isnumber=8615748>

Tang Z, Wang C, Hoang P, Liu S, Cai W, Soligo D, Oliver R, Barnett M. (2018) Automatic Segmentation of Thigh Muscle in Longitudinal 3D T1-Weighted Magnetic Resonance (MR) Images. In: Melbourne A. et al. (eds) Data Driven Treatment Response Assessment and Preterm, Perinatal, and Paediatric Image Analysis. PIPPI 2018, DATRA 2018. Lecture Notes in Computer Science, vol 11076. Springer, Cham

Christogianni A, Bibb R, Davis SL, Jay O, Barnett M, Evangelou N & Filingeri D (2018) Temperature sensitivity in multiple sclerosis: An overview of its impact on sensory and cognitive symptoms, *Temperature*, 5:3, 208-223, DOI: 10.1080/23328940.2018.1475831

Hardy, TA. Regulatory B cells: the key to post-alemtuzumab rebound phenomena in multiple sclerosis? *Mult Scler*. 2018.

Hardy, TA. How should we diagnose acute disseminated encephalomyelitis? *Dev Med Child Neurol*. 2018 Nov;60(11):1070.

Invited Talks

Emily Mathey. Autoantibody responses to nodal and paranodal antigens in chronic inflammatory neuropathies: targets, pathogenesis and clinical relevance. 14th ISNI Congress, Brisbane, Australia, August 27 – 31, 2018. Speaker

Michael Buckland. Molecular heterogeneity in diffuse gliomas. 19th International Congress of Neuropathology (ICN), Tokyo, Japan, September 23 – 27, 2018. Plenary lecture

Ambrose Chan. Photobiomodulation in dentistry. International Dental Exhibition and Meeting Congress, Suntec Convention Centre, Singapore April 11 – 13, 2018. Keynote speaker

Ambrose Chan. Lasers – enhancing dentistry. International College of Dentists Sections XV and XIII, International Scientific & Induction Ceremony Congress, Conrad Convention Centre, Macau, SAR China, June 21, 2018. Speaker

Ambrose Chan. Photobiomodulation delivered target in pre-emptive dental anaesthesia. Launching PBMt into Mainstream Medicine: Breaking Down the Barriers, Australian Medical Laser Association Annual Meeting, Sydney, Australia, September 15 – 16, 2018. Speaker

Ambrose Chan. The effects of photobiomodulation delivered by pulsed Nd:YAG laser on cultured rat DRG neurons: relevance to clinical pre-emptive dental anaesthesia. 16th World Congress of World Federation for Laser Dentistry, Aachen, Germany, October 1 – 3, 2018. Speaker

Ambrose Chan. Laser (photons) – enhancing dentistry: understanding the clinical utility and performance. Gulf Dentex Congress, ADNEC, Abu Dhabi, October 21, 2018. Keynote speaker

Roberta Chow. Introduction to Photobiomodulation - Photobiomodulation therapy (PBMt): New Frontiers in Neurological Disorders & Practical Applications in Dentistry & Primary Care Settings in Medicine & Allied Health. Australian Medical Laser Association, Melbourne, Australia June 30 – July 1, 2018.

Roberta Chow. Introduction to Laser Safety. Launching PBMt into Mainstream Medicine: Breaking Down the Barriers, Australian Medical Laser Association, Sydney, Australia, September 15 – 16, 2018. Speaker

Roberta Chow. Photobiomodulation – (i) Mechanisms for Analgesia for Veterinary Medicine (ii) Overview of PBM and Neck Pain. Mechanisms and Clinical Application, World Association of Laser Therapy, Biennial Meeting, Nice, France October 2 -3, 2018. Speaker

Matthew Kiernan. (i) The use of nerve excitability testing in understanding ion channel dysfunction in Neuropathy (ii) MND: Therapeutic Landscapes (iii) Acquired distal motor syndromes. 15th International Congress on Neuromuscular Diseases, Vienna, Austria, July 2018. Invited speaker

Matthew Kiernan. Transmission: Roadmaps to therapy in ALS. European Network For The Cure Of ALS (ENCALS), Oxford, UK June 2018. Invited speaker

Matthew Kiernan. MND in Australia: where we have been, where we are and where we are going. Fight MND Australasian Symposium, Melbourne, Australia, March 22 – 24 2018. Organizer, Invited speaker

Matthew Kiernan. The impact of Medical Research. British Medical Journal (BMJ) Editors Retreat, London, UK, March 2018. Invited speaker

Matthew Kiernan. Clinical trials experience – the good, the bad and the ugly. Palliative Care Clinical Studies Collaborative (PaCSC), 9th Annual Research Forum, Sydney, February 27, 2018. Invited speaker

Conference Presentations

Garg N., Park SB., Howells J., Yiannikas C., Vucic S., Noto Y., Krishnan A., Spies J., Mathey EK., Pollard, JD., Kiernan M. Mechanisms of nerve dysfunction in immune-mediated neuropathies. MC ANZAN, Darwin, Australia, May 2018.

Garg, N., Park S., Howells J. Anti-MAG neuropathy: Role of IgM antibodies, the paranodal junction and juxtaparanodal potassium channels. Annual Meeting of the Peripheral Nerve Society, Baltimore, USA, July 2018.

Kaplinovsky T., Chan A., Armati P. Ratiometric imaging of mitochondrial membrane potential in cultured dorsal root ganglia cells. 19th International Microscopy Congress, Sydney, Australia, September 2018.

Books and Chapters

Chan, A. & Armati, P. 2018. Pre-emptive dental anaesthesia by pulsed Nd:YAG photobiomodulation. *In: BRUGNERA, A. & NAMOUR, S., eds. Laser Dentistry: Current Clinical Applications.* Florida: Universal Publishers, 263-284.

Dharmadasa T, Huynh W, Matamala JM, Zoing M, Kiernan MC. Balance, Gait and Falls in Motor Neuron Disease. In Brian Day, Stephen Lord (Eds); *Handbook in Clinical Neurology.* Elsevier (In Press 2018).

Huynh W, Dharmadasa T, Agarwal S, Caga J, Kiernan MC. Motor Neuron Disease. In Darren Hocking, John Bradshaw and Joanne Fielding (Eds); *Degenerative Disorders of the Brain.* Psychology Press, Taylor & Francis Group (In Press 2018).

Dharmadasa T, Huynh W, Kiernan MC. Transcranial magnetic stimulation in the dementias. The Neuroscience of Dementia. Kings College London (In Press 2018).

Simon NG, Kiernan MC. Disease definitions: Motor neurone disease and related disorders. International Classification of Diseases (ICD) – 11th Revision. Geneva: World Health Organization. (In press)

Certification Course Provider and Coordinator

Dr. Ambrose Chan

- World Federation for Laser Dentistry - Asia Pacific Division: International Dental Exhibition and Meeting - 2018 Pre-congress Laser Workshop: Incorporating Laser Technology into Clinical Dentistry, Suntec Convention Centre, Singapore, April 12, 2018.
- International College of Dentists Sections XV and XIII International Scientific & Induction Ceremony Pre-Congress Laser Certification Course, Conrad Convention Centre, Macau, SAR China, June 20, 2018.
- Gulf Dentex – Pre-congress Laser Certification Course, ADNEC, Abu Dhabi, October 20, 2018.

New Academic Appointment

Ambrose Chan. Honorary Assistant Professor, Faculty of Dentistry, University of Hong Kong, August 2018. The University of Hong Kong's Dental School has just been ranked Number 1 in dental research, three years in a row (2016-2018), in the QS World Universities Rankings.

Research monies granted to researchers associated with the NRF

Recipient of Grant	Title	Granting Body	Amount of Grant
Kiernan M, Lin C, Pollard J, Mathey E, Park S, Vucic S	Nodal Function in Peripheral Neuroinflammatory Disorders: Target Antigens, Functional Significance and Treatment Response	National Health and Medical Research Council (NHMRC)/Project Grants.	\$605,172 2016-2019
Barnett M	SOAR Research accelerator Fellowship	The University of Sydney	\$150,000 2017-2018
Barnett M, Barton J, Klistorner A, Wang T	Vision in Multiple Sclerosis	Sydney Neuroimaging Analysis Centre and Genzme-Sanofi	\$600,000 2016-2018
Calamante F, Tao D, Barnett M	NVIDIA Medical Imaging Computational and AI platform;	National Health and Medical Research Council (NHMRC)/Equipment Grants.	\$180,000
Wang C	Probing demyelination, remyelination and axonal loss: development of multi-modal, quantitative neuroimaging biomarkers in multiple sclerosis;	Multiple Sclerosis Research Australia/Postdoctoral Fellowships.	\$180,000
Sydney Neuroimaging Analysis Centre, The University of Sydney, I-MED Radiology	AI: new smarts for the medical imaging industry;	Cooperative Research Centres Projects (CRC-P) Grants	\$2.36m
Garber J	MRI Biomarkers and Mechanisms of Progression in Multiple Sclerosis.	Trish Foundation and MS Research Australia Postgraduate Scholarship	\$78,000
Beadnall H	Measuring changes in brain tissue volume over time using MRI.	Brain Foundation Gift	\$30,000
Hardy TA	Clinical and pathological characteristics of Baló's concentric sclerosis.	MS Research Australia Ian Ballard Travel Award.	\$5,000
Barnett M (MS Research Group)	MS Research - support research in Psychological/cognitive treatments for multiple sclerosis.	The Goodridge Foundation.	\$72,513

Nerve Research Foundation Financial Statements

The University of Sydney

Nerve Research Foundation

Notes to the Financial Statements for the year ended 31 December 2018

1. Statement of Significant Accounting Policies

- (a) These financial statements are special purpose financial statements that have been prepared on an accrual basis.
- (b) Income tax is not applicable to activities of the Foundation.

2. Unrealised Gain/(Loss) on Investments

The business model that relates to unitisation supports the classification and measurement of the majority of University financial assets at fair value. The unrealised gains/ (losses) as at 31 December are shown as “Unrealised Gain/ (Loss) on Investments” in the Income Statement. Long term investments are shown at market value in the Balance Sheet.

3. Accumulated Funds Adjustments

In 2017, funds relating to the Ignacy Burnett Bequest, accumulating to \$440,986 were transferred to the area in charge of its administration.

4. Contributions to University areas

In 2018, funds amounting to \$415,745 were transferred to Central Clinical School for a Neuroanalytics Platform.

The University of Sydney
Nerve Research Foundation

Income Statement
for the year ended 31 December 2017

	Notes	31 December 2018	31 December 2017
INCOME			
Scholarships, Donations and Bequests		110,213	22,468
Business and Investment Income		4,033	12,106
Realised Gain / (Loss) on Investments		84,634	4,648
Unrealised Gain / (Loss) on Investments		6,452	90,473
Internal and Other Income		0	0
Total Income		205,332	129,695
EXPENDITURE			
Services and Utilities		0	32
Contributions to University areas	4	415,745	88,085
Other expenses		(1,934)	8,879
Total Expenditure		413,811	96,996
Surplus / (Deficit)		(208,479)	32,699
Accumulated Funds		1,539,792	1,948,079
Accumulated Funds Adjustments	3	5,496	(440,986)
Total Accumulated Funds		1,336,809	1,539,792

The University of Sydney
Nerve Research Foundation

Balance Sheet
as at 31 December 2018

	Notes	31 December 2018	31 December 2017
ASSETS			
Current Assets			
Short Term Investments		342,464	440,767
Total Current Assets		<u>342,464</u>	<u>440,767</u>
Non Current Assets			
Long Term Investments		994,343	1,099,025
Total Non Current Assets		<u>994,343</u>	<u>1,099,025</u>
TOTAL ASSETS		<u>1,336,807</u>	<u>1,539,792</u>
NET ASSETS		<u>1,336,807</u>	<u>1,539,792</u>
EQUITY			
Accumulated Funds		1,336,807	1,539,792
TOTAL EQUITY		<u>1,336,807</u>	<u>1,539,792</u>

I certify that the Income Statement and Balance Sheet of the Foundation have been prepared in accordance with the University's accounting practices and procedures. These Foundation accounts form part of The University of Sydney's financial reports.

Petrus Swemmer
Finance Director
Faculties of Health
January 29, 2019

We again thank the Brain & Mind Centre of the University of Sydney, the Charles Perkins Centre and Australian Centre for Microscopy and Microanalysis for providing research facilities and support