BRAIN RESEARCH NEW ZEALAND

ANNUAL REPORT 2016

Brain Research
NEW ZEALAND
Rangahau Roro Aotearoa

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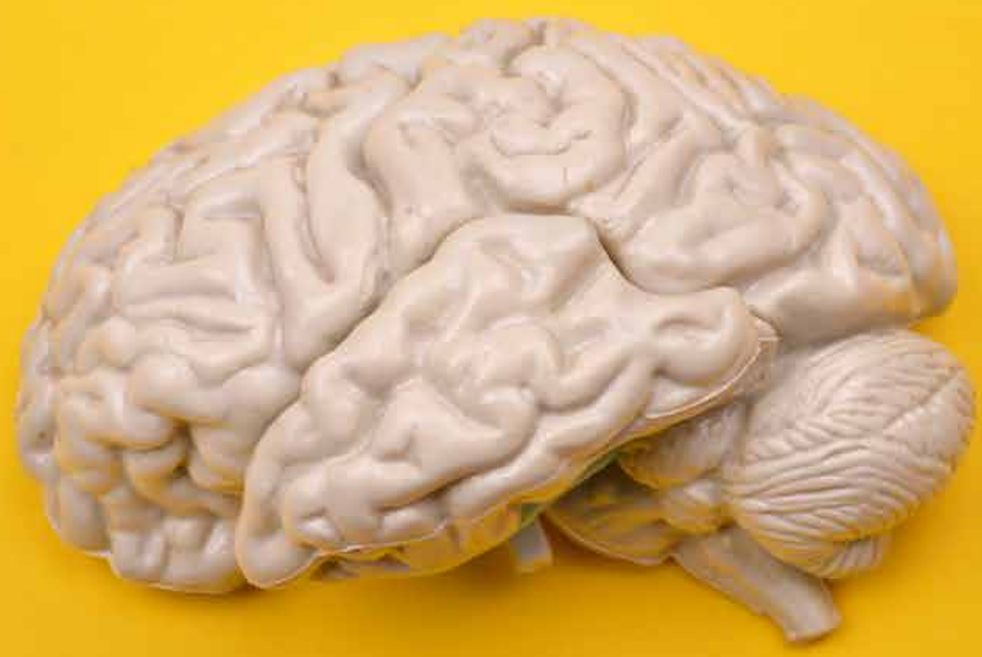
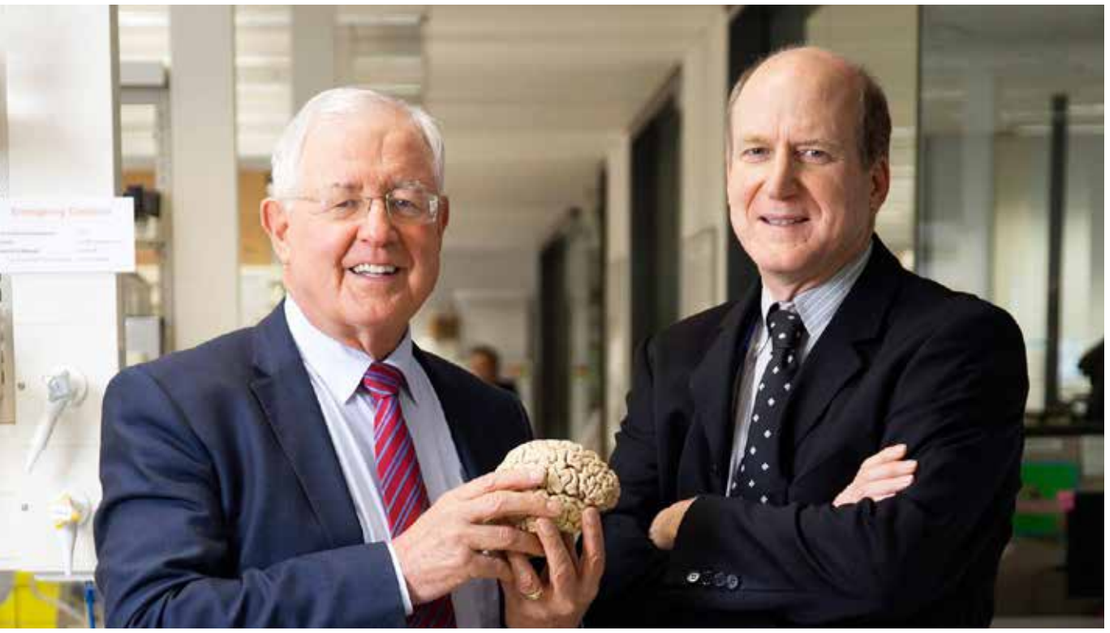
ABOUT US

Brain Research New Zealand - Rangahau Roro Aotearoa (BRNZ) is a national Centre for Research Excellence (CoRE) undertaking ground-breaking research on the ageing-brain and ageing-related neurological disorders.

We are a collection of leading neuroscientists and clinicians from across the country who are working alongside community organisations to combat neurological disorders, such as stroke, Parkinson's and Alzheimer's diseases and hearing loss, that pose the greatest medical and social challenge of our generation.

Our interdisciplinary approach, founded on the pillars of excellence and innovation, is the driver for undertaking biomedical research that will be translatable to the clinical setting, with the ultimate aim of improving brain health for all New Zealanders in the years to come.





A WORD
FROM OUR CO-DIRECTORS

Looking back over 2016 it is hard to believe it has been a mere two years since the launch of Brain Research New Zealand –Rangahau Roro Aotearoa and our mission to enhance lifelong brain health for all New Zealanders.

With the percentage of New Zealanders aged over 65 increasing year by year, New Zealand is facing a virtual tsunami of ageing-related neurological disorders – a challenge that will take a truly national effort to overcome.

In this our second annual report, you will read about the remarkable efforts that our scientists and clinicians have made in quickly establishing Brain Research New Zealand as a world-class research centre. With 69 investigators and 154 students across our four partner universities, BRNZ has the diverse talent and expertise to make pioneering discoveries that will fundamentally change our ability to detect and treat ageing-related neurological diseases. We are proud to report that the projects we began funding in 2015 are starting to bear fruit and that our visionary research strategy is coming to life. Our research into diagnostic techniques such as imaging and biological markers is bringing us closer to being able to identify specific groups of people at risk of cognitive decline and to use this knowledge to improve the development of new treatments.

Adding to the BRNZ-funded research portfolio, in 2016 our members secured over $30 million in external funding for related research projects, including prestigious Health Research Council Programme grants and Marsden Fund grants, indicative of the standout talent in our research team. Professors Donna-Rose Addis, Warren Tate, Richie Poulton and Valery Feigin were also formally recognised for their immense contribution to health research efforts nationally and abroad. The international and national profile of BRNZ was further enhanced by our members' frequent engagement with the media, radio and TV. We reached millions through regularly featuring in national and international new articles, and "Who am I" – the four-part documentary on the world-renown Dunedin Study - was picked up for screening by thirty networks syndicating in seventy countries worldwide.

But it's not just our seasoned researchers who are making a difference. BRNZ kicked off 2016 by celebrating the exceptional 'young talent' we have in our CoRE. Their enthusiasm, dedication and research skills are the critical ingredients for our success, now and in the future. In February 2016 we brought them together for BRNZ's first Early Career Researcher workshop. Over sixty of New Zealand's brightest young neuroscientists descended on Christchurch for two days of training, networking and dare we say it, fun. It was clear for all to see that BRNZ has an extraordinary cadre of young researchers rising through the ranks, and we are doing our utmost to make sure they experience the excitement and opportunities of collaborative CoRE research.

2016 also saw the continued development of our innovative Dementia Prevention Research Clinics, one of our signature initiatives. Associate Professor Lynette Tippett and her team have been working extensively with researchers, clinicians, District Health Boards and community groups to ensure our clinics meet international "gold standards". In 2017, we'll reap the harvest of this groundwork when we launch two more clinics in Dunedin and Christchurch, an immense achievement made possible by the support of the Dementia Prevention Trust and many generous philanthropists.

BRNZ also accelerated our community engagement in 2016, to encourage the uptake of our research by the community and the many stakeholders we serve. Members of our CoRE, for instance, participated in, and even led, numerous Alzheimer's Awareness Month events –memory walks, informative public forums, and presentations on cutting-edge research. Whether addressing a small care group in Balclutha or leading a march of hundreds of people in Taranaki, BRNZ was a regular voice to be heard in communities throughout New Zealand.

In early 2016, Dr Hinemoa Elder joined BRNZ as our Kaiwhakahaere Māori. We asked Hinemoa to join our CoRE to guide us in partnering with Māori in a meaningful way, and to help us build a thriving Māori neuroscience and healthcare workforce for New Zealand. Hinemoa has led us down exciting pathways of Māori engagement. We had our first wānanga with our Māori community partners - Te Kura Kaupapa Māori o Hoani Waititi in Tāmaki Makarau and Puketeraki Marae, Ōtepoti – and we are providing regular opportunities to meet in order to ensure our Māori communities are at the forefront of research collaboration. Our Māori research funding is supporting an exciting variety of opportunities for Māori career development in neuroscience. And importantly, we have had our first wānanga in Te Reo Māori with kaumātua to explore the mātauranga of this field of research.

At its core, Brain Research New Zealand's mission is to combine world class scientific research with the clinical expertise of New Zealand's best health professionals to advance the diagnosis and treatment of ageing-related neurological disorders. We are your centre; and with every year we work together, our vision of lifelong brain health for all New Zealanders becomes closer to reality.

Distinguished Professor
Richard Faull, KNZM, FRSNZ
University of Auckland

Professor
Wickliffe Abraham, FRSNZ
University of Otago

OUR GOAL
FOR NEW ZEALAND

OUR VISION

Lifelong Brain health for all New Zealanders.

OUR MISSION

To unlock the secrets of the ageing brain and develop new therapies and better clinical and community care to enhance life-long brain health for all New Zealanders.

OUR STRATEGIC OUTCOME TARGETS

01
Better health outcomes, improved quality of life and positive ageing for older persons and their families, including reduced physical, emotional, social and financial costs of ageing-related neurological disorders, through public dissemination of the latest research and the creation of partnerships with patients, families, community organisations and NGOs across NZ.

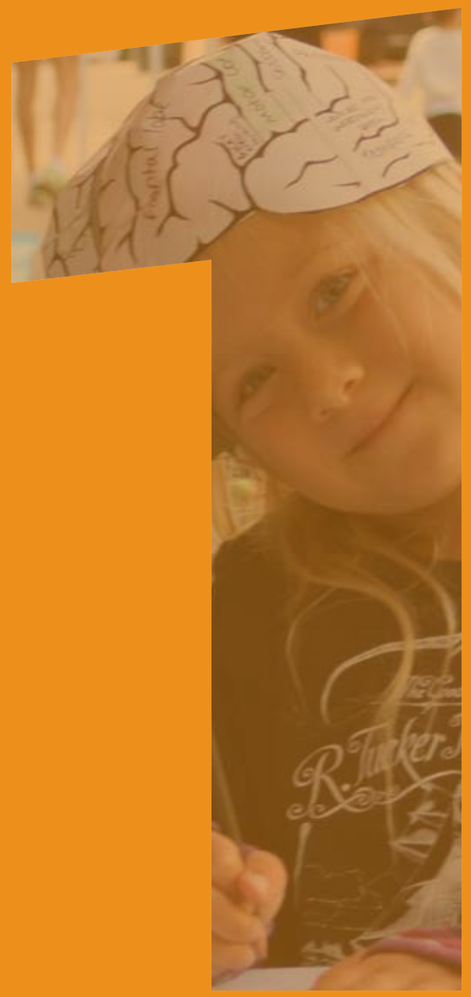
02
A Centre of Neuroscience Research Excellence that is nationally and internationally recognised and sought after for its expertise and innovation in the study of the ageing brain.

03
Improved strategies for prevention, early detection and slowing of progression of ageing-related neurological disorders, through identification of early biomarkers and an improved understanding of the mechanisms of ageing-related neurological disorders.

04
Improved clinical practice by translating scientific knowledge into treatments, strategies and care pathways aimed at delaying or moderating ageing-related neurological disorders.

05
Increased scientific, clinical, translational and leadership capability that will improve research output, patient outcomes, productivity and health industry research capacity.

06
Improved Māori health and wellbeing during ageing by working with Māori communities to understand their needs and value and build equal relationships, incorporating Mātauranga into innovative research and clinical methods, and by supporting Māori to determine their own pathways to brain health through training of Māori neuroscientists and clinicians.



IN THE

COMMUNITY

The population demographic of New Zealand, like other developed nations, is an ageing one.

The rate of change is so fast, in fact, that by 2040 almost one quarter of the population (between 1.28 and 1.37 million New Zealanders) will be over 65. And as the number of older New Zealanders grows, so too will the number of people affected by neurological disorders.

Once a person is over 65, their risk of developing Alzheimer's or Parkinson's disease increases exponentially. Once over 85, their risk of dementia is close to 1 in 2. Yet despite this, a large majority of New Zealanders know very little of what lies ahead in their ageing years and how substantially their lives will be affected by disorders of the brain.

A major aim of BRNZ is to invest in an extensive community outreach programme that gives our scientists the opportunity to share their research and scientific knowledge with the public - through the media, public lectures, community engagement days, Q&A forums and countless other channels. Looking back over 2016, we are humbled by the level of support we have received from community organisations, patients and their families- all of whom share our unwavering commitment to improving the quality of life of New Zealand's ageing population.

BRAIN AWARENESS WEEK

Neuroplasticity *is the brain's amazing ability to grow, adapt, and rewire itself, not only for the purpose of memory storage, but also to compensate for injury and disease. Harnessing neuroplasticity has far-reaching implications for new models of healthcare.*

The backbone of BRNZ's community outreach programme is Brain Awareness Week, a global campaign to increase public awareness of the progress and benefits of brain research.

Brain Awareness Week (BAW) was founded by the Dana Alliance (based in New York) over twenty years ago, and now serves as a means of uniting the efforts of some 22,000 organisations around the world to bring attention to advances in brain research and to advocate for science funding. In New Zealand, the Neurological Foundation has been supporting BAW events for 11 years. BRNZ is proud to have been involved since its inception.

In 2016, the public turned out in force to participate in informative and entertaining events led by BRNZ scientists, clinicians and students at BAW events across the country. In Auckland, our younger scientists were also on hand to introduce children to the wonders of the human brain through the use of games and interactive activities. Associate Professor Cathy Stinear, Professor Peter Thorne and Dr Melanie Cheung also explained in an informal panel discussion how our brains can change through neuroplasticity.

In Dunedin, Neurological Foundation of New Zealand Professor of Neurosurgery, Dirk De Ridder, Professors Leigh Hale, Warren Tate, and Russell Snell gave public presentations at the Otago Museum, highlighting what is being done locally and abroad to tackle Alzheimer's disease, Huntington's disease, stroke and Parkinson's disease. Professor Snell kick-started the series with a talk on his revolutionary research involving the genetics of Alzheimer's, Huntington's and autism. Recent progress in these areas of research is setting the world stage for innovative new breakthroughs – with leading contributions from Professor Snell's lab. Neurological Foundation Chair of Neurosurgery Professor De Ridder sat down with Sue Giddens of the Neurological Foundation to update the public on his exciting research into brain implants and their potential to combat addiction, yet another health issue facing ageing New Zealanders.

BRINGING IN THE BIG GUNS

PROFESSOR EMERITUS DAVID SMITH / LEFT
The University of Oxford

PROFESSOR JOHN ROTHWELL / RIGHT
The University College London

In February 2016, BRNZ held two highly successful public lectures in partnership with the Neurological Foundation of New Zealand.

On February 3rd, BRNZ Science Board member **Professor Emeritus David Smith** of the University of Oxford, gave a lecture titled "Can we prevent Alzheimer's Disease?" at the Faculty of Medicine in Auckland. His answer, presented with a significant amount of evidence, was a resounding "yes". David has been at the forefront of research into novel treatments for Alzheimer's disease and dementia for over fifty years. In February, the public were relieved to hear that contrary to popular belief, dementia is not an inevitable part of ageing. By adopting healthy behaviours such as stopping smoking, eating fish, watching your blood glucose levels, exercising and keeping mentally and socially active, you can age successfully and with a healthy brain. February also saw BRNZ and the Neurological Foundation host another Science Board member, **Professor John Rothwell** of University College London. John is a world-leader in human movement function research and non-invasive brain stimulation techniques for enhancing brain function in neurological disorders. He gave a public lecture in Dunedin on the ability of electrical stimulation to harness the natural power of the human brain. The brain is an electrically excitable organ, and stimulation of the brain is proving an increasingly popular technique being used by researchers to find treatments for neurological disorders such as Parkinson's disease, stroke and Tourette's syndrome, and psychological disorders like depression. In his lecture, John talked about how cutting-edge stimulation technologies may be able to change the excitability of neurons in specific regions of the brain, so that functions such as cognition, movement or memory may be restored or improved.

Through our public lecture series, Brain Research New Zealand aims to bring the world's most inspired researchers and clinicians to the public's front door to share their expertise, to spark conversation, and to equip New Zealanders with the information they need to look after their brain health.

WORLD ALZHEIMER'S MONTH 2016

World Alzheimer's Month is an international campaign held in September each year to raise awareness of, and challenge, the stigma that surrounds dementia.

World Alzheimer's Month started in 2012, and this year BRNZ supported the campaign efforts. When faced with a parent, partner or friend suffering from Alzheimer's, people often find themselves grappling with decisions about a loved one's care that they simply don't understand. They can also feel scared and overwhelmed by what the future holds. To help allay these fears, and to shed some light on Alzheimer's, we took to the road, running an extensive month-long campaign with regional New Zealand Alzheimer's organisations to increase public understanding of the disease.

BRNZ ran public forums and Q&A sessions out in the community in partnership with Alzheimer's organisations in Manawatu, Napier, Nelson, Northland, Otago, Taranaki, Tauranga, Waikato, Whakatane and Wairarapa. These face-to-face forums gave people the opportunity to meet our researchers, to learn about what we do and to share their own experiences of living with the disease.

We supplemented our public forum series with a month-long social marketing campaign, taking the message to thousands of Kiwis from Cape Reinga to Bluff.

ALZHEIMER'S NEW ZEALAND CONFERENCE

FROM LEFT / **SIR RICHARD FAULL, JAN WHITE, NGAIRE DIXON AND DIANA FAULL**

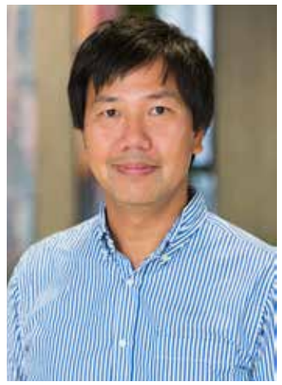
ASSOCIATE PROFESSOR MAURICE CURTIS

2016 culminated in the Alzheimer's New Zealand and 19th Asia Pacific Regional Conference for Alzheimer's disease in Wellington in November.

Alzheimer's NZ is our country's leading dementia support organisation, with eighteen regional branches throughout the country. Each year, it supports tens of thousands of New Zealanders affected by dementia by raising awareness, providing information and resources, advocating for quality care services, and by promoting research about prevention, treatment, cure and care of people affected by the disease.

Like BRNZ, one of Alzheimer's New Zealand's core values is to collaborate with like-minded organisations to ensure a standard of excellence which is in the best interests of all those affected by dementia. Alzheimer's NZ's values, expertise and community outreach make them the ideal partner for BRNZ, and we were privileged to sponsor their conference "Dementia Today: Diverse Communities, Collective Action". With nearly four hundred people in attendance, we met people from health, education, government, and residential care and dementia services and talked to them about our Dementia Prevention Research Clinics and about BRNZ's research more broadly. BRNZ researcher Associate Professor Maurice Curtis gave a keynote presentation "Is the brain flexible in Alzheimer's disease". He talked about the way the brain changes to compensate for dying cells caused by toxic proteins that build up in the brain of a person with dementia. One of our leading clinicians, old-age psychiatrist **Dr Gary Cheung**, was also at the conference running a training workshop for health professionals on Cognitive Stimulation Therapy (CST), alongside Dr Kathryn Peri.

CST is an evidence-based structured group treatment for mild to moderate dementia. It has been shown to have significant benefits for participants including a positive effect on mood, improved memory and improved quality of life.



DR GARY CHEUNG

The University of Auckland

ON THE

GLOBAL STAGE

2016 has seen BRNZ develop into a nationally recognised research centre bringing together New Zealand's neuroscience elite.

Over the past year we have contributed greatly to advances in global health research efforts, established strong partnerships with the community, NGOs and healthcare providers, and invited eligible New Zealanders to participant in the country's first Dementia Prevention Research Clinic.

We have grown in global prominence too – strengthening our bond with Duke University in the U.S.A, and forging new links with the New Zealand-China Non-Communicable Diseases Research Collaboration Centre, Macquarie University in Sydney, the International Alzheimer's Disease Research Portfolio (founded by the National Institutes of Health in the USA) and Sheffield Hallam University in the United Kingdom.

EXCEPTIONAL TALENT. EXCEPTIONAL ACCLAIM.

DR TRACY MELZER / RIGHT
——The University of Otago

PROFESSOR DONNA-ROSE ADDIS / LEFT
——The University of Auckland

In 2016, BRNZ's researchers continued to make a real difference to the health and well-being of New Zealand.

While some were recognised for their immense contribution to health research, others achieved significant success in highly contestable external funding rounds.

Dr Tracy Melzer, from the University of Otago, Christchurch, was awarded a highly prestigious Sir Charles Hercus Fellowship from the Health Research Council. Most people associate Parkinson's disease with its motor symptoms - tremors, slowness and stiffness - but the brain changes which lead to motor symptoms in PD can result in cognitive issues too, such as memory difficulties, slowed thinking, confusion and in some cases, dementia. Tracy's aim is to identify early signals in the brain that could predict the later development of dementia. He plans to do this by using MRI scans and cognitive data that have been collected from a group of people at different stages of Parkinson's disease, as part of the longitudinal study BRNZ is supporting in Christchurch. If Tracy and his colleagues can discover what is happening in the brains of these patients with PD, this might lead to the discovery of a biomarker which would tell us about the risk of a person developing dementia in the near future.

This year the Royal Society of New Zealand announced **Professor Donna-Rose Addis** (University of Auckland), as one of only nineteen New Zealanders elected as Fellows of the Royal Society of New Zealand. This honour recognises outstanding achievement in the sciences, technologies and humanities, and is one of the highest accolades that can be given in New Zealand for research. Donna-Rose is known for her pioneering research into the brain mechanisms involved in 'future thinking' and episodic memory, and how they change during ageing and disease. This work has the potential for improving early screening for diseases such as Alzheimer's, and point to new targets for therapies. The recipient of a raft of prestigious grants and prizes – including a Rutherford Discovery Fellowship, the Prime Minister's MacDiarmid Emerging Scientist Prize and the 2015 Young Investigator Award from the International Cognitive Neuroscience Society (being the first recipient outside of the Northern Hemisphere)- Donna-Rose joins seven other BRNZ researchers regarded amongst our country's most eminent scientists.

CELEBRATING EXCELLENCE

PROFESSOR WARREN TATE
——One of the HRC's Celebrating Research Excellence Award recipients

On 1 January 2017 Brain Research New Zealand will turn two. But many of the researchers and clinicians at the heart of our CoRE have spent decades working to improve the lives of New Zealanders.

In 2016, BRNZ Co-Director **Professor Sir Richard Faull**'s services to brain research was recognised at the highest level - he was made a Knight Companion of the New Zealand Order of Merit, and received a Celebrating Research Excellence Award by the Health Research Council. Three further BRNZ researchers, **Professors Richie Poulton, Warren Tate and Valery Feigin**, were also awarded Celebrating Research Excellence Awards from the HRC, in recognition of their outstanding contribution to health research excellence, leadership, and impact.

Richie is the Director of the Dunedin Study, one of the most far-reaching and comprehensive studies of human health and development in the world. The impact of this research has been immense, both in New Zealand and internationally.

Warren and his team's work is widely recognised for having revolutionised our understanding of how proteins are synthesised in living cells, and provided important insights into the mechanisms behind diseases as diverse as Alzheimer's, HIV and chronic fatigue syndrome.

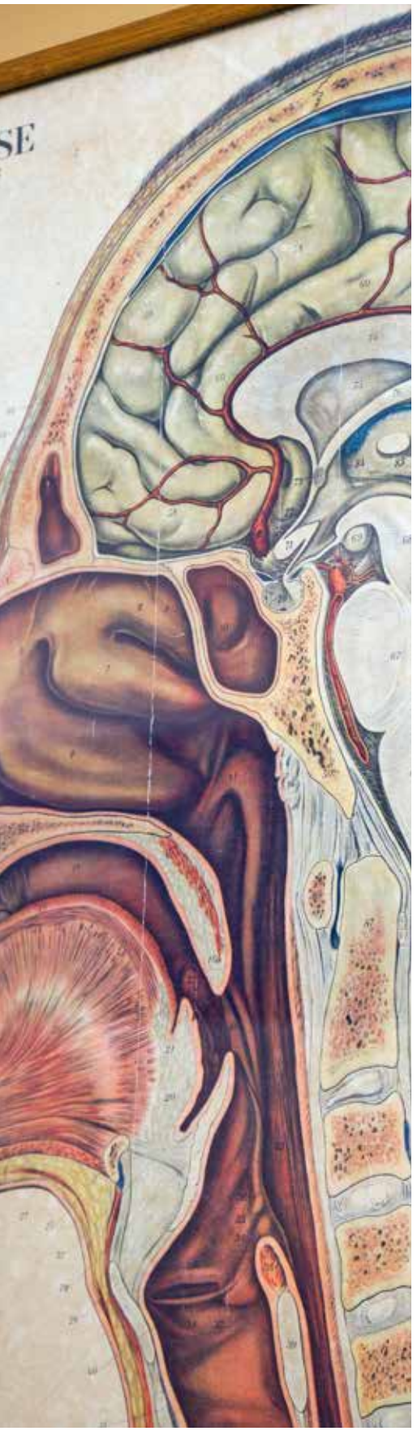
Valery's outstanding contribution to stroke and traumatic brain injury epidemiology and treatment was also recognised by the HRC. Valery recently revealed diverging trends in stroke burden between developed and developing countries. His work remains of critical importance for evidence-based health care planning for strokes and traumatic brain injuries.

SIR RICHARD FAULL

A LIFE IN SCIENCE IS A LIFE SPENT HELPING OTHERS

"From the moment I laid my hands on it, I was hooked. It just seemed like magic,"

said Professor Sir Richard Faull, recalling a memory from the 1960s. Richard was in his third year at the University of Otago's Medical School when he first saw the organ that would go on to define his career – the human brain. Now aged 71, married to Diana and with five grown-up children and four grandchildren, his fascination with the human brain is stronger than ever.



Richard is an internationally recognised expert on the workings of the human brain, and on the neurodegenerative diseases that can affect it, like Alzheimer's, Parkinson's and Huntington's. He is founder and director of the University of Auckland's Centre for Brain Research, and an ardent advocate for collaborative science. "I could never have dreamed that I'd build such an incredible team, or collaborated with so many international research groups, throughout my career," he said. "But we can do so much more when we work together."

It was this idea that drove Richard to team up with Cliff Abraham – an internationally leading Professor of Neuroscience at the University of Otago – to bid for a national Centre of Research Excellence - Brain Research New Zealand - Rangahau Roro Aotearoa (BRNZ). Launched in early 2015, BRNZ has brought together almost 70 research groups and clinicians from across New Zealand, with the aim of unlocking the secrets of the ageing brain.

> *"We want to fundamentally change the way brain research is done – not just in New Zealand, but in the wider world," said Richard.*

By 2036, one in four New Zealanders aged over 65 will be disabled by an ageing-related brain disorder. Ageing-related neurological disorders like Alzheimer's are accompanied by immense social, economic and healthcare costs, and place huge burdens on individuals, their family and whanau. "I've worked with so many families impacted by Alzheimer's, a most tragic disease that destroys the human mind. We may not be able to cure it, but if we can slow it by five years, we'd cut the prevalence of the disease in New Zealand by 50%, allowing people to live longer and have a higher quality of life," Richard said.

It's very clear that helping people is a deep and enduring passion of Richard's – one that he credits to his upbringing in Tikorangi, a tiny rural town in North Taranaki. The second son in a family of five, with parents who ran the area's general store, Richard grew up in a busy, yet traditional household. "The town was small, so we sold everything," he said. "And my parents were like social counsellors for the whole community – people came first. We didn't have much money, but my mum often said that we were the luckiest family in the world, because we were surrounded by friends."

Richard has carried that attitude through his entire career. And not only has it endowed him with a humility rarely seen at the upper levels of academia; it has also opened the doors to some truly ground-breaking research. It all started in 1970. After taking a year out of his medical studies to pursue a research degree, Richard qualified as a doctor at the turn of the decade. A PhD on movement disorders in the rat brain followed, after which he was offered a Harkness Fellowship. That gave him the opportunity to work in the US for three-and-a-half years – first at NASA, and then at MIT and Harvard. He returned to New Zealand and joined the University of Auckland, inspired and motivated to further his work on the human brain.

And it was a conversation with a genetics professor that sealed his fate. "He'd been looking after 400 NZ families with Huntington's disease. We knew that it was caused by a dominant gene, so if you had the gene, you'd get the disease; and once the first symptoms appeared, you'd be dead within 15-25 years. Getting that diagnosis was a literal death sentence," explained Richard. "But the problem was

that no-one had identified the gene that caused it. That meant that we couldn't test for it, so couldn't be sure that the diagnosis was correct." A number of these families then did something that Richard describes as "the ultimate gift, which changed my life" – they donated the brain of their deceased loved one to science, in the hope that they could use it to further their understanding of the disease. And so, working closely with a neuropathologist, Richard started to investigate cell damage in the basal ganglia – the area of the brain that controls movement. Their findings were rather unexpected. "We found that the pattern of pathological cell death was different in each and every case. This really worried me – it contradicted all of the text books!" They realised that they needed more information about each brain donor, so in collaboration with a psychologist, they collected the histories and doctor's notes related to every person whose brain they were investigating. When they put the two stories together, they discovered that the variations in the pathology matched the variations in the symptoms. "We could say that this patient had this pattern of symptoms because of the damage in this particular portion of the brain. It was revolutionary," said Richard. These results kick-started an entirely new approach to human brain research, and the relationships he had developed with these families allowed Richard to set up the now word-famous Neurological Foundation Douglas Human Brain Bank.

> *"Using this brain tissue, we've been able to do incredible research – we were the first to show that the human brain has stem cells in it, and that it continues to produce new brain cells from these stem cells throughout life," he said. "In more recent years, we've shown that we can keep donated brain cells alive in a dish, and trial new drugs against them. Our ability to do all this is due entirely to the generosity of these very special families."*

Richard's warmth and positivity, as well as his commitment to openness and collaboration, makes him a fantastic mentor for younger scientists. He has spent forty years teaching medical students, and he regularly takes plastinated brains into schools and youth groups to inspire children. He also instigated the now-annual Brain Day that invites the community to the university campus to learn more about neurological diseases. In January of this year, Richard was made a Knight Companion of the New Zealand Order of Merit, for services to brain research. Modest to the core, Richard accepted his knighthood by saying, "It's important to realise that the recognition is not just for me, it's actually for the brain researchers across the country and the way we work together as a team. I share this with all of those research groups and all the families touched by brain disease who have supported our research in the most special way."

With Cliff, Richard continues to lead BRNZ's research efforts, and work closely with families with brain disease. There is no sign of him slowing down, and that's because, ultimately, he loves what he does. "My career is a privilege. Every day that I get to work with incredible clinicians and scientists, or help a family to navigate the latest research, is a privilege. I am incredibly lucky to live this life."

EXTERNAL FUNDING

PROFESSOR JOHN REYNOLDS

Recipient of $4.8M MBIE grant

BRNZ's researchers secured over $30 million in new research funding in 2016.

Dr Andrew Clarkson and **Associate Professor John Reynolds** enjoyed major success in Ministry of Business Innovation and Enterprise (MBIE) funding round this year. John was awarded over $4.8 million to develop new technology that will enable non-invasive drug delivery to the brain, revolutionising the treatment of disorders with underlying neurochemical imbalances such as Parkinson's disease. The technology could also target chemotherapy to brain cancers and arrest epileptic seizures at the site of origin. Andrew received a $1 million Smart Idea grant to develop and test a range of potential drugs that may help patients recover from stroke. Such novel compounds have wide-ranging potential as they have the ability to modulate many biological and physiological processes in the brain. Beyond holding great promise for treatment of stroke, they too could aid in improving outcomes for other neurological conditions in the future.

HEALTH RESEARCH COUNCIL FUNDING

PROFESSOR CLIFF ABRAHAM

BRNZ Co-Director

BRNZ researchers also achieved outstanding success in the latest Health Research Council of New Zealand funding round.

Attracting over $16million in new health research funding, their success is testament to their world-class research proposals. The world-renowned Dunedin Study led by Professor Richie Poulton — which has followed nearly all aspects of the health and development of more than 1000 people born in Dunedin in 1972-73 — received $4.9M to investigate ageing processes in its members to inform early intervention strategies to help people age as healthy as possible. BRNZ Co-Director **Professor Cliff Abraham** and his colleagues received a five year programme grant to investigate the mechanisms of Alzheimer's disease so that more effective therapies can be developed. Cliff's team will study molecules that may be key players in the disease process, and use new and improved models of the disease to determine if those molecules are closely related to the development of the disease from its earliest stages. **Professor Michael Dragunow**'s team also received a programme grant to study the underlying causes of neurodegeneration, focusing on brain inflammation and blood vessels of the human brain that allow blood cells and proteins to seep into diseased brain tissue. They will also test compounds directly on diseased human brain cells to identify novel treatments.

DESIGNING FOR THE AGEING BRAIN

FROM LEFT / **KAROL CZUBA, GUY COLLIER, ASSOCIATE PROFESSOR NICOLA KAYES AND NICK HAYES**

In 2015, BRNZ funded a key piece of research by Associate Professor Nicola Kayes into what it means to live with Mild Cognitive Impairment.

While much is known about deficits in functioning caused by MCI, we know very little about how people live with the condition, the strategies they find most helpful, and what kinds of services they find most supportive. This kind of knowledge, so crucial to our understanding of MCI, would improve our ability to develop new interventions and break down barriers to accessing health care. One such barrier can be the physical environment in which people seek treatment and care.

The growing number of people with dementia and co-morbidities means that they are often seen by multiple units when they visit hospital - acute hospital wards, rehabilitation settings, radiography departments, general wards – and for the cognitively impaired, it can be very hard to find your way. The design of many of these environments has been shown to increase disorientation. It can also worsen the perceptual and cognitive difficulties that individuals living with dementia face. Nicola has been interested in the therapeutic potential of design for some time and, in 2016, she secured catalyst funding to collaborate with AUT's Design for Health and Wellbeing Lab and Lab4living on an exciting new initiative. Lab4Living is a multidisciplinary design laboratory based in Sheffield Hallam University in the United Kingdom. Along with Dr Richard Worrall from Auckland District Health Board, the group plans to develop design-led solutions to promote well-being of people living with dementia in New Zealand and the United Kingdom. Though new, this fledgling international partnership holds real promise for New Zealand's health services.

INTERNATIONAL ALZHEIMER'S DISEASE RESEARCH PORTFOLIO

The International Alzheimer's Disease Research Portfolio (IADRP) was launched in 2010 as a joint collaboration between the National Institute on Aging (part of the NIH) and the American Alzheimer's Association.

Essentially, the IADRP is a global database that gives users the ability to assess the portfolios of major organisations (currently 30+) for areas of overlap as well as areas of opportunities in which to collaborate and coordinate in a collective effort to advance Alzheimer's disease research. In 2016, BRNZ established friendly ties with the IADRP, helping us to identify new opportunities in promising areas of growth alongside major funders of Alzheimer's disease research across the globe.

THE DUNEDIN STUDY

PROFESSOR RICHIE POULTON

Director of the Dunedin Study and recipient of the Prime Minister's Science Prize 2016

The Dunedin Study, arguably the world's most successful longitudinal study, turns 45 this year. And as the study members reach midlife, Professor Richie Poulton, the study director, can see the work taking on an exciting new focus.

"After 45 years," he says, "I feel like we're on the crest of a new wave. We were originally a child health and development study, and then we moved to being a study of young adulthood and lifestyle… Now we're starting to see the effect of ageing. We're trying to link what we know from the past to set the stage for the future."

The participants in the study – a thousand people born between April 1, 1972 and March 31, 1973 - will be forty five when the next phase of research kicks off. In this next phase, Richie and his team will be looking out for early signs of ageing, conducting kidney, hearing, vision and musculoskeletal examinations, and now, state of the art brain imaging. "The idea that you have to study old people to learn about ageing is nonsense," he explains, "in some ways the horse has bolted. What you want is to identify people who are ageing faster earlier so you can change things, put them on a better trajectory."The brain imaging project has already begun, with over 150 of the study's 1,000 members having now been through the new 3T Siemens MRI scanner. The information from just this first 15% of members has been astounding. "The associations we had hypothesised we would see in the first 150 participants are actually there," he says, "and they are there more strongly and more clearly than anyone could have believed or really even dreamed of."

But the road to this new technology has been a long one, stretching back almost 15 years, and was only made possible by pooling the resources of Brain Research New Zealand, the Health Research Council and international funders like The National Institute of Aging in America. The global scientific community stepped up and made it happen because they needed the study to do it. "They don't do it because they're particularly generous or because they've got stacks of money laying around," Richie stresses, "it's because it helps them, and you can see that in their policy documents. They do it because [the study] is something special, and they can get answers from it which they can apply to their own countries." The value of the study has been shown time and again through national and international investments, with the NZ Health Research Council supplying over $6 million New Zealand dollars, the US National Institute of Health having ensured over $15.3 million New Zealand dollars, and the UK Medical Research Council ensuring $2.27 million New Zealand dollars for the study in the past five years alone.

Prime Minister Bill English is the latest in a long line up to recognise the value of the study, recently presenting Richie with the Prime Minister's Science Prize for 2016. According to Richie, the prize amounted to a watershed moment for the study and recognised ''the efforts of so many people, over so many years''. Perhaps, most importantly, it ''recognises the generosity and commitment of the study members themselves''.

With almost 1,000 study members and a 95% retention rate, the Dunedin Study is in a unique position to be able to truly identify early ageing risk factors, not just for kiwis but for people across the developed world. "The people who are lost [from longitudinal studies] are not random," he says. "The people that are lost, or hard to get back in, tend to be people for whom multiple difficulties aggregate and those are the people you really want to keep." It is the retention rate which has set the study apart from other longitudinal studies, and ensured that the information put out by the study can be generalised to other nations; it is why national and international politicians and researchers have come to take the study so seriously.

> *"I start with the assumption that we're going to get 100% of study members each time and then I work from there," Richie says, "whereas other studies might be satisfied with 50%. It's really the bloody-mindedness of it all. We'll be at 80% and there's still 15% or 20% of people out there we could get in, so we set the clock back to zero." No one gets left behind; no one is given up on.*

It's no wonder, then, that the study has managed to attract scientists from around the world to contribute. Currently, collaborating experts come from as far afield as Duke University in the USA, King's College London in the UK, as well as a handful of researchers based in Canada, Australia, and Singapore. These international researchers include the likes of Professors Terrie Moffitt, Avshalom Caspi, and Ahmad Hariri, some of the foremost experts in their fields. Then there are those researchers spread across most New Zealand universities, including BRNZ's own Professors Peter Thorne, Suzanne Purdy and Valery Feigin based at the University of Auckland and AUT respectively. While they may still be based in their namesake, The Dunedin Study has well and truly gone global.

As it crests this new wave of enquiry, the study is building on 45 years of data and momentum. "The data that we hold already could show predictors of a person at age 45 being much older than their peer group, and if we find a predictor that is modifiable we can tell policy makers and practitioners 'Focus on this, change this!'". Given the significant financial investments, of not only the New Zealand government but also the UK and USA governments, it is clear that once the data is processed all eyes will be keenly focused on those findings.

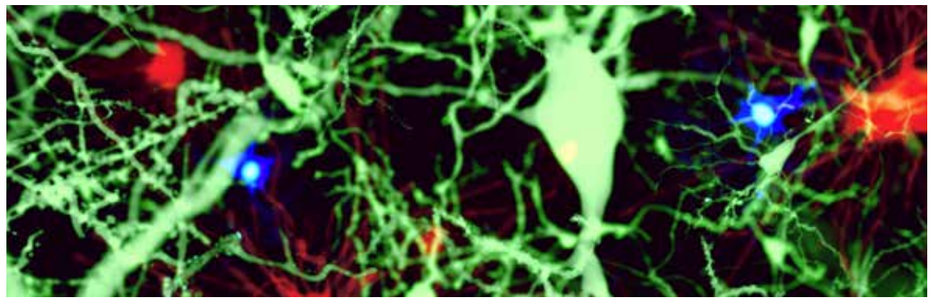
IN THE

LAB

Brain Research New Zealand's research programme is devoted to enhancing understanding of the causes and pathology of ageing-related neurological diseases.

Armed with this greater knowledge, researchers will be better able to develop new therapies to attack the disorders. But already BRNZ researchers have new and innovative ideas for how to tackle brain diseases, and BRNZ is providing significant funding to underpin their research.

USING BRAIN CELLS AS THERAPEUTIC AGENTS



Can the power of healthy brain cells be harnessed to treat brain diseases? Many of our researchers are very interested in the opportunities that may be on offer from this line of approach.

In one set of experiments, a particular type of cell found near blood vessels, called pericytes, is attracting interest. Pericytes, which have some properties of stem cells, may be able to promote brain repair where damage has occurred, for example after stroke. Research findings could pave the way for using those cells collected from around the patient's own vasculature to promote "self-repair" of their brain, while eliminating the immuno-suppressants needed with "non-self" stem cell treatment.

NEW STRATEGIES FOR DRUG THERAPIES

Parkinson's disease is a severely disabling neurodegenerative disorder that is managed by delivery of the drug levodopa, which helps replace some of the neurochemical dopamine that is brought to dangerously low levels by the disease.

Unfortunately levodopa gradually loses its potency after prolonged administration. Our research is targeting drugs that can prevent or slow dopamine removal after its release, with the prediction that they will increase the availability of dopamine and thus identify potential new targets for co-therapies to improve short and long-term effectiveness of levodopa. Another study is examining a new drug therapy for Alzheimer's disease, focusing on receptors for a different neurochemical, GABA. Reducing the action of this inhibitory chemical is predicted to be effective in the fight against the cognitive decline that is so devastating in this disorder.

NEW CONCEPTS IN BRAIN STIMULATION AS A THERAPEUTIC APPROACH

Given the proven success of deep brain stimulation in treating Parkinson's disease, our researchers are building on this concept for not only Parkinson's but also other disorders.

Of particular note are state-of-the-art experiments aimed at genetically delivering light-sensitive proteins to cells in damaged brain areas, and then implanting special light emitting probes to awaken these brain areas to restore function. These exciting new techniques are being applied to models of Parkinson's disease to improve motor function, and of stroke to reverse memory loss, which may also prove to be relevant to the treating Alzheimer's disease or head injury. Interestingly, brain stimulation may also be generated through sensory signals. Clinical researchers are investigating whether visual "biofeedback" signals can be used to generate brain states that enhance cognitive function in people who have mild cognitive impairment, an early stage of Alzheimer's disease.

IDENTIFYING BIOLOGICAL "TELL-TALES" OF NEUROLOGICAL DISEASE

It is vital that the development of new treatments for progressive neurodegenerative disorders, as described above, is done hand-in-hand with improving early detection of these brain diseases.

Our groups are hot the trail of "biomarkers" that will reveal the earliest stages of various diseases so that treatments can be started as soon as possible. New funding was provided by BRNZ for studies into Alzheimer's disease, Huntington's disease, Parkinson's disease and frontotemporal dementia, using animal models, human cohorts and computer modelling. Blood samples from people in different stages of the disease are being analysed for diagnostic molecules, while other studies are employing MR imaging and EEG analysis of brain function to identify early changes in brain function predictive of disease onset.

LIVING WELL WITH AGEING-RELATED NEUROLOGICAL DISORDERS

Our researchers are also interested in treatments that improve quality of life for both those ageing in a relatively healthy way as well as for those developing ageing-related neurodegeneration.

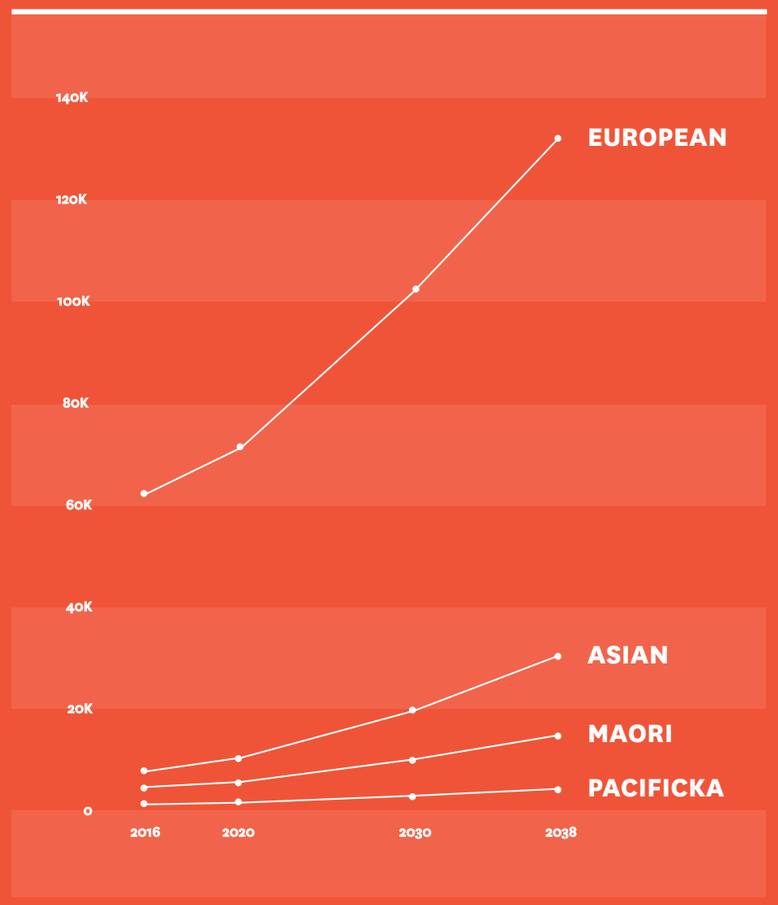
For example, one project is aimed at investigating whether more physical exercise, as well as more social interaction (as evidenced by volunteering in the community), has the potential to slow or even reverse ageing-related cognitive decline.

Ageing is also associated with impaired motor function, and a higher incidence of falls which often cause head injuries that can exacerbate risk and symptoms of neurological disorders. People with dementia have ten times more falls than older people without dementia. Body-worn sensors will be used to understand the gait patterns of older people both with and without dementia to aid in the development of strategies to reduce the risk of falls in these people.

Support workers and caregivers give critical support to people with cognitive decline in accessing health services and facilitating the uptake of interventions. Our investigators are working to find out how these unheralded workers and carers that are supporting older adults with cognitive decline can be valued for the important work they do. The aim is to use this knowledge to optimise access to services and interventions for those living with cognitive decline.

DEMENTIA PREVALENCE

BY ETHNICITY IN NEW ZEALAND



170,212

New Zealanders are predicted to have dementia by 2050... that's

2.9%

of the population, nearly triple current rates!

BY 2038

MĀORI DEMENTIA PATIENTS WILL INCREASE FROM 5.1 TO

8 PERCENT

$1.7 BILLION NZD

total economic cost of dementia in New Zealand in 2016

INDIVIDUALISED MEDICINE & THE

PREDICTION OF DEMENTIA

Predicting the onset of dementia in patients with Parkinson's disease (PD) is a huge challenge, but it's one that Professor Tim Anderson from the University of Otago, Christchurch, is determined to overcome. Funded by BRNZ, Tim is leading a multi-centre research project into the progression of cognitive impairment in a group of 150 PD patients around New Zealand.

As a neurologist with expertise in movement disorders, Tim is an expert on both PD and Huntington's disease, and hosts regular clinics at the university. But his research effort focuses on Parkinson's, and on the specific form of dementia that tends to accompany it. PD is a progressive neurodegenerative condition, that usually starts with movement issues – either too little, or in case of tremors, too much. But as the disease progresses, the major concern becomes the impairment to the cerebral parts of the brain, which causes hallucinations, depression and dementia.

> *"We know that around 80% of those diagnosed with Parkinson's disease will go on to develop dementia," Tim explained, "But what we can't say, with any certainty, is exactly when that will happen."*

For patients already dealing with the diagnoses of Parkinson's, such uncertainty can be deeply troubling.

So Tim, working with Professor John Dalrymple-Alford at the University of Canterbury, is working with patients that show the earliest symptoms of dementia – those with mild cognitive impairment (MCI). MCI is a midway phase between having normal cognition, and being impaired such that you can't live independently. "We know that about half of the people we identify with MCI will go onto develop dementia in the following four years. So if we can catch them early enough, we stand a chance of predicting the onset of their dementia." This BRNZ study is following a group of patients in Christchurch, Dunedin and Auckland, to investigate how their MCI develops over several years, in the hope of pinpointing the specific triggers that lead to dementia.

The team are using a number of tools to carry out this work – for example, because there are differences in the brain scans of people with normal cognition, with MCI, and those with dementia, every patient involved is undergoing magnetic resonance imaging (MRI). They're also taking a series of cognitive tests, and well as providing blood samples to help Tim search out genetic susceptibility factors, or signposts in the genes, that have been linked to PD.

Half of the patients are also having positron emission tomography, or PET scanning, which uses radioactive tracers to seek out abnormal proteins in a person's brain. Already used widely in the diagnosis of Alzheimer's, PET scanning is a vital but expensive tool in our understanding of disease. "The dementia in PD is probably multi-factorial, so we're trying to reflect that in this study," said Tim. "Our hope is that by combining PET scanning, blood screening, and cognitive tests, we'll be able to determine the combination of factors that contribute to a patient's risk of developing dementia."

The outcomes of this study will also feed into a collaboration run by the International Parkinson and Movement Disorder Society, which Tim and his team are part of. Though New Zealand offers a smaller sample size than a global study, it has many advantages – the patient cohort is very stable and they are keen to contribute to research, with many of Tim's patients pledging to donate their brain after death. This relationship, combined with previous Health Research Council funding, means that the Christchurch arm of the study is at an advanced stage, while progress is accelerating in Dunedin, under Dr Nick Cutfield. With Dr Barry Snow now at the helm in Auckland, the identifying and screening of patients will soon begin.

Ultimately, the goal of this project is to individualise the process of dementia prediction – to determine the prospects of each, individual patient, so that neurologists can better answer their questions about what the next few years hold for them, and their carers. For Tim, the 'holy grail' in Parkinson's research is to find a way to stop the disease progressing at all. "We're not going to answer that here, but our skills can certainly help identify those most at risk of developing the debilitating dementia that comes with it," he said, "If and when treatments become available, we'll be able to directly target those who most need our help, and ultimately improve their quality of life."

TAILORED GENE THERAPY

FOR THE HUMAN BRAIN

Associate Professor Debbie Young from the University of Auckland never planned to become an academic.

Her career began with a degree in biochemistry at the University of Otago, but after that, she was keen to start her working life, so took on several research technician roles – first at the Dental School in Dunedin, and later in the Department of Pharmacology & Clinical Pharmacology at the University of Auckland. Her attitude to academia changed when she was offered a position at a large pharmaceutical firm doing quality control work.

> *"It was a pivotal point in my career. I applied for the role mostly because the salary was fantastic. But it quickly became clear that money wasn't the main driver for me – the work itself needed to be challenging," said Debbie. "I realised that I wasn't ready to give up research, so I applied to do a neuroscience PhD, and haven't looked back."*

She also admits that part of her success was being in the right place at the right time. Debbie's first post-doc came in the late 1990s, when gene therapy was a cutting-edge technology that, for the first time, offered a way to replace the defective genes responsible for genetic disorders, with normal healthy genes. "At the time, gene therapies were just beginning to be explored as a potential treatment route. I've spent the intervening 25 years developing and applying them to brain diseases." These days, Debbie's group has a broad range of interests that cover the full spectrum, from the molecular basis of learning and memory, to gene therapy of neurological disorders.

Her latest research effort, funded by the BRNZ, is a world-first. Debbie has developed a new gene regulation system that kick-starts production of the therapeutic gene, only in response to signals produced by a brain cell when it is getting sick. This means the therapy is regulated by the cell itself, and made only when it is needed, reducing the possibility of side-effects of the therapy on normal, healthy cells.

BRNZ COLLABORATORS PROFESSOR MIKE DRAGUNOW / LEFT ASSOCIATE PROFESSOR DEBBIE YOUNG / RIGHT

Efficient transfer of a green fluorescent reporter gene (GFP) in pericytes using viral vectors / FAR RIGHT

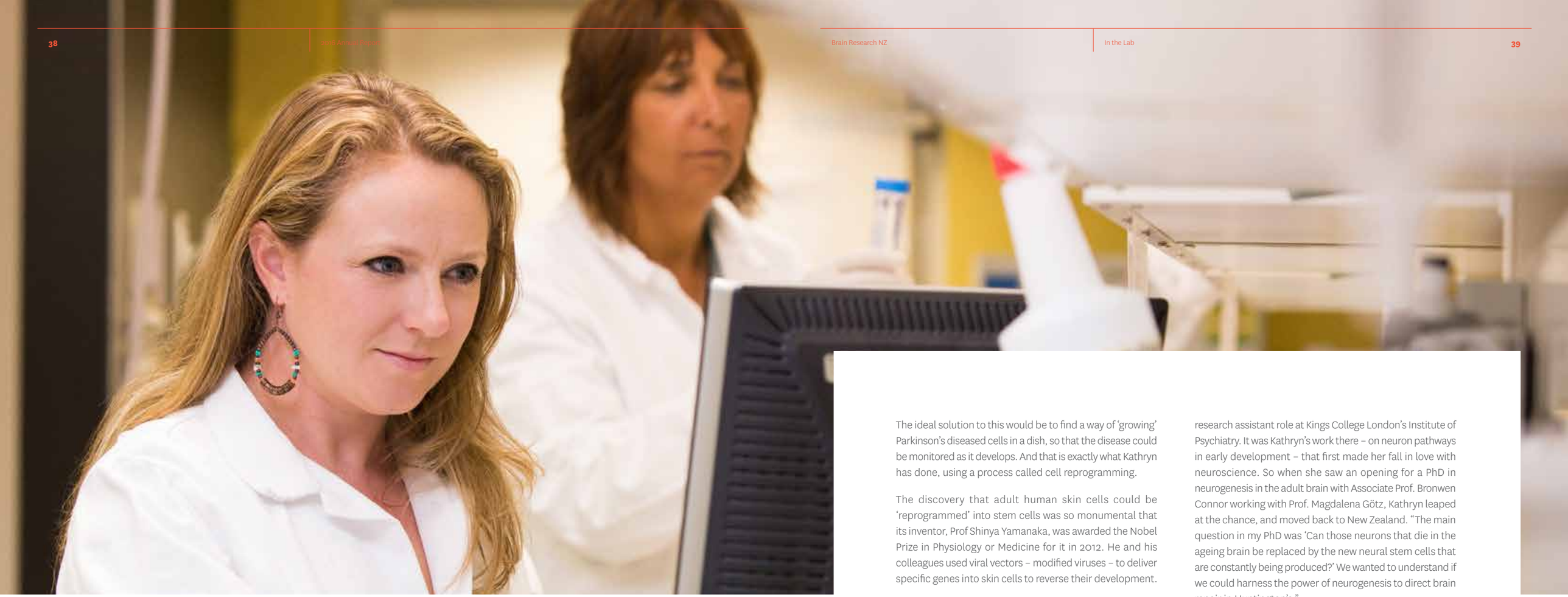
The role of these specially-designed genes is to stop the production of proteins that have been linked to cell death in Parkinson's disease. But that's only half of the story. Debbie has actually developed a dual therapy that not only knocks down the target; it also supplements the neurons with another factor that boosts their resilience to further damage – a double-whammy approach to gene therapy. To deliver these, she is using viral vectors – viruses that have had their DNA replaced with other genes tailor-made to treat a specific disease. "We remove 96% of the original viral material," Debbie explained. "So the vector is like a Trojan horse – it might look like a virus from the outside, but on the inside, it's filled with therapeutic genes."

"Another huge hurdle in applying gene therapy to humans is the sheer size of the human brain," said Debbie. "For a therapy to work, especially in diseases like Alzheimer's that impact entire hemispheres, it may need to be delivered globally." To do this, Debbie has been working closely with Professor Mike Dragunow, also at the University of Auckland. He's been growing human brain cells in the lab, specifically from pieces of the leptomeninges – the thin membrane that encases your brain and its surrounding fluid. A specific class of these cells, called pericytes, are known to play an important role in sustaining the blood-brain barrier, as well as acting as a communication tool between brain cells. And as Debbie and Mike have discovered, being able to deliver gene therapies to pericytes could potentially enable delivery of the therapies to the entire brain.

So while they have found a vector that is very good at delivering the therapeutic genes to pericytes, another part of the equation are the promoters, or as Debbie described them, the "battery packs for genes", that drive the production of the protein encoded by the therapeutic gene. The strengths of these promoters can differ as well as their activity in different types of brain cells, which means that they could potentially deliver therapy to cells that don't need it. Debbie has found that in a whole animal brain, the promoter they are currently using is not very specific, so it will drive production of proteins in all types of brain cells, rather than in pericytes alone. So, now half way through the project, their focus is shifting to designing promoters to use in combination with the vector so that the therapeutic proteins are only made in pericytes, taking the therapy one step closer to a clinical reality.

According to Debbie, gene therapy for brain disease offers huge advantages over traditional drug-based treatment. "Rather than saying to a patient 'ok, you must now take this cocktail of drugs for the rest of your life', we could potentially deliver a life-long therapy in just one operation. Once you put the therapeutic gene in, our gene regulation system will allow your cells to just continue the process itself." Gene therapy also opens the door to early-intervention treatments. If those at risk of developing diseases like Parkinson's and Alzheimer's can be identified early enough, it may be possible to deliver therapeutic genes that lay dormant until the cell begins to 'get sick'. Then, once specific biochemical signals are released by the cell, the treatment triggers itself, and gets to work delivering the therapy, one cell at a time.

It might sound like a faraway dream, but genetic treatments like these are already in clinical trials all over the world. And if they succeed, they could have a huge impact on the lives of those facing a future with a neurodegenerative disease.



PROGRAMMED FOR SUCCESS

Dr Kathryn Jones is a BRNZ Postdoctoral Research Fellow based in the University of Auckland's Neural Reprogramming and Repair Lab, and she is well on her way to achieving a remarkable goal.

Working with Associate Professor Bronwen Connor, Kathryn is transforming skin cells, donated from patients with Parkinson's disease (PD), into live dopamine neurons that carry the signature of PD. This work has the potential to revolutionise the way we study, and eventually, treat Parkinson's.

PD is a long-term, degenerative disorder of the central nervous system – over time, a patient's nerve cells, which usually produce the vital neurotransmitter dopamine, become sick and die. But until now, researchers have had no way to examine exactly how the disease progresses within those cells. And according to Kathryn, "This lack of access to live-but-disease-affected human neurons is a huge barrier to our understanding of PD."

The ideal solution to this would be to find a way of 'growing' Parkinson's diseased cells in a dish, so that the disease could be monitored as it develops. And that is exactly what Kathryn has done, using a process called cell reprogramming.

The discovery that adult human skin cells could be 'reprogrammed' into stem cells was so monumental that its inventor, Prof Shinya Yamanaka, was awarded the Nobel Prize in Physiology or Medicine for it in 2012. He and his colleagues used viral vectors – modified viruses – to deliver specific genes into skin cells to reverse their development.

> *This process turns them back into embryonic stem cells – the 'youngest' cells we have. But, when it comes to Parkinson's disease, young, rejuvenated cells aren't relevant – as a disease of ageing, the neurons studied should be old too.*

So Kathryn had to take a new approach to cell reprogramming; one than can produce neural stem cells that have the age-related characteristics of PD. To do this, she moved from viruses to specially-modified RNA, produced by Dr Carsten Rudolph in Germany. This stable, non-toxic molecule carries the genetic message into skin cells donated by a Parkinson's patient, reprogramming them until they become stem cells. From there, Kathryn has grown them into mature, human dopamine neurons, hallmarked with PD, in a dish in the lab. And working with Professor John Reynolds at the University of Otago, Kathryn is now preparing to transplant these cells into animal models, to test whether this can correct behavioural deficits.

This completely novel technique builds on Kathryn's extensive previous experience – her career began with a BSc (Hons) degree in cell and molecular biology from Victoria University of Wellington. A stint overseas led her to a research assistant role at Kings College London's Institute of Psychiatry. It was Kathryn's work there – on neuron pathways in early development – that first made her fall in love with neuroscience. So when she saw an opening for a PhD in neurogenesis in the adult brain with Associate Prof. Bronwen Connor working with Prof. Magdalena Götz, Kathryn leaped at the chance, and moved back to New Zealand. "The main question in my PhD was 'Can those neurons that die in the ageing brain be replaced by the new neural stem cells that are constantly being produced?' We wanted to understand if we could harness the power of neurogenesis to direct brain repair in Huntington's."

The move from investigating Huntington's disease – a progressive brain disorder that usually appears in a person's thirties or forties – to Parkinson's, which primarily affects the elderly, was a natural one for Kathryn, and it chimes closely with the broader work carried out by her supervisor, Bronwen Connor. Her progress seems all the more remarkable, though, when you consider that for the past four years, Kathryn has worked part-time, while raising her two young children. Speaking about what that has meant for her career, she says, "It can be difficult doing science part-time – the field doesn't wait for you! But Bronwen has always been a very supportive supervisor, and seems determined to give all of the researchers in her lab an equal opportunity to reach their full potential." Now back in the lab full-time, Kathryn is relishing the chance to step up activity on this and other projects.

On completion of her BRNZ Fellowship, she will build on her cell reprogramming work to include high-throughput drug screening, "These live-but-disease-affected human neurons offer us a unique opportunity to look for neuroprotective compounds that can slow down diseases like Huntington's and Parkinson's," she explained. "Being on the cutting-edge of any field can be a challenge, but knowing that our work is directly relevant to New Zealanders and the health of their ageing brains is hugely important to me."

NEURO-VASCULAR COUPLING

AND ITS CONNECTION TO ALZHEIMER'S

Professor Tim David is the Director of High Performance Computing at the University of Canterbury, and a Principal Investigator at BRNZ, but he describes himself as a "late starter."

PROFESSOR TIM DAVID WITH PHD STUDENT ALLANAH KENNY (NGAI TAHU)

He jumped straight into the world of work when he finished school, but at age 26, the lure of academia called to him. Tim received a BSc in Mathematics from the University of Leeds, followed by a PhD in the same subject.

Before completing his PhD, he was offered a lectureship at Leeds – "When you're given an opportunity like that, you don't say no," he said, and in total, he spent twenty years in the UK city. It was in his final four years at Leeds that Tim first became interested in modelling blood flow in the brain. "I knew that Professor Peter Hunter had done a huge amount of work at the University of Auckland, which focused on the heart. So I wanted to take on the challenge of doing something similar for the brain."

His change of direction coincided with an opportunity to move to New Zealand, and a wider push towards multiscale modelling, whereby entire organs are simulated by integrating small, detailed models.

What started with an interest in a circular set of arteries at the base of the brain, has now led Tim to ask much larger question, "Can we simulate certain chemical pathways in order to identify the early biomarkers of neurodegenerative disease?" A project that aims to answer this question is now underway, thanks to funding from BRNZ, and it starts with a specific mechanism called neurovascular coupling. "There's a growing body of evidence that links the way a cell gains its glucose and oxygen, with the development of Alzheimer's," Tim explained. "But it is difficult, and sometimes impossible, to explore this mechanism in the wet lab."

Neurovascular coupling relies on a cell called an astrocyte. The arms of this star-shaped cell connect not only with neurons, but also with the arteries that perfuse brain tissue, providing glucose and oxygen to the neurons. However, if an astrocyte or neuron fails to get enough oxygen, the chemistry of the cells start to alter. That causes certain proteins to be cut incorrectly by the cell – and in some cases, producing the amyloid plaques synonymous with Alzheimer's disease. And so, Tim and his team are now exploring this complex chemical pathway, using computation.

> *"A computer model can do experiments that you can't do, logistically or ethically, in the lab. We're trying to find a way to alleviate the production of amyloid plaques, by looking further up the chemical pathway."*

Tim is working with another BRNZ researcher, Dr Tracy Melzer, on this project, because of his expertise in functional MRI. Tracy is leading a project to understand the development of Parkinson's disease through blood-oxygen-level dependent, or BOLD, signals obtained with an MRI. Tim's model can simulate these fMRI signals, so by working with Tracy, they will be able to compare their model with actual BOLD signals obtained from Parkinson's patients. A second collaborator is Dr Jason Berwick, from the University of Sheffield. He's looking at the same process in mice, adding another dimension to the work. "We have already developed the BOLD signal model from a small piece of cortical tissue," said Tim. "Now, we need to do it for a large piece of tissue, so that we can directly compare it to Tracy's real-world data." Assisting Tim in this effort is one of his PhD students – Allanah Kenny. "We are very lucky to have two fantastic Māori researchers in my group. Allanah's work is central to this cortical tissue project, and Michelle Goodman's work, on how waves of potassium can damage brain tissue, will further our understanding of stroke."

Of course, like all good scientists, Tim has interests outside the lab too. For him it is music – he's been playing the flute for over 50 years, and even toyed with the idea of becoming a professional musician. But he's happy to keep those two parts of his life rather separate, saying "There is an unexplained reason why certain music brings tears to my eyes – I'd much rather maintain that mystery than try to unpick it!" But when it comes to understanding brain disease, his approach is very different. In the short term, Tim's goal is to understand why amyloid plaques form in the brain, but ultimately, he wants to be able to do something about it. "We're all going to get old," he said. "I just want to do science that contributes to improving our quality of life when we do."

IN THE

CLINIC

In 2016 our scientists continued to make significant headway against ageing-related neurological disease.

With 175 publications in leading international neuroscience and clinical journals during the year, BRNZ's researchers have been making significant contributions to science, health research and academia. But to truly have an impact on the lives of New Zealanders, our research also aims to offer practical benefits to healthcare professionals, community groups, and most importantly, to patients and families.

Perhaps BRNZ's most ambitious initiative is the establishment of a network of Dementia Prevention Research Clinics (DPRCs) in Auckland, Christchurch and Dunedin. Through our clinics, our investigators have started to follow a group of individuals with early signs of dementia, acquiring serial blood samples, brain imaging and cognitive testing. The group will also be invited to participate in a range of preliminary clinical trials, developed as part of our research programme. These trials may involve testing novel drugs, nutritional supplements, and cognitive, social and physical interventions designed to prevent, delay or ameliorate Alzheimer's disease (AD) and other related dementias. Through exposure to novel methods that may delay the development of AD, patients involved in our clinical research stand to directly benefit from early access to new technologies. If successful, these technologies will quickly be applied to non-research participants too, by virtue of the DHBs' relationship with Brain Research New Zealand.

Alongside the clinics, BRNZ is investing in research into novel cognitive stimulation and physical activity strategies to moderate ageing-related neurological disorders. Our overarching goal is to identify therapies for future large scale trials that can then be rolled out in a community setting for the benefit of New Zealand. Collectively, this research will lead to the development of new technologies and therapies, and ultimately a notable improvement in New Zealand health care and public health.

FEEL THE RHYTHM

HOW MUSIC AND MOVEMENT CAN HELP US AGE BETTER

When it comes to advanced ageing research, Professor Ngaire Kerse from the University of Auckland is a force to be reckoned with. Ngaire credits her grandmother as her major source of inspiration – "She lived a fulfilled, independent life until her death at 95. And I guess I wanted to understand how and why she managed to do it, while others don't". And now, as Head of the School of Population Health and a Professor of General Practice, Ngaire dedicates her career to the care of the elderly. She is a world-renowned expert on falls, physical activity, and maximising health for older people, and has led multiple projects that aim to understand the factors that contribute to a long and healthy life.

One thread of this research led Ngaire and her PhD student Kristina Zawaly, to undertake an ambitious feasibility study, with BRNZ's support. Titled 'Complex cognitive activity to prevent mild cognitive impairment (MCI) progression', it aimed to examine the impact of dance on people with MCI.

> *"Numerous studies have shown that taking part in social, mental and physical activities reduce an older person's risk of developing dementia, but to date, there have been very few randomized controlled trials specific to dance in persons with mild cognitive impairment," said Kristina.*

Music has also long been suggested as a potential therapy for older people experiencing cognitive decline. There have been some positive results for those with Parkinson's disease, but concerns around the quality of the methodology used has limited its wider acceptance.

So, Ngaire and Kristina designed a study that would combine these factors to form a cognitive challenge specifically for older people experiencing MCI. A cohort of 30 signed up for the 12 week programme, and they were split into three groups. The control group would listen to music for one hour, while sitting still. The second group were encouraged to dance freely while listening to music, and the third were trained in the Ronnie Gardiner Method. This rhythm technique is named after the talented jazz musician who developed it in the late-1900s. It uses a combination of language, movement and music to stimulate the brain and body, while encouraging social interaction.

Each of the participants had cognition and mobility tests at the start of the study, with the same tests repeated 12 weeks later. Though only a small sample, the results were impressive – the participants in the third group were found to perform considerably better in the concluding tests than they'd done in the initial tests. And the largest differences in performance were found between the first and third groups, suggesting that the most challenging activity had the largest positive effect on the participants. Qualitatively too, the study was well-received, "It was a huge amount of fun, and the feedback has been overwhelmingly positive," said Kristina. "We had people ask if the course could carry on indefinitely!"

With so many people living longer, the prevalence of dementia and other cognitive impairments will certainly grow, but we need to recast the challenge, according to Ngaire. "I want to get away from this idea that all people in their 80's have some form of disability – it's just not true. Many older people continue to contribute to society, and we need to find better ways to help them stay independent for as long as possible. So, developing therapies that could delay the onset of dementia should be a priority for our healthcare system." The findings from this study suggest that cognitively challenging dance-based activities could be just such a therapy. A larger more definitive trial is needed before widespread adoption, but the Ronnie Gardiner Method could improve clinical practice, and ultimately inform a new health policy specific to the impending dementia crisis.

"We know that there was recently a large study in the UK that taught stroke patients the Ronnie Gardiner Rhythm Method, but the results have yet to be published," said Kristina. "We'll certainly be getting in contact with them to compare our results, and to see if we can collaborate." Longer-term too, the team has plans to make further use of BRNZ's network, "We have lots of unanswered questions, in terms of the physiology and cellular biology behind these results, so we'd love to combine our physical study with brain imaging with collaborators," explained Ngaire.

Ultimately, Ngaire and Kristina hope that their work helps to improve the lives of older people with mild cognitive impairment. "I am passionate about helping people to experience a healthier old age. And if we can do that while having fun, then that's even better"

APP-SOLUTELY FABULOUS

TACKLING THE STROKE EPIDEMIC WITH THE TOUCH OF A BUTTON

When health experts talk about our growing use of smartphones, it is rarely for positive reasons. But a new app, developed by Kiwi scientists, has the potential to literally save lives, thanks to its novel approach to stroke prevention.

Endorsed by leading charities and research organisations, and supported by BRNZ, the Stroke Riskometer™ app is already in use in 104 countries, and has been downloaded more than 100,000 times. Its developer, Professor Valery Feigin, is the Director of the National Institute for Stroke and Applied Neurosciences, at Auckland University of Technology, and he is passionate about reducing the burden of stroke worldwide.

In a paper published in The Lancet in 2016, Valery showed that 74% of the factors that increase someone's risk of stroke are behavioural – particularly smoking, poor diet, and low physical activity. "That's the main thing to realise about stroke", he said. "Though it is devastating, in most cases it's also highly preventable. Lifestyle changes can greatly reduce an individual's risk."

Despite this, around the world, public health efforts have largely focused on treatment, rather than prevention of stroke, partly thanks to two recent breakthrough techniques – thrombolysis, which dissolves dangerous clots in blood vessels, and thrombectomy, in which a blood clot is physically pulled from the brain. While both are incredibly effective, according to Valery thrombectomy has been used for just 90 people in the whole of New Zealand, and thrombolysis is given to only about 7% of ischaemic stroke patients. "We have 9,000 cases every year – and that number is on the rise." In addition, most screening programmes target only those traditionally considered 'high-risk' –smokers, diabetics or those with high blood pressure or cholesterol. By definition, this approach to prevention misses people with low to moderate risk, which is where the vast majority – up to 80% – of today's strokes and heart attacks actually occur.

The solution then, as Valery sees it, is to take a more population-wide view on stroke prevention – to target everyone, regardless of their risk. With three out of every four New Zealanders now using a smartphone on a daily basis, producing a mobile app offered an easy way to reach a large audience. "Our motivation for developing it was to deliver information on stroke risk and prevention to as many people as possible, for little or no cost." The Stroke Riskometer™ was born in 2015 after consultation with other leading experts, and is now fully endorsed by the World Stroke Organization, World Heart Federation, World Federation of Neurology, European Stroke Organisation, Australian Stroke Foundation, Stroke Association of China and the International Association of Neurology and Epidemiology.

The interface is simple – users are asked 20 questions which are known to contribute to stroke. Their answers are used to calculate their absolute risk of stroke in the next five to ten years, as well as their relative risk compared to someone else

of the same age and sex. It also provides information on F.A.S.T. which summarises the early signs of stroke, and the 'pro' version of the app gives users information on how they can reduce their risk of stroke or heart attack. In addition, those who give informed consent also contribute, through the app, to a global study on stroke called RiBURST.

But Valery and his team wanted to take the app further – to demonstrate how effective it really is as a prevention tool. And this is where the BRNZ stepped in – the Stroke Riskometer™ is now undergoing a randomised control trial, with users across New Zealand. "This funding has been vital to us – we hope the pilot study shows that the app works as a standalone or add-on tool for education, behaviour modification and primary prevention of stroke."

Valery also hopes that the study will begin to offer answers to questions specific to New Zealand. "Maori and Pacific populations are two to three times more likely to suffer cardiovascular disease than those of European descent. And contrary to what you might have read elsewhere, this difference cannot be explained solely by conventional risk factors!" So a central part of their research effort is to culturally tailor the app for each community that uses it, to encourage widespread adoption, and they've made it available in multiple languages too. For Valery, the best research is that which engages with a global audience.

> *"If we develop only expensive, high-technology solutions, they will never be used in developing countries. They are the ones suffering most from the stroke epidemic, so we must always think globally when it comes to health."*

There is no doubt that the burden of cardiovascular diseases is growing faster than our ability to treat them. So, primary prevention is gaining in importance. Some national governments have lobbied the food industry to reduce salt and sugar, while others have taxed alcohol and tobacco. "We know that these population-wide strategies work incredibly well, but they can be hard to implement," said Valery. "We hope that the use of mobile technology can finally help us defeat the epidemic of stroke."

PROFESSOR VALERY FEIGIN

Director of the National Institute for Stroke and Applied Neurosciences at AUT

TUNING OUT TINNITUS

Imagine having to live with a persistent, irritating noise, such as a buzz, a ringing sound, or an ever-present whistle. That's the reality facing up to one in five people in New Zealand. They suffer from tinnitus, a condition described by the University of Auckland's Dr Grant Searchfield, as "the perception of sound in the absence of an external auditory source."

Though it is known to be a problem within the auditory system, no two cases of tinnitus are the same – the condition's severity, symptoms and triggers vary significantly between individuals, which makes finding a suitable treatment a huge challenge.

> *"We once thought that tinnitus originated in the ear," said Grant, "But in more recent years, we've realised that it is actually a brain network problem that even involves parts of the brain not normally associated with hearing."*

With a system as complex as this, Grant and his team employ an array of techniques to explore and treat tinnitus in their patients, including magnetic resonance imaging, behavioural studies and electrophysiology – measuring brain waves in response to sound simulation. But what unites them all is a theoretical model that Grant has developed. It looks at the relationships between psychosocial factors (e.g. stress), background sound, and the tinnitus symptoms, producing a map that a patient's experience can be plotted onto. "The idea of this is to try to understand and quantify the variation between individuals, and then develop a treatment plan unique to that person," Grant said.

Unsurprisingly, sound is the main weapon in their arsenal. Over the years, Grant and his team have collected a huge library of sounds that can be used for 'brain training' – providing short-term relief to sufferers from their tinnitus, or even helping them to manage it in the longer-term. But however many successes they've had in their specialist tinnitus clinic, Grant wanted to find a way to reach a wider audience.

So he collaborated with Tom Donaldson, a colleague at Auckland, to create Tinnitus Tunes – a website that acts as a repository for the group's knowledge, and a safe source of easily-accessible information for sufferers. Sound therapy files can be selected and then downloaded direct to an individual's smartphone, or even streamed to their hearing aid, to help them manage their tinnitus. Importantly too, Tinnitus Tunes is rapidly becoming a space for collaboration amongst researchers and clinicians. "As well as allowing us to connect with the community, the site has made us more nimble in our research," said Grant, "and has led to interest from international funding bodies."

Grant's group is one of three within BRNZ that focuses on tinnitus – the others are at the University of Otago – and this is because age is a significant factor in the prevalence of tinnitus. Some of its symptoms have been linked to the general impairment of a specific hearing nerve that occurs with ageing. As Grant explained, "Our research in tinnitus is beginning to feed back into general studies of sensory systems. With BRNZ support, we're now exploring brain networks involved in ageing, which are similar to those impacted in tinnitus. We're particularly interested in the effect that age has on the interaction between hearing and vision."

To learn more, visit: www.tinnitustunes.com

THE DEMENTIA PREVENTION RESEARCH CLINICS

Dementia is a leading cause of death in New Zealand. There is no cure.

In April 2016, Brain Research New Zealand officially launched its first Dementia Prevention Research Clinic in Auckland, the first of three across New Zealand.

Attendees included kaumatua, BRNZ PIs, as well as Hon Stephen Joyce, community groups, funding body representatives (HRC, Neurological Foundation), Memory Services clinicians, and our two pilot participants for the clinics. It was a positive celebration, infused with hope for the future.

The goal of BRNZ's Dementia Prevention Research Clinics is to recruit individuals with mild cognitive decline or the early stages of Alzheimer's disease. We provide them with thorough assessment and feedback on their condition and then enrol theme in one of our longitudinal or intervention studies.

> *Dementia is an umbrella term used to describe a group of symptoms including impaired thinking abilities, memory loss, confusion, difficulty with day-to-day tasks, and often behavioural and mood problems. It is caused by various diseases of the brain, with the most common cause being Alzheimer's disease.*

Through our network of research clinics, BRNZ aims to study ~400 people over 4 years to determine which biomarkers, cognitive characteristics, and health and lifestyle factors determine subsequent development of Alzheimer's disease (AD). Alternatively, people who attend the clinics may be invited to participate in one of a range of preliminary clinical trials, with the goal of identifying treatments and interventions that might prevent, delay or ameliorate AD or related dementias.

One of the main issues with AD is that by the time a clinical diagnosis is made, a significant amount of irreversible brain damage has already occurred. Yet biological indicators occur up to fifteen years before clinical symptoms show. If we can diagnose patients at risk for dementia early in the disease, they will have the opportunity to access drug and non-drug treatments that could improve their cognition, delay progression of the disease and thereby enhance their quality of life. Discovering new diagnostic tests and interventions for AD is no small task and it will take immense and coordinated efforts. Brain Research New Zealand is in the unique position of being able to unite New Zealand's best scientists and clinicians to tackle the disease head-on, and we have already begun.

With just on 9 months of operation under its belt, BRNZ's Auckland-based clinic is on its way to establishing a well characterised patient cohort that our researchers can use for our longitudinal and intervention studies. Here BRNZ's National Clinic Director, Associate Professor Lynette Tippett, provides an overview of progress in this exciting area:

ASSOCIATE PROFESSOR LYNETTE TIPPETT

BRNZ's National Clinic Director

OVERVIEW

"Following obtaining ethical approval for the Dementia Prevention Research Clinics at the end of 2015, there was a rigorous period of testing the implementation of each of the protocols for the clinic:

1. clinical assessment
2. neuropsychological assessment
3. MRI protocols
4. diagnostic procedures
5. blood-taking and preprocessing of blood.

This was most intensive for the MRI protocols and the protocols associated with the blood-bank. The MRI platform PIs, Professor Ian Kirk and Dr Tracy Melzer worked closely with international colleagues including those involved with the Alzheimer's Disease Neuroimaging Initiative and the UK Biobank Imaging Study, to determine the precise protocols needed for scanning of this type. Critical quality control processes have been developed with the expert input of MR physicist Catherine Morgan, who joined us from University College, London and who has experience in multi-site longitudinal MRI studies. Professor Donna-Rose Addis has been working on the essential data storage infrastructure for this large multi-site longitudinal study.

Equally demanding has been the development of processes relating to the DPRC bloodbank, with recent international recognition that preanalytical variation in study procedures is a crucial limiting factor in the search for blood-based biomarkers of MCI and early dementia. To this end our Blood-bank Fellow, Dr Erin Cawston worked closely in the first months of the year with scientists involved in large international studies. In particular she has worked to precisely align our protocol with those currently used by Professor Ralph Martins, co-PI of the Australian Imaging Biomarkers and Lifestyle Study of Ageing. Though the protocols are time-intensive, this has increased our compatibility with international studies, and ensured our processes are at the cutting edge of international research. Dr Cawston and PI Joanna Williams attended the Alzheimer's Association International Conference® 2016 in Toronto as well as other research

centres to learn more about international standards for blood processing for longitudinal dementia studies. These international links are ensuring that our blood-bank processes are of the highest international calibre.

The DPRC has also benefitted from the sage input of Science Board member Professor David Smith. His input, plus that of Professor Linda Clare of the University of Exeter (visited by Associate Professor Tippett in May), a prestigious UK researcher working in the area of dementia, encouraged us to develop a strategy to meet the challenges associated with retention of participants in longitudinal studies of this sort. We have strived to have ongoing conversations and input from community partners including Alzheimer's Auckland (now named Dementia Auckland), Alzheimer's New Zealand, and the national Dementia Co-operative. At the heart of these clinics will always be the people – those participants who generously chose to be part of the research journey.

Staffing

Prior to launching the Auckland DPRC, we needed to recruit our part-time clinical specialists to join the clinical research nurse (Karen Smith until October, 2016, then replaced by Christine Brennan) and neuropsychologist (Dr Christina Ilse). We were fortunate to recruit Dr Kiri Brickell, a neurologist with a special interest and expertise in dementia and Dr April Clugston, a consultant older age psychiatrist (from CMDHB). They have been welcome additions to the clinical team, that also comprises myself, Dr Gary Cheung (Older age psychiatrist), and Dr Phil Wood (geriatrician and current Health of Older Person Chief Advisor in the Ministry of Health), all of whom bring clinical and research expertise to the DPRC. In 2017 we will recruit a part-time geriatrician to increase our capacity.

We have seen 50 participants in 2016, the details of which are outlined in the table on the next page.

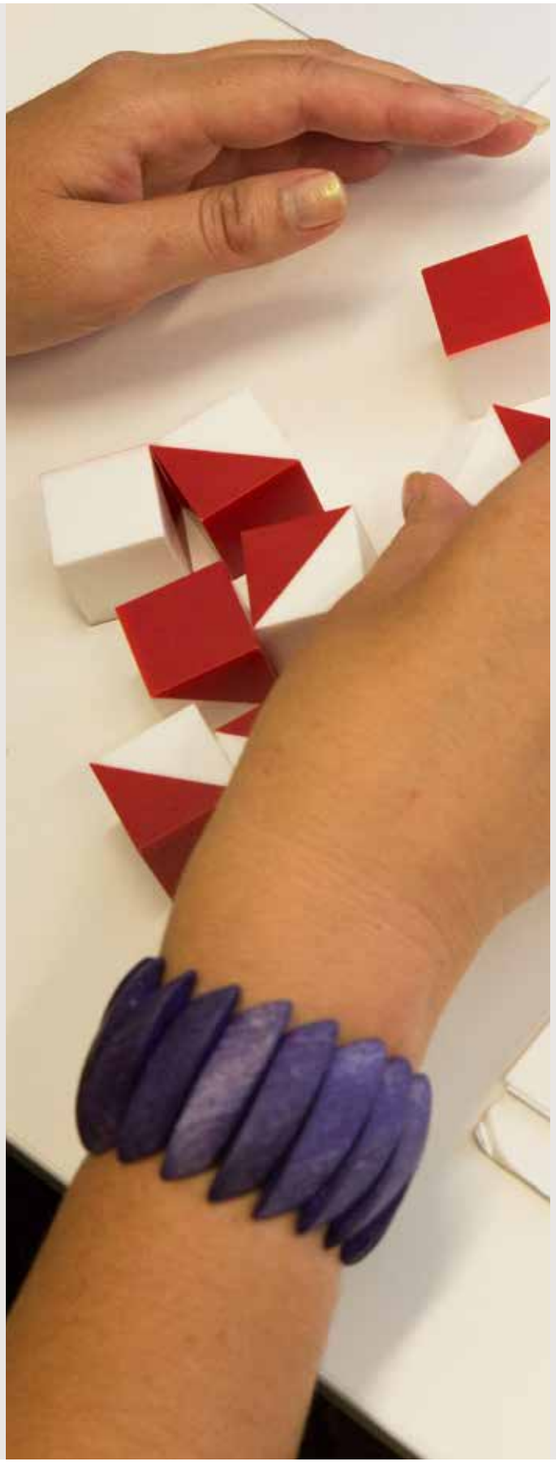


TABLE 1. TOTAL PARTICIPANTS SEEN AT AUCKLAND DPRC (COMPLETED OR IN PROGRESS, N=50)

Subjective Cognitive Decline	8
Mild Cognitive Impairment	8
In Progress	11
Early Alzheimer's Disease	4
Moderate Alzheimer's Disease	4
Dementia - Other	5
Other (post head injury)	2
Control Participants	4
Strong Family History of AD	4

Of the total seen, 11 participants do not meet our criteria, and we are examining ways of reducing inappropriate referrals, and of improving the hit rate of those with MCI or subjective cognitive decline. To address these issues, the DPRC team has engaged in a number of targeted speaking opportunities this year. In addition we have established a link to information about our clinic, eligibility, and the referral process inserted into the newly developed eLearning Dementia Education Resources for GPs and Practice Nurses being established at the Goodfellow Unit at Auckland University.

Dunedin and Christchurch DPRCs

The directors of the upcoming Dunedin (Dr Nick Cutfield) and Christchurch DPRCs (Professor John Dalrymple-Alford) have been fully involved in development of the protocols to be used across the three clinics. Both clinics are planning to open in 2017, with appointments and training of staff already beginning in 2016 for the Dunedin clinic.

The Auckland DPRC Team
FROM LEFT / **DR PHIL WOOD, DR KIRI BRICKELL, DR ERIN CAWSTON, A/P LYNETTE TIPPETT, CHRISTINE BRENNAN, DR CHRISTINA ILSE AND DR GARRY CHEUNG**

DR JOANNA WILLIAMS / THIRD FROM LEFT / and her team at the University of Otago

"It may well be that we already have the perfect cures, but they're just not given at the right time."

UNCOVERING THE HALLMARKS OF

ALZHEIMER'S IN THE BLOOD

The University of Otago's Dr Joanna Williams started life as a molecular neurobiologist. After great success from her early work on how the brain changes when memories form, her research interests now not only include fundamental science, but she has also embraced something more directly applicable to the clinic.

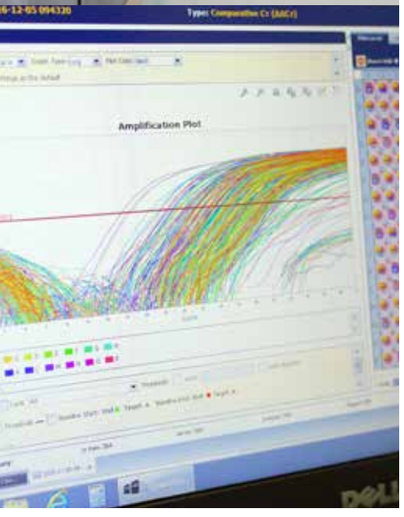
"The desire to contribute more than just knowledge led, rather naturally, into examining the other side of memory formation – how memories fail to form in patients with Alzheimer's," she explained.

> *Alzheimer's is a degenerative disease, in which neurons are progressively damaged over a long period of time. It begins silently – for the first 15 years or more of the disease's progression, a patient won't display any obvious symptoms. By the time the symptoms of memory loss, behavioural change or cognitive impairment appear, much damage has already been done.*

So, before clinicians can effectively treat Alzheimer's, they must first be able to detect the earliest stages of the disease, even before overt symptoms become apparent. This is also the period when the brain tissue will be most receptive to treatment.

There are, of course, practical issues with diagnosing Alzheimer's using brain tissue from a live patient, so Joanna had to find another way in. "If we want to screen for people who are likely to develop Alzheimer's, we have to start early, and that means targeting people in their 40s," she explained. "Expensive imaging techniques aren't going to be an option." Another screening tool that has been widely touted is cerebrospinal fluid (CSF) collection. CSF is the clear, viscous fluid that surrounds the brain, and it is typically accessed via a lumbar puncture, commonly called a spinal tap. While this fluid can provide a lot of information about the molecular status of the brain, for Joanna, it is too invasive to become a practical screening technique.

So, she turned to the human circulatory system. Though incredibly complex, it is fundamentally tasked with moving blood around the body. The heart may lie at the centre of this system, but all of the major organs, including the brain, are nourished by it. As blood passes through each organ, it picks up molecules – called biomarkers – that are unique to each organ.



In addition, specific combination of biomarkers are now being linked to a small but growing number of disorders, including cancer and cardiovascular disease. “I remember the moment where I naïvely thought, ‘if only we could do this for neurological conditions like Alzheimer’s”, said Joanna. “Once we started looking into it properly, we realised that, actually, we can!”

Initially, her work – in collaboration with Dr Nick Cutfield, and Professors Bob Knight, Cliff Abraham and Warren Tate – has focused on developing a simple blood test that screens for specific molecules, in particular microRNA, in blood plasma. But transforming that into a clinical tool that correctly identifies Alzheimer-specific biomarkers requires a much greater effort. For this, Joanna turned to one of the BRNZ’s major initiatives – the Dementia Prevention Research Clinics, a national collaborative effort focused on investigating the factors that contribute to dementia.

Funded by BRNZ and the New Zealand Dementia Prevention Trust, and as part of a wider team of clinicians and researchers, Joanna and Research Fellow, Dr Erin Cawston, will lead the development of a world-class blood biobank within BRNZ’s research clinics. Importantly too, this approach will allow Joanna and other BRNZ investigators the opportunity to carry out longitudinal studies that cover the entire progression of Alzheimer’s.

“There are two major challenges with biomarkers for ageing disorders – 1) there are very, very few studies that have been around for long enough to encompass the full progression of a neurodegenerative disease, and 2) due to inconsistencies in how blood samples are processed, everyone keeps finding different answers!” said Joanna. “Those issues are, fundamentally, what we’re trying to address with our clinics.” Joanna and Erin will be using the Australian Imaging, Biomarker & Lifestyle Study of Ageing (AIBL) as the gold standard for blood biomarkers in neurodegenerative diseases. This landmark study has been taking blood samples from over 1000 patients for a decade, with the aim of identifying those factors that contribute to the development of Alzheimer’s disease. The samples that are being collected via the Dementia Prevention Research Clinics will be directly compared to those from the AIBL study, as well as to existing samples at Otago.

> *The hope is that this will lead to a first of its kind – a standardised, internationally-respected processing methodology for biomarkers. In addition, the information gleaned from a combined study will add a greater depth of knowledge, “... allowing us to pinpoint the exact biomarkers for Alzheimer’s, not just in New Zealand, but also in Australia, and beyond,” said Joanna.*

In addition, BRNZ is funding a second study with Joanna – this one is looking at blood in an even more sophisticated fashion, by analysing exosomes, recently discovered communication bodies that carry information and proteins between cells. Once thought to be nothing more than a ‘trash collection’ service for cells, early stage results suggest that exosomes could offer vital information on how neurological disorders progress between different regions of the brain.

Fundamentally, Joanna’s hope is that a biomarker-based approach would not only help to identify Alzheimer’s at a much earlier stage, but it could also open the door to improved drug interventions for the disease too. “All of the drugs that target the diagnostic principles of Alzheimer’s have failed in clinical trials. But that’s because they are only given to people who are well-advanced in the disease,” Joanna explained. “It may well be that we already have the perfect cures, but they’re just not given at the right time. So it’s all the more vital that we try to detect the disease as early as possible.”

A PENNY FOR YOUR THOUGHTS?

THE NEW ZEALAND DEMENTIA PREVENTION TRUST

Dementia is an enormous global health challenge. In New Zealand today, over 50,000 people are living with the condition and this is projected to reach 75,000 in the next twenty years.

As New Zealand’s ageing population grows, the number of people suffering from dementia will impose a significant economic and social burden on our society. The direct costs associated with dementia are estimated to have increased by 75% - from $955 million on 2011 to $1,676 million in 2016[1]. Yet despite the prevalence and costs of dementia, dementia research in New Zealand is significantly underfunded in relation to other chronic diseases, making philanthropic funding a crucial source of income for our centre.

In 2015, the New Zealand Dementia Prevention Trust (NZDPT) began life with a significant amount of hope, but no funding to its credit.But through the dedication of Sir Eion Edgar KNZM, (Chair), Mr David Mace ONZM, Sir Don McKinnon ONZ GCVO, Lady Barbara Stewart QSO and Sir Ralph Norris KNZM, the Trust has witnessed exciting growth. Through the generosity of family foundations and individual donors, the NZDPT now has over $3million in pledged donations. In 2016, funding from the Trust enabled us to purchase vital research equipment and to hire talented research staff. In Auckland, we appointed a Clinical Trials Coordinator to oversee the operations of all three clinics, while in Dunedin we hired a Research Nurse and Clinical Neuropsychologist. The Dunedin staff will help in the recruitment of adults with mild cognitive impairment or the earliest stage of Alzheimer’s disease, and to carry out detailed diagnostic evaluations.

The NZDPT provides funding for our researchers so they can make a difference to the lives of New Zealanders, without its support, this research would not be possible.

To donate contact Alex Sweetman at Alexandra.sweetman@otago.ac.nz

1. Deloitte Dementia Economic Impact Report, New Zealand.” Report prepared for Alzheimer’s New Zealand. Retrieved from http://www.alzheimers.org.nz/Alzheimers/media/alz/NewsInfo/ReportsandStats/Economic-Impacts-of-Dementia-2017.pdf

IN THE

CLASSROOM

BRNZ is deeply committed to training the next generation of New Zealand neuroscientists and clinicians.

But to build the health and research workforce of the future, we need to start early and attract the best students from secondary school and undergraduate programmes to postgraduate study and careers in health research. In 2016, we continued to support the Brain Bee Challenge to inspire and encourage secondary school students into neuroscience training programmes. We also invested in the development of an exciting new primary and intermediate school outreach initiative spearheaded by Professor Bronwen Connor.

In the two years since our launch, we have provided funding to seventeen PhD students (including two MB ChB-PhD students and two Māori PhD students), six postdoctoral fellows, two research fellows and two Māori summer scholars. We also supported the research and career development of undergraduate and postgraduate students from a broad range of disciplines working on BRNZ funded and aligned projects.

In 2016, we awarded three new postdoctoral fellowships, and ten new PhD scholarships. The three postdoctoral fellow awardees; Dr Owen Jones (University of Otago), Dr Pritika Narayan (University of Auckland) and Dr Brigid Ryan (University of Auckland), come from labs in the departments of Psychology and Physiology, Biological Sciences and Anatomy and Medical Imaging respectively. In addition to receiving fellowship support, our postdoctoral fellows have the opportunity to learn new research techniques and different fields of study, and to present their research to peers and senior investigators at our annual research meeting in Queenstown. BRNZ's annual research meeting presents a valuable opportunity for our students and postdoctoral fellows to gain a multidisciplinary perspective by meeting senior national and international neuroscientists from differing fields as well as clinicians who provide opportunities for students to participate in neurological clinics.

EARLY CAREER RESEARCHER WORKSHOP FEBRUARY 2016

BRNZ's 2016 Early Career Researcher (ECR) workshop was the first national meeting of emerging researchers from across our CoRE. Held in Christchurch on 2-3 February, over 60 registrants and ten presenters from a range of backgrounds including academia, theatre, government, NGOs and medicine attended the two-day event.

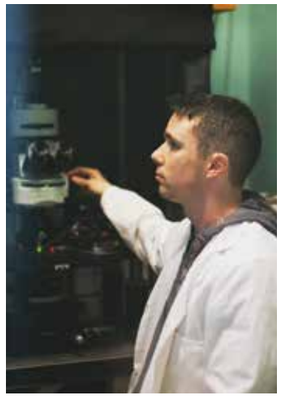
The workshop, full of fascinating and motivating presentations, was designed to provide our ECRs with professional development and networking opportunities, whilst also giving them the chance to meet and be inspired by individuals living with neurological disease.

To shed some light on the experience, on day one our ECRs started their day learning about MRI acquisition and data analysis in a joint presentation by Professor Donna-Rose Addis and Dr Tracy Melzer. One of our leading neurologists, Professor Tim Anderson, took the MRI theme a step further by explaining how imaging techniques can be used in the clinical setting, to diagnose and treat patients with Parkinson's disease (PD). What it means to live with Parkinson's disease is not something that is front of mind for researchers, so Tim introduced one of his patients to the group, sparking conversation about the real life challenges of PD, the impact such a condition has on family life, and the degree of trust involved in a patient's relationship with their clinician.

A highlight for many was listening to Rosie Belton - drama teacher, director and producer and author of "Just a bang on the head" - explain how a seemingly minor slip at a friend's wedding resulted in Traumatic Brain Injury that completely altered her life. For our young researchers, the opportunity to meet people like Rosie who live with debilitating neurological conditions is a powerful and inspirational experience and one that squarely puts their research in context - "I could see the real world impact of my little piece of research". Next to be invited onto the podium, was Professor Richie Poulton, Director of the Dunedin Multidisciplinary Health and Development Research Unit, which conducts the Dunedin Longitudinal Study — one of the most detailed studies of human health and development ever undertaken, and the longest-running project of its type in the world. Richie took the opportunity to share the many successes of the study, as well as highlight some of the challenges, such as how to maintain high retention rates and sufficient funding to continue running the study.

To round off the programme, Dr Ngaire Dixon, Chair of Alzheimer's New Zealand, shared her experience in leadership positions and developing effective teams. Ngaire emphasised the need for graduates to build great and collaborative people skills, develop their leadership skills, and participate wholeheartedly in team environments. Professor Kathryn McPherson, CEO of the Health Research Council, also gave her time to talk about the New Zealand funding environment in New Zealand, explaining current funding priorities and sharing some useful insights with some eager young minds.

CLINICIAN SCIENTISTS IN TRAINING



One of BRNZ's many workforce development goals is to increase the number of clinician-scientists, that is, clinicians who have experience with basic research.

Doctors, nurses, audiologists, physiotherapists, psychologists and other allied health professionals that have direct experience in research learn to "think like scientists". By becoming familiar with the process of conducting scientific research, they learn how to discover and apply new knowledge about the mechanisms, diagnosis and treatment of disease – leading ultimately to the delivery of better care for New Zealand patients.

In 2016, BRNZ provided funding to two young medical students to enrol in the University of Otago's MB-ChB PhD programme - Tim Galt and Rosie Melchers. BRNZ started offering MB-ChB PhD scholarships to support talented medical undergraduates to undertake PhD training while still an undergraduate. There is an acknowledged need for well-trained clinician-scientists worldwide and BRNZ is doing its best to bridge the gap in New Zealand.

COMING SOON TO A SCHOOL NEAR YOU!

The Being Brainy science programme is the brainchild of BRNZ investigator Bronwen Connor, Associate Professor in Pharmacology and head of the Neural Reprogramming and Repair Lab at the University of Auckland.

Struck by the lack of brain science being taught in schools, Bronwen was determined to come up with a fun and practical way of sharing her passion for neuroscience with as many Kiwi kids possible. And so it was that with a little financial backing from Brain Research New Zealand, and a significant amount of elbow grease, the Being Brainy science programme was born.

> *Being Brainy was developed by neuroscientists at the Universities of Auckland and Otago to enable science and technology engagement with primary and intermediate schools using the example of the human brain.*

It is a free teaching resource that gives primary and intermediate school teachers everything they need to take students on an exciting 8-week programme full of hands-on activities, experiments and inquiry about the human brain. A web-based initiative, students and teachers can also talk with BRNZ members online, or in person during school visits and access an extraordinary library of web-based resources.

BRNZ's Being Brainy programme will be officially launched across the country early 2017. So far, it has been trialled at two Intermediate schools (Blockhouse Bay Intermediate; Northcote Intermediate) and four Primary schools (Upper Harbour Primary, Sunnybrae Normal Primary, Birkenhead Primary and Orere Point School) in the North Island and the feedback has been outstanding. Formal and informal feedback from both teachers and students has shown that the programme generated a high level of learning and inquiry from students, whilst connecting school learning to real-world contexts and providing students with an insight into a career in science. Several schools found they could easily incorporate aspects of the lesson plan into other curriculum topics including art, literacy and/or numeracy. What sets Being Brainy apart is the easy access to support and professional learning that our researchers provide to teachers to give them the knowledge and confidence they need to inspire future Kiwi scientists.

Being Brainy

BRIDGING THE DIVIDE

FOSTERING SCIENTIFIC RESEARCH AMONG TRAINEE HEALTH PROFESSIONALS

Medicine and science have always enjoyed a fruitful, shared history. Breakthroughs in one field have invariably led to advancements in the other. It is this understanding that has driven Otago Professor John Reynolds to encourage more medical students to seriously pursue scientific research. Some, he hopes, may get the research bug and pursue their investigations as clinician-scientists; others may transition wholly into a research career and enjoy a life of science, just like him.

PROFESSOR JOHN REYNOLDS / RIGHT / WITH MB ChB-PhD STUDENT ROSIE MELCHERS

John's message to doctors-in-training has already started to resonate. Rosie Melchers is one such medical student who has taken the opportunity to pursue her love of neuroscience, whilst still completing her medical training. After her third year of medicine, Rosie completed a year-long medical science degree. She was immediately grabbed by lab-based research, and knew she wanted to do more. That is when she decided to apply for one of a BRNZ's newly offered MB-ChB PhD scholarships, which combine medical and scientific training to produce outstanding clinician-scientists.

Rosie's doctoral research explores how brain stimulation techniques can be used to improve recovery after a stroke.

> *Following a stroke, there is a reduction in functional brain tissue in the lesioned, or damaged, part of the brain. For that function to be regained, other healthy areas of the brain need to take over for the damaged parts, a process that requires neuroplasticity.*

According to Rosie, if you can find a way to increase the neuroplasticity of the areas next to the lesioned part of the brain, you would improve a person's chance of recovery. But, like everything in science, it is not that simple. In patients with motor cortex stroke, there is an increase in inhibition from the hemisphere opposite the stroke lesion, onto areas surrounding the lesioned cortex. Rosie thinks this increase in interhemispheric inhibition (IHI), as it is called, limits recovery, and that if you could decrease it, then you could improve a patient's chance of recovery. "I'm looking at ways to measure that (IHI) and then modify it using stimulation techniques to hopefully produce some additional benefits, over and above traditional rehabilitation". Rosie's project has the potential to lead directly to changes in clinical practice. It also has implications for a study that John is doing, which could yield opportunities for cross-pollination in their respective investigations.

Rosie has set herself an ambitious workload: she is juggling her PhD at the same time as completing her medical training. But John, her primary supervisor, is confident she will take the challenge in her stride: "What Rosie is embarking on is incredibly demanding but she's got the mettle to do it. There are very few people who do this because it is such a commitment, but we need more."

And John is quick to point out that all of Rosie's hard work will pay great dividends: "It is a fantastic bridge for Rosie's career. She will go on to understanding the scientific process, and hopefully end up running a large research programme, as well as her clinical practice."

Rosie herself would not hesitate to encourage other medical students to consider pursuing scientific research seriously, as a means to supplement their clinical training:

"There's no point doing anything in medicine if it doesn't have a good scientific backing. So I think that's what's valuable to me - and if it leads to career opportunities, that's great as well."

YOUNG SCHOLARS TAKE FLIGHT

2016 saw the launch of BRNZ's Young Ambassadors scheme, designed to support the development of promising young neuroscientists through funding their travel to international conferences, to training workshops and to visit laboratories around the world.

Breaking into today's research environment is difficult. To be internationally competitive, New Zealand's young scientists need to be able to demonstrate their contribution to knowledge and gain recognition for their work- no mean feat when you live in a remote corner of the world.

In 2016 BRNZ provided the means for twenty of our top young scholars to present at major international conferences. Our Young Ambassadors scheme has seen the highest calibre of young Kiwi neuroscientists pack their bags to promote New Zealand neuroscience and Brain Research New Zealand on the global stage.

In doing so, they have had the opportunity to create new connections and increase the odds of coming across a new contact or idea. They have also increased international awareness of Brain Research New Zealand, and the leading-edge research we undertake.

1/ SOUTH KOREA
Computational Neurosciences Meeting 2016

2/ SAN DIEGO
Society for Neuroscience

3/ SLOVENIA
11th international congress on non-motor dsyfunctions in PD and related disorders, NMDPD 2016

4/ NEW LONDON, NH, USA
Barriers of the CNS, Gordon Research Conference; 2nd Annual Blood-brain Barrier, New Understanding, Strategies and Tools for Delivering Therapy to the Brain

5/ DENMARK
10th Federation of European Neurosciences Societies. Forum of Neuroscience

6/ BOSTON, MA, USA
2nd Annual Blood-Brain Barrier: New Understanding, Strategies and Tools for Delivering Therapy to the Brain. World Preclinical Congress

7/ BOSTON, MA, USA
SIAM Conference in the Life Sciences

8/ LISBON, PORTUGAL
The 10th World Congress on Controversies in Neurology (CONy)

9/ MELBOURNE, AUSTRALIA
World Congress on Active Ageing

10/ SEOUL, SOUTH KOREA
Barany Society Meeting and Satellite conference

11/ CALGARY, CANADA
2016 National Falls Prevention Conference: Applying Integrated Approach

12/ BRISBANE, AUSTRALIA
Australian Course in Advanced Neuroscience

13/ VIENNA, AUSTRIA
Dopamine 2016

FROM NZ TO THE WORLD

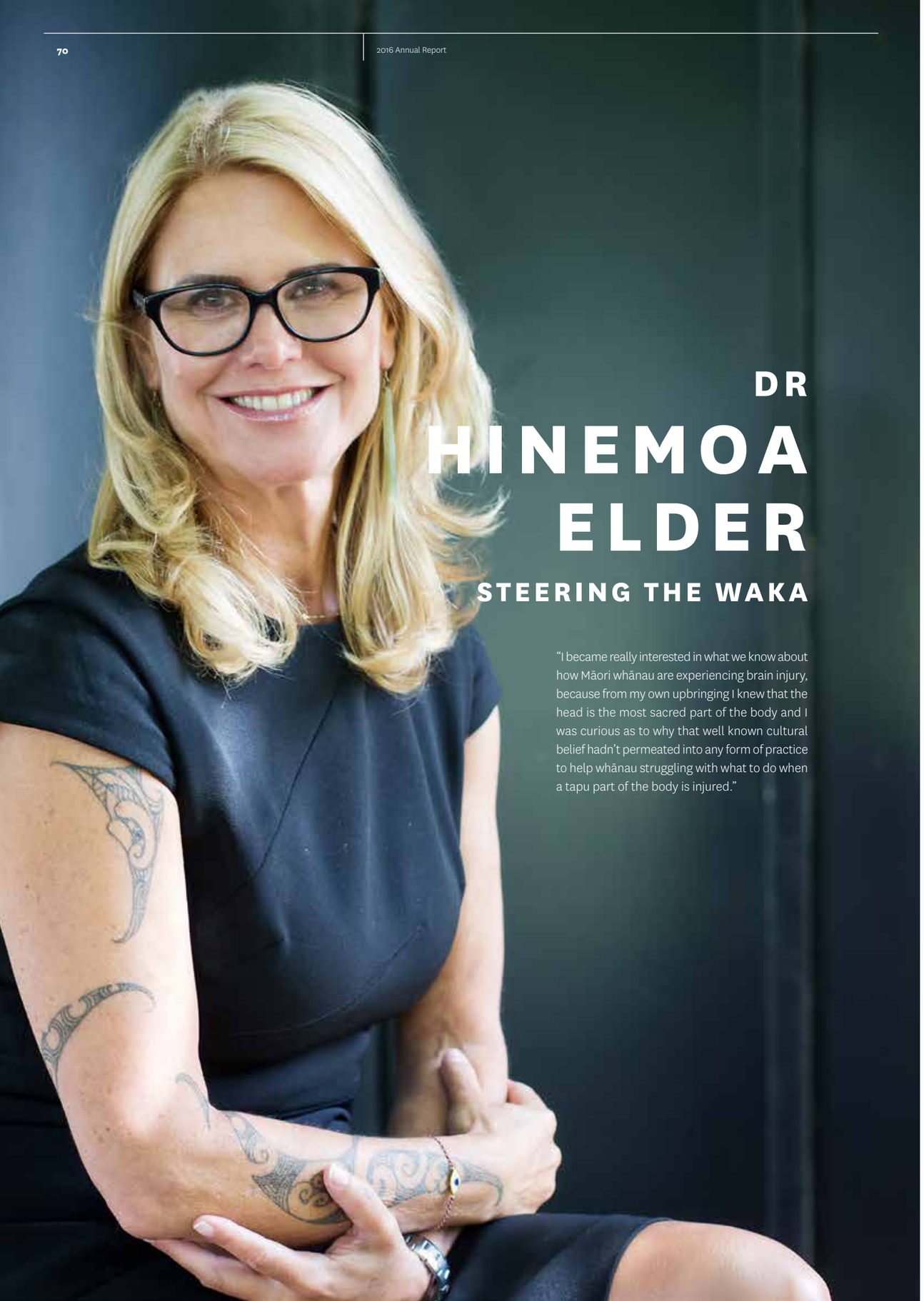
BRNZ's Young Ambassadors travel destinations 2016

HAUORA MĀORI

E kitea ai ngā toanga o te moana me mākū koe – If you seek the treasures of the ocean, you need to get wet.

With the baby boomer generation reaching their 60s and 70s, New Zealand's elderly population continues to grow. However, our Māori population is ageing at the most rapid rate. In the next twenty years, the number of Māori aged 65 years or more will grow at almost double the rate of non-Māori. Issues of dementia, falls and cognitive decline will become increasingly relevant, making it more important than ever for researchers and clinicians to partner with Māori to understand their needs and values, and through enhanced cultural awareness undertake and promote relevant and appropriate research. Research for Māori is best done by and with Māori. It is therefore vital to foster a thriving Māori neuroscience and healthcare workforce, to ensure Aotearoa - New Zealand provides culturally responsive models of care for Māori and their whanau.

In 2016 BRNZ made significant progress towards addressing these Māori health imperatives by focusing on four key areas: partnering with Māori; capacity building; Māori specific research and Mātauranga Māori. Under the leadership of our Kaiwhakahaere Māori (Māori Strategic Leader) Dr Hinemoa Elder, 2016 saw BRNZ develop new and meaningful ties with two thriving Māori communities: Te Kura Kaupapa Māori o Hoani Waititi Marae in Auckland and Puketeraki Marae in Dunedin. We also invited two exceptional Māori clinicians on board and provided funding to talented Māori PhD students and summer scholars. A Māori researcher hui and Māori keynote speaker were also highlights of the CoRE's meeting in association with the Australasian Winter Conference of Brain Research (AWCBR). To cap off the year, we funded our first tranche of Māori research projects that directly address Māori health needs with Māori investigators at the helm.



DR HINEMOA ELDER

STEERING THE WAKA

"I became really interested in what we know about how Māori whānau are experiencing brain injury, because from my own upbringing I knew that the head is the most sacred part of the body and I was curious as to why that well known cultural belief hadn't permeated into any form of practice to help whānau struggling with what to do when a tapu part of the body is injured."

For Dr Hinemoa Elder, her first contact with human brain research came from a deeply personal place.

"When my mother died in 1991 she wanted to donate her body to the Medical School. My father and I first got to know Sir Richard through that bequest. Little did I know that I would soon be at Medical School myself. Later, Sir Richard would be on the supervisory panel of my doctorate and eventually I would end up working with him in this exciting role."

Hinemoa's decision to pursue psychiatry, with advanced training in child and adolescent psychiatry, grew from a fascination with the hinengaro (mind) and wairua (spritual connection). "These are foundational aspects of hauora that drew me to psychiatry and wanting to make a difference in this area of medicine. From a Western perspective the features of the mind such as consciousness, feelings and thoughts, memory, attention, and decision making focus on the workings of the brain itself. It is exciting that wider aspects of human experience such as social support and other organs of the body, like the gut, are being shown to have a key influence on the mind in ways we previously associated only with the brain. These findings align with Māori ways of thinking about the interconnections of human experience. I suspect exploring these aspects will illuminate novel enhancements in the experience of ageing that will benefit Māori and all New Zealanders."

Establishing an approach that reflects Māori culture and belief systems (Mātauranga Māori) soon became a priority for Hinemoa. Her PhD focused on developing new theory and practice around working with whānau and this was followed by her current Eru Pōmare Postdoctoral Research Fellowship, funded by the NZ Health Research Council (HRC), saw her develop a new tool for assessing the cultural needs young Maori who have sustained a traumatic brain injury (TBI) – a risk factor for the development of neurodegenerative disease.

When Sir Richard Faull asked Hinemoa to take on the role of BRNZ's Kaiwhakahaere Māori (Māori Strategic Leader) at the beginning of 2016, it was a true stroke of genius. Talented, tenacious and inspiring, she is using her experiences and personal history to encourage Māori into neuroscience and researchers onto the marae.

One of Hinemoa's first steps after joining the CoRE, was to ensure BRNZ lived up to the commitment it made to Māori communities, working with them to understand their needs and values, and incorporating Mātauranga Māori.

> *"Māori knowledge systems are difficult to articulate or bring forward if you're not using Te Reo Māori. So I've been very clear we have to think very carefully about how we begin to move into that territory and begin incorporating Mātauranga using Te Reo."*

One vital step is to build CoRE members' overall skills in Te Reo Māori and also to develop culturally robust technical language. "Speaking Te Reo really makes a difference when you go into a Māori community. It signals that you've taken some time, that you really respect our ways of communicating, that you mean business and it's not some sort of token thing, and you're not going to just come in and take information away. Those days are long gone," Hinemoa adds. "We also need to support Māori to determine our own pathways to brain health through the training of Māori neuroscientists and clinicians."

In a short time, the impact Hinemoa has had on BRNZ is extraordinary. She is singlehandedly changing the way researchers engage with Māori – brokering relationships with iwi and creating real partnerships that are a two-way street. She is also driving funding for Māori neuroscientists to lead Māori-specific studies, "As we go along and the people within those projects become alumni" she says "we can begin to develop a vertical stream or whānau structure where we're growing more senior Māori researchers, but we're also bringing onboard kura and school students, undergraduate, Honours and Masters students."

INTRODUCING

DR MARGARET DUDLEY

"I love pragmatic research, although I do understand the need to have theory-based evidence for what we do. But If I can be involved in research that affects the actual practice of our discipline then I'm all for that."

DR MARGARET DUDLEY
BRNZ Principal Investigator

Dr Margaret Dudley's path to becoming a BRNZ Principal Investigator is anything but conventional but absolute proof even a relative latecomer to the world of academic research can have a vital impact. Before taking on tertiary study in 1990, Margaret had spent 20 years working in varied roles from RNZAF sergeant to courier driver.

> *After returning to New Zealand in 1990 a friend suggested she head to University under a New Start course for mature students and it was during that time a lecture on the ramifications of splitting the brain to control epilepsy captivated her. "That just absolutely fascinated me and I thought that's the pathway I want to go down."*

After completing a degree in psychology she spent 15 years as a clinician before being asked if she wanted to undertake a PhD, working with patients in the early recovery of stroke. "I got the research bug and I love the whole world of conducting research in academia, so I applied for funding." Margaret found herself specialising increasingly in the field of assessing cognition for Māori and was approached by Professor Ngaire Kerse, Head of School of Population Health at the University of Auckland, to be part of a large longitudinal study. "They had been conducting assessment on the elderly Māori cohort within their study, for mild cognitive impairment. According to the assessment tool these kaumātua were assessed as having cognitive impairment but when the researchers actually met them and there was follow-up they realised that these individuals did not have mild cognitive impairment or early signs of dementia. Ngaire was talking to me about that and we both agreed that the assessment tool itself is wrong and likely not measuring in a culturally valid way." One example Margaret points to was a test using pictures of objects to test verbal abilities and test language to gauge whether there is a problem. "The current pictures are of animals such as a camel and a lion but maybe we should include pictures of a kiwi or a pukeko that are more relevant and familiar to elderly Māori and therefore more accurately tap into their memory for word finding abilities." They decided to apply for funding to develop a more accurate tool for detecting mild cognitive impairment or dementia in elderly Māori and are now more than six months into the three year Health Research Council-funded project. "Our goals are to develop a Māori theory of dementia and develop assessment tools to help diagnose or detect dementia in Māori in a more accurate way," she says. "We want a tool that is Māori friendly and Māori appropriate. It's going to be contextually Māori and therefore more relevant and lead to more accurate detection of dementia." For Margaret, being a researcher in Brain Research New Zealand - Rangahau Roro Aotearoa is a way to bring greater change for Māori.

Working as a clinician meant she could help one to one, but it became quite frustrating because she could see there needed to be a lot of changes made to make brain research more relevant to Māori and result in better health outcomes for Māori. "I find being involved with BRNZ at this level allows you to have more influence to make changes that are more far reaching to a wider audience. It's really having the backing to make more of a difference." Margaret sees developing more Māori researchers as a key priority: "They are very much under-represented in terms of workforce capacity in brain research. We want to build it exponentially."

Nevertheless, the number of new young Māori researchers starting to come into the field is encouraging and Margaret is keen to help develop them. "I feel the call is getting out there and they're hearing it. I think the future looks bright for us. As long as we look after the young Māori research students then I think our knowledge base of brain research from a Māori world view is going to develop over the next decade," she says. "For me, the interface of Mātauranga Māori, that is Māori knowledge or a Māori world view, with western science is important. I think you can take the best from both I think that's the way ahead and I think that's going to be the most successful pathway for us to take. We're at a place where we have the resources, the people and the commitment to build this area of research for Māori health. It's an exciting time."

TĀMAKI AND OTEPOTI WĀNANGA

2016 saw BRNZ's first wānanga with with two Māori community groups take place in BRNZ's two main hubs - Tāmaki Makaurau (Auckland) and Ōtepoti (Dunedin).

On October 11th 2016, BRNZ's Auckland-based members attended the CoRE's first official wānanga at Hoani Waititi marae in West Auckland. Hoani Waititi is New Zealand's first urban marae named after Hoani Waititi, a notable New Zealand teacher and community leader celebrated for his services to Māori education. Founded in 1980, the marae was set up by the large Māori community of West Auckland to foster identity, self-respect and a sense of belonging amongst young urban Māori. Like its namesake, the marae dedicates much of its time to the promotion of Māori knowledge and practice. It started up one of the first kōhanga reo (Māori language preschools) in Auckland, and now provides language immersion at pre-school, primary and secondary levels along with Tikanga Māori Programmes that use Maori philosophy, values and practice to support young people embrace their Māori heritage. We came to partner with Hoani Waititi marae through Hinemoa and her connections with the then Principal, Rawiri Wright, and kaiako Te Kura Taiaho Lonoholoikahiki Kapea, Joni Gordon and Griffa Rivers and with the support of academic and politician Sir Pita Sharples. Hinemoa identified Te Kura Kaupapa Māori o Hoani Waititi marae as a possible partner for the CoRE because of the community's dedication to learning and commitment to Māori advancement and wellbeing. The October 11th wānanga was an extraordinary day. BRNZ researchers were welcomed onto the marae by a full pōwhiri, ope tāua and wero organised and led by the tauira (students). The kohanga, kura tuatahi and whare kura students met us at the gates and led our group to the main whare where Dr Michael Steedman, kaiarahi University of Auckland, Lloyd Popata, Kaumatua BRNZ and Board member and Akuhata Rangi, Kaumatua, Te Whare Wānanga o Awanuiārangi addressed the room. The food was healthy and delicious and we were privileged to be entertained by the Auckland Regional Champions kapa haka team from the Whare Kura.

A month later, and at the opposite end of the country, Puketeraki Marae hosted Brain Research New Zealand for the very first time for a three day wānanga in November. The wānanga, jointly presented by the University of Otago, Kāti Huirapa ki Puketeraki, Ngā Pae o te Māramatanga, Brain Research New Zealand – Rangahau Roro Aotearoa and Water Safety New Zealand saw dozens of students, investigators and hau kāinga (locals) gather to make new connections and to learn more about each other's perspectives and values. We were privileged to experience an extraordinary degree of manaaki (hospitality), being treated to an exploration of the moana, waka and awa of the local pepeha and an eye-watering haukai.

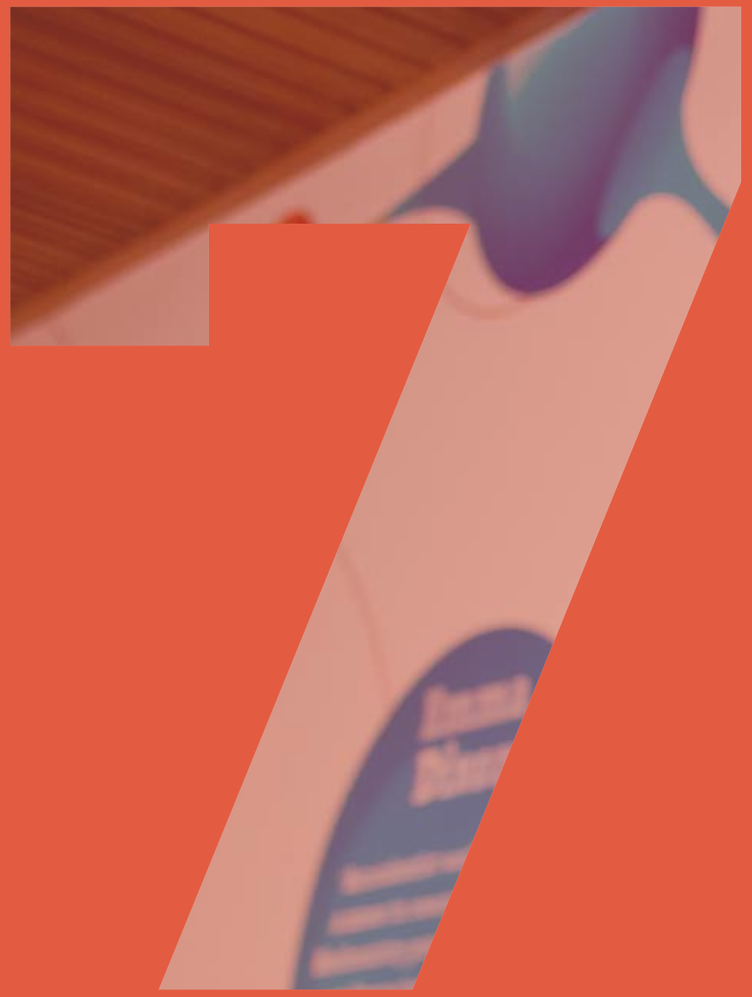
These first two official BRNZ wānanga provided an invaluable opportunity for our researchers to sit down with local Māori and to gain a better appreciation of the values of each community. The wānanga at Tāmaki Makaurau brought young Māori people face to face with researchers and scientists, while at the same time giving many of our researchers their first experience of marae manaakitanga. We had the opportunity to directly communicate the opportunities and value of research for Māori and to spur interest in science amongst Māori students. Meanwhile, the wānanga at Puketeraki Marae saw Māori and non-Māori researchers becoming part of a wider discussion about relationships with the hau kainga (home whānau).

MĀTAURANGA RESEARCH

Neuroscience research by Māori is about Tino Rangatiratanga, the right for Māori to determine their own pathways of knowledge and wellbeing in accord with the Treaty of Waitangi.

Just over 13% of our investigators are Māori and, with our Māori engagement strategy well underway, this number is already on the rise. A key part of our strategy involves funding neuroscience research by, with and for Māori. Neuroscience research with Māori is about whanaungatanga, maintaining and strengthening partnerships with Māori so that we can better understand their challenges and aspirations, and manaakitanga, caring for and being of service to Māori communities with neurological disease.

In June 2016, BRNZ held its first Māori specific funding round to create greater visibility for Māori researchers. As a result of that round, we funded three new studies that directly address questions of particular relevance to Māori. In Christchurch Dr Toni Pitcher, Research Fellow in the University of Otago's Department of Medicine is leading a study with Professor Tim Anderson that seeks to understand some of the reasons why Māori experience lower rates of PD than non-Māori. In Auckland, Professor Suzanne Purdy (Te Rarawa), is leading a two year study "Te Tino rangatiratanga o te mate ikua roro" that aims to develop community-led peer support systems for Māori with stroke. Also in Auckland, Professors Peter Thorne (UoA), Grant Searchfield (UoA) and Hinemoa Elder, will use their funding to explore Māori perspectives on hearing loss and hearing health services, an area of high significance for Māori. Hearing is particularly important to Maori because of the oral culture which means that elders will struggle to carry out their leadership roles if they cannot hear.



REACHING OUT

This year, though our knowledge and expertise have been communicated in a variety of ways, our mission has remained the same: to have a positive influence on individuals, organisations and communities who stand to directly benefit from our work.

We want people to understand how our brain research can give hope and inform actions across all sectors of the community and thus lead to an improved quality of life for all New Zealanders.

IN THE MEDIA

Newspaper articles, radio programmes, television appearances, and even podcast interviews - these were just some of the ways that we captured the public's attention, shedding lighting on research of ageing related neurological diseases.

In 2016 our researchers and their work appeared in print media across the country nearly three times a week, with news articles potentially reaching tens of millions of national and international readers. Internationally, over one hundred and eighty articles featured our researchers - appearing in newspapers and magazines in China, the USA, the United Kingdom, Germany, India to name a few. Examples include:

- Neurological Foundation Professor of Clinical Neurology, Alan Barber, gave numerous interviews to Australasian newspapers such as The Sydney Morning Herald, The Age, and The Dominion Post on issues related to stroke. One article on clot retrieval, in The Age (Melbourne), was syndicated to over 130 regional and local Australian papers. The article detailed a new technique that is revolutionizing stroke treatment.
- Prof. Valery Feigin's research on stroke was also featured heavily in the news, both domestically and internationally. He gave interviews to The Guardian and The New Zealand Herald, among many other newspapers. He was also featured in Neurology Today, and provided a podcast interview to The Lancet, related to his article on stroke risk. On July 23, he was also interviewed by TVOne's health reporter, Lorelei Mason, on the flaws of current stroke screening tests.
- Prof. Richie Poulton's internationally renowned longitudinal study, which was the subject of a four-part New Zealand documentary series that screened in June, also generated considerable media attention. In addition to regular appearances on radio and television, he featured as the lead story in both the New Zealand Listener and North and South magazines.
- Prof. Donna Rose Addis was featured in a New Zealand Herald article on the role of brain scans. She also appeared on RNZ National's Nine to Noon segment with Kathryn Ryan. She discussed memory and the ageing brain, with the segment proving to be the most popular audio download of the day.
- Assoc. Prof. Lynette Tippett was again in the news in 2016 in relation to her role as the Director of the Dementia Prevention Research Clinics. She gave interviews on the work of the clinics to NewstalkZB and RNZ National.
- Dr Grant Searchfield was interviewed on RNZ National by Jesse Mulligan on the causes and impact of Tinnitus. (September.)
- Prof. Warren Tate was interviewed by Eva Radich on her RNZ Concert programme "Upbeat Interview". Tate spoke about research on music and the ageing brain.
- Dr Liana Machado's research on ageing and cognitive functioning was featured in the New Zealand Herald.
- And Assoc. Prof. Ruth Empson was interviewed by the Otago Daily Times about an App that aids movement, the Cerebellar Training app.

IN THE COMMUNITY

Without community support, BRNZ could not achieve what we do. As well as participating in Brain Day and Brain Week, BRNZ members gave numerous presentations to community groups and NGOs across New Zealand in 2016. Some examples include:

- Throughout the year, Dr Grant Searchfield gave eight public talks on Tinnitus to a variety of organisations such as Age Concern, Fellowship New Zealand (formerly Probus), and the Hastings and Napier Hearing Associations.
- In New Plymouth, Associate Professor Lynette Tippett led the 'Memory Walk' on behalf of Alzheimer's Taranaki. (18 September). Geriatrician Dr Phil Wood also conducted a well-attended public forum on behalf of Alzheimer's Taranaki about the work of the Dementia Prevention Research Clinics (20 September).
- In Auckland, Professor Louise Nicholson addressed the Otahuhu Rotary Club on 23 August, speaking on the issue of "Connexins and the ageing brain". Neurological Foundation Professor of Clinical Neurology, Alan Barber, also gave a public talk at the Remuera Rotary Club on new stroke treatments (April).
- As part of Huntington's Awareness Month, Distinguished Professor Sir Richard Faull, patron of the Huntington's Disease Association, gave the introductory lecture at the National Huntington's Disease Conference.
- Dr Rita Krishnamurti gave several presentations to the Asian Network Incorporated (TANI) on stroke awareness and prevention. (July, October).
- Professor Mike Dragunow addressed the New Plymouth Epilepsy Association in November, where he spoke about developing new treatments strategies.
- Dr. Louise Parr-Brownlie addressed the Blenheim Parkinson's Society on how optogenetics may aid Parkinson's patients. She also gave a lecture on future Parkinson's treatments at the International Science Festival in Dunedin. In addition, she participated in Brain Health Forums in Balclutha and Oamaru.
- Professor Tim Anderson also addressed the Christchurch branch of the Neurological Foundation of New Zealand. Over 600 people attended his public panel discussion, which discussed the "Ageing Brain". Whilst in India, he was also invited to give a lecture at the Mumbai Parkinson Society, where he discussed new treatments for Parkinson's disease.
- As part of a Public Health Lecture series in Christchurch, Dr Tracy Melzer spoke about how brain imaging serves as a window into Parkinson's disease. (March).
- Professor Cliff Abraham delivered a talk in Geraldine at U3A on memory and Alzheimer's disease.
- Professor Brian Hyland and Warren Tate gave presentations on ageing brain research to the Summerset Retirement village in Dunedin. (August).

WORKING WITH HEALTHCARE PROFESSIONALS

BRNZ is wholeheartedly committed to ensuring that New Zealand's health workforce is apprised of the latest developments in ageing-brain research. In sharing this knowledge, we are confident that health professionals will be equipped to provide the best care to ageing New Zealanders. The following is a sample of the knowledge exchange our researchers provided to further the education of New Zealand health professionals:

- Associate Professor Cathy Stinear spoke to the Eastern Doctors Gerontology Peer Review Group, where she talked about using algorithms for predicting motor outcomes after a stroke. She also addressed the National Upper Limb Group at Auckland's Middlemore Hospital on 28 September. Early in April, she also addressed the Capital and Coast DHB in Porirua on two subjects: predicting recovery of upper limb function; neuroplasticity and recovery from stroke.
- Professor Donna Rose Addis organised and spoke at a "Symposium for Auckland Radiologists". Her lecture was entitled "Applications of MRI in Neuroscience Research."
- Professor Ngaire Kerse presented the implications of her LiLACS longitudinal study to the Bay of Plenty District Health Board (Funding and Planning sections; August).
- Professor Mike Dragunow addressed the Canterbury District Health Board at the Nurse Maude Neurone Disease Seminar on 11 March.

WORKING WITH SCHOOLS

As in previous years, a number of our senior investigators continued their partnership with the Australasian Neuroscience Society and the Queensland Brain Institute, to organise the national secondary schools' Brain Bee Challenge (www.abbc.edu.au/abbc/index.html).

The Brain Bee is a global neuroscience Q&A competition for Year 11 secondary school students that aims to motivate them to learn about the brain. In the New Zealand Brain Bee Challenge (NZBBC), Year 11 students compete to determine who has the "best brain" on such topics as intelligence, memory, emotions, and ageing. The mission of the NZBBC is to inform students about the latest advances in neuroscience, its value to the community, and to encourage and inspire young people to consider a career in science. The University of Auckland and the University of Otago host the regional finals for the New Zealand competition, with individuals competing for a place at the Australia-New Zealand Brain Bee Final. The national Brain Bee Challenge winner then has the opportunity to compete in the International Brain Bee. Brain Research New Zealand investigators are heavily involved in the NZ and Australasian Brain Bee challenge. Professor Louise Nicholson and Associate Professor Maurice Curtis direct the national programme (Prof. Curtis served as host of the North Island challenge), and in 2016, almost 300 students from 56 secondary schools competed. Other 2016 activities aimed at educating teachers and inspiring future generations of scientists and clinicians include:

- Dr Tracy Melzer was an invited presenter (for six sessions) at INSPIRE 2016, an educational festival for primary and secondary students held in Nelson, NZ. He also undertook multiple high school field trips (at Rangi Ruru Girls' School and Riccarton High School).
- Assoc. Prof. Bronwen Connor coordinated the development of the "Being Brainy" Brain Education Program for Primary / Intermediate school students.
- Assoc. Prof. Ruth Empson served in the Otago University School Ambassador Program, and gave lectures and hosted a research lab (July 2016). She also organised a "Lab in a Box" visit to East Otago High School, in Palmerston, Otago, research lab and demonstration to low decile school students.

SERVICE

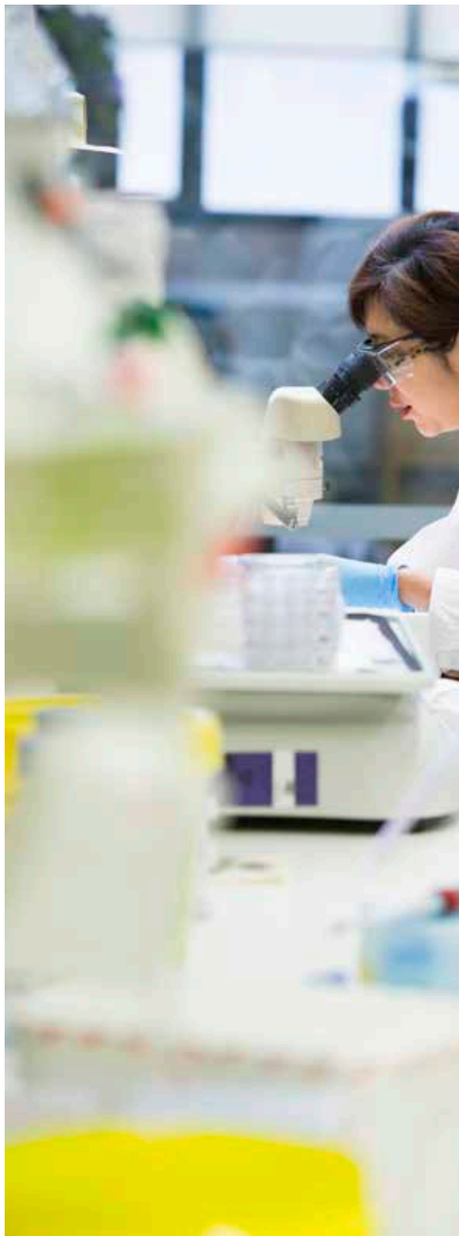
Brain Research New Zealand's researchers are dedicated members of the local and international science community and hold leadership and research advisory positions in many professional bodies, Non-Government Organisations and New Zealand-based charities. In 2016 we continued to dedicate our time and expertise to the following national and international entities:

NATIONAL

- Age Concern Otago
- Alzheimer's Foundation (Auckland)
- Alzheimer's Otago
- Alzheimer's Auckland Charitable Trust
- Alzheimer's New Zealand Charitable Trust
- Community Care Trust Otago
- Deafness Research Foundation
- Huntington's Disease Association (Auckland)
- Health Research Council, Biomedical Advisory Board
- Motor Neurone Disease Association of New Zealand (Inc.)
- Ministry of Health National Stroke Network Leadership Group
- Multiple Sclerosis Otago
- Neurological Foundation of New Zealand
- Neuromuscular Research Foundation Trust
- Neurology Association of New Zealand
- Parkinson's New Zealand (Otago)
- Stroke Foundation Otago
- Stroke Foundation of New Zealand

INTERNATIONAL

- Australasian Neuroscience Society
- Controlled Release Society
- European Federation of Neurological Societie
- Human Frontiers Science Programme Organisation
- International Society of Vestibular Physiologists
- Society for Neuroscience (North America)
- Neurosurgical Society of Australasia
- World Stroke Organization
- World Health Organisation Global Burden of Disease (GBD) 2013 TBI Panel
- World Health Organisation - Integrated Care for Older People



INVITED LECTURES

BRNZ members were also frequently called upon to provide invited lectures to a variety of organizations in 2016. A few examples include:

- Dr Grant Searchfield was invited to address both the American and British Tinnitus Associations (12 January; 22 September).
- Dr Jian Guan was invited to the University of Santiago, Spain, in July, where she spoke on the theme of 'the road to discovery'. She also addressed the Malaghan Institute in April on the issue of Microcirculations.
- Prof. Donna Rose Addis was invited to address the Sir George Elliot Charitable Trust Scholarship Luncheon (9 December).
- Distinguished Prof. Sir Richard Faull spoke at the following gatherings: Science Communications Workshop (Auckland; 23 February), Australasian Doctors' Conference (Auckland; 18-19 March), Jade Software Corporation (Christchurch; 5 August).
- Prof. Valery Feigin was invited to deliver a lecture at the 10th Anniversary celebration of NeuroAid in Singapore (24 September). In addition, Prof. Feigin delivered 21 additional conference presentations in 2016, including three at the 10th World Stroke Congress, five at the European Stroke Organization, a further three at the Asia Pacific Stroke Conference, and 11 at the New Zealand Applied Neurosciences Conference.
- Prof. Cliff Abraham gave an invited conference paper at a symposium in Heidelberg, Germany. He also gave presentations at the University of Texas, Austin; the University of California; and at the Florey Institute of Neuroscience and Mental Health (Melbourne, Australia).
- Prof. Peter Thorne was an invited speaker at a 'Symposium on the Blood-Labyrinth Barrier', an event hosted by the Australasian Neuroscience Society. The conference took place in Hobart, Australia, in December.

EDITORIAL BOARDS

BRNZ researchers serve on numerous journal editorial boards. Some examples include:

- *Australasian Journal on Ageing*
  Professor Ngaire Kerse
- *BMC Family Medicine*
  Professor Ngaire Kerse
- *Neuroepidemiology*
  Professor Valery Feigin (Editor-in-Chief)
- *Frontiers of Neuro-Otology*
  Dr Yiwen Zheng
- *Brain and Neurosciences Advances*
  Professor Cliff Abraham
- *Hippocampus*
  Professor Cliff Abraham
- *Neurobiology of Learning and Memory*
  Professor Cliff Abraham
- *Experimental Brain Research*
  Professor Cliff Abraham
- *Journal of Neurology and Therapeutics*
  Associate Professor Srdjan Vlajkovic
- *American Journal of Physiology*
  Associate Professor. Johanna Montgomery
- *Neuroepidemiology*
  Neurological Foundation of New Zealand (NFNZ)Professor of Clinical Neurology Alan Barber
- *Journal of Clinical Neuroscience*
  NFNZ Professor of Clinical Neurology Alan Barber
- *Journal of Neurology, Neurosurgery, and Psychiatry*
  NFNZ Professor of Clinical Neurology Alan Barber

NEW CONNECTIONS. NEW IDEAS.

BRNZ places a high priority on hosting top researchers from around the world at local conferences and symposia. To nurture the best research teams, we strive to support an ongoing exchange of ideas between clinicians and scientists, and give our researchers the opportunity to share their views, test their hypotheses and ultimately, make new scientific advances:

- In April, Professor Ralph Martins - recognised as a world leader of research into Alzheimer's disease - gave a keynote presentation to BRNZ's investigators at our strategic planning meeting at the University of Auckland. Professor Ralph Martins is Chair of Alzheimer's and Ageing at Edith Cowan University and Director of Research at Australian Alzheimer's Research Foundation. Ralph explained the work being done in the Australian Imaging Biomarkers and Lifestyle (AIBL) study which aims to identify biomarkers that may allow for early diagnosis. The AIBL study is the world's largest and most comprehensive study to develop an early diagnostic test for Alzheimer's disease.
- In April, BRNZ invited Professor Christine Milligan, Director of the Lancaster University Centre for Ageing Research to lead a seminar called 'A Life More Ordinary': How can we create dementia-friendly spaces by integrating the arts? Christine's research focuses on voluntary and community interventions to support active and healthy ageing; informal (family) care-giving; the role of technology in supporting older people; and the changing nature of home and community. In her seminar, she discussed how theatre and Age UK worked together to develop spaces in which people with dementia and their carers could continue to participate in ordinary everyday activities, crucial to maintaining a sense of belonging.
- Professor Perminder Sachdev, Scientia Professor of Neuropsychiatry, Co-Director of the Centre for Healthy Brain Ageing (CHeBA) in the School of Psychiatry, University of New South Wales, visited the University of Auckland to give a lecture on the extent to which we can prevent Alzheimer's disease. Perminder's talk focussed on the extent and quality of evidence, suggesting that education, more stimulating environments and better control of vascular risk factors might contribute to declining age-specific prevalence and incidence of dementia.
- In August 2016, Professor Ahmad Hariri, Director of the Laboratory of NeuroGenetics (LoNG) at Duke University visited the University of Otago, to present a seminar on how variability in brain circuit function associated with threat, reward, and executive control helps shape an individual's sensitivity to future life stress. He also discussed how he plans to elaborate and extend his findings by analysing neuroimaging data in the Dunedin Longitudinal Study.
- Seelye Fellow Professor Juan Carlos Arango-Lasprilla visited the University Auckland in October to teach us about his experience in culturally sensitive assessment and recovery from brain injury and neurodegeneration. An international expert in the psychological needs of individuals with brain injury, Juan Carlos has conducted numerous research studies in Spain, Mexico, Colombia, Argentina, Peru, and the USA focused on understanding and addressing the psychological, emotional, and family needs of individuals with brain injury. Juan Carlos came to New Zealand to learn how our country has taken a leadership role in cultural affairs, building healthcare and research models that are specific to Māori.

THE ENGINE ROOM

BRNZ's accomplishments are the product of the efforts of innumerable exceptional individuals.

Our dedicated students, researchers, and clinicians work together on a daily basis for the betterment of New Zealanders' brain health. Our Scientific Advisory Board provides us with valuable insights and ensures our research is of the highest international standard. While our Governance and Māori Advisory Boards oversee our efforts and help to shape our CoRE into a strong and thriving research centre.

BRNZ IN BRIEF

OUR PEOPLE

69 RESEARCHERS & CLINICIANS

39% WOMEN

9 MĀORI MEMBERS

45 UNDERGRADUATE STUDENTS

109 POSTGRADUATE STUDENTS

3 DHBS | **4** UNIVERSITIES | **1** CRI

OUR RESEARCH

418 PEER-REVIEWED PUBLICATIONS IN 2 YEARS

OVER **$51 MIL** IN ALIGNED RESERACH FUNDING IN 2 YEARS

06 PATENT APPLICATIONS

01 PATENT GRANTED

GOVERNANCE BOARD

BRNZ is privileged to have the support of leading New Zealanders and experienced governance board members who are committed to helping us achieve our goals. Our Governance Board members in 2016 were:

Sir Don McKinnon

Chair of Brain Research New Zealand

Mrs Wendy Fleming

Chair of Alzheimer's New Zealand Charitable Trust, Vice-Chair of Alzheimer's Disease International and Past-Chair Alzheimer's New Zealand

Mr Tony Offen

Dunedin accountant, entrepreneur and member of the Council of the Neurological Foundation of NZ

The Venerable Lloyd Nau Pōpata

Archdeacon of Tāmaki Makaurau, Pou Tikanga – of Ngāti Kahu of Northland

Professor Richard Blaikie

Deputy-Vice-Chancellor (Research and Enterprise) at the University of Otago and Professor in Physics

Professor Max Abbott

Pro-Vice-Chancellor and Dean of the Faculty of Health and Environmental Sciences at AUT, and the Director of the National Institute for Public Health and Mental Health Research

Professor John Fraser

Dean of the Faculty of Medical and Health Sciences at the University of Auckland

Professor Keith Hunter

Pro-Vice-Chancellor (Sciences) at the University of Otago, and newly appointed Fellow of the Royal Society of New Zealand

Professor Jim Metson

Deputy-Vice-Chancellor (Research) at the University of Auckland

SCIENCE ADVISORY BOARD

BRNZ's Science Advisory Board is made up of five internationally recognised experts in the neurosciences and neurology. The Board is chaired by:

Professor Stephen Davis

Professor of Medicine at the University of Melbourne, and President of the Australian and New Zealand Association of Neurologists.

Joining Professor Davis on the Scientific Advisory Board are:

Professor John Rostas

Emeritus Professor, Deputy Head of Faculty Research, Faculty of Health and Medicine, University of Newcastle, past-President of the Australian Neuroscience Society

Professor Mark Bear

Professor of Neuroscience of the Picower Institute for Learning and Memory, Massachusetts Institute of Technology, and Howard Hughes Medical Institute

Professor John Rothwell

Institute of Neurology, University College London

Professor A. David Smith

Emeritus Professor, University of Oxford, Founding Director of Oxford Project to Investigate Memory and Ageing

DIRECTORATE

DISTINGUISHED PROFESSOR SIR RICHARD FAULL

- Co-Director
- MBChB, PhD, DSc; KNZM FRSNZ
- Neurodegenerative diseases of the human brain

PROFESSOR WICKLIFFE ABRAHAM

- Co-Director
- BA with highest distinction, PhD; FRSNZ
- Synaptic plasticity, metaplasticity and the neural mechanisms of memory and Alzheimer's disease

PROFESSOR PETER THORNE

- Strategic development
- BSc, DipSci, PhD; CNZM
- Diseases of the inner ear and the effects of noise and consequences of ageing on the auditory system

PROFESSOR JOHN REYNOLDS

- Leadership development and capability building
- MBChB, PhD
- The role of neuromodulation and synaptic plasticity mechanisms in brain areas affected by Parkinson's disease and stroke

PROFESSOR ALAN BARBER

- NFNZ Chair of Clinical Neurology
- Clinical engagement
- MBChB, FRACP. PhD
- Neurology with special interest in stroke

ASSOCIATE PROFESSOR LYNETTE TIPPETT

- Dementia Prevention Research Clinics
- MSc (1st), DipClinPsych, PhD
- The clinical and neuropsychological effects of neurological disorders

PROFESSOR HINEMOA ELDER

- Māori engagement and strategic development
- MBChB, FRANZCP, PhD
- Psychiatrist with a special interest in working with Māori whanau with traumatic brain injury

MĀORI ADVISORY BOARD

BRNZ is privileged to be able to call on the expertise of our Māori Advisory Board to provide guidance on the funding of neuroscience research that will have a positive impact on Māori health outcomes.

The Venerable Lloyd Nau Popata

(Chair), (Ngati Kahu), Priest in Charge of the pastorate of the Church of the Holy Sepulchre in Grafton.

Professor Michael Walker

BSc, MSc, PhD, Fellow of the Royal Society of New Zealand and the Royal Institute of Navigation in London.

Dr Louise Parr-Brownlie

BSc, PhD, (Ngāti Maniapoto and Ngāti Pikiao), neurophysiologist and Kaiārahi at the Otago School of Medical Sciences, University of Otago.

Dr Waiora Port

BA, MA, PhD (Te Aupouri [Ngāti Pinaki], Te Rarawa [Ngāti Maroki]), a respected Kuia with long-standing community knowledge of Māori health issues.

Associate Professor Papaarangi Reid

DipComH, BSc, MBChB, DipObst, FNZCPHM (Te Rarawa), Tumuaki and Head of Department of Maori Health at the Faculty of Medical and Health Sciences, University of Auckland.

Te Kaanga Skipper

(Tainui), Te Roopu Taurima o Manukau within the Kaupapa Māori Disability Support Service (Korowai Aroha).

Dr Emma Wyeth

BSc (Hons) PhD. Director of Te Rōpū Rangahau Hauora Māori o Ngāi Tahu (Ngāi Tahu Māori Health Research Unit) and a Lecturer in Māori Health, both in the Department of Preventive and Social Medicine at the University of Otago.

RESEARCHERS

NAME	POSITION TITLE	INSTITUTION	BRNZ STATUS
Richard Faull	Professor	University of Auckland	Co-Director, PI
Wickliffe Abraham	Professor	University of Otago	Co-Director, PI
Alan Barber	Professor	University of Auckland	Directorate member, PI
Peter Thorne	Professor	University of Auckland	Directorate member, PI
Lynette Tippett	Associate Professor	University of Auckland	Directorate member, DPRC Leader, PI
John Reynolds	Professor	University of Otago	Directorate member, Theme Leader, PI
Brian Hyland	Professor	University of Otago	Theme Leader and PI
Tim Anderson	Professor	University of Otago	Theme Leader and PI
Ngaire Kerse	Professor	University of Auckland	Theme Leader and PI
Donna Rose Addis	Professor	University of Auckland	Principal Investigator
Nigel Birch	Associate Professor	University of Auckland	Principal Investigator
Margaret Brimble	Professor	University of Auckland	Principal Investigator
Winston Byblow	Professor	University of Auckland	Principal Investigator
Bronwen Connor	Associate Professor	University of Auckland	Principal Investigator
Garth Cooper	Professor	University of Auckland	Principal Investigator
Maurice Curtis	Associate Professor	University of Auckland	Principal Investigator
Mike Dragunow	Professor	University of Auckland	Principal Investigator
Margaret Dudley	Dr	University of Auckland	Principal Investigator
Jian Guan	Dr	University of Auckland	Principal Investigator
Ian Kirk	Professor	University of Auckland	Principal Investigator
Janusz Lipski	Professor	University of Auckland	Principal Investigator
Johanna Montgomery	Associate Professor	University of Auckland	Principal Investigator
Suzanne Purdy	Professor	University of Auckland	Principal Investigator
Grant Searchfield	Dr	University of Auckland	Principal Investigator
Russell Snell	Professor	University of Auckland	Principal Investigator
Cathy Stinear	Associate Professor	University of Auckland	Principal Investigator
Debbie Young	Associate Professor	University of Auckland	Principal Investigator
Valery Feigin	Professor	Auckland University of Technology	Principal Investigator
Nicola Kayes	Associate Professor	Auckland University of Technology	Principal Investigator
Andrew Clarkson	Dr	University of Otago	Principal Investigator
Nick Cutfield	Dr	University of Otago	Principal Investigator
Dirk De Ridder	Professor	University of Otago	Principal Investigator
Ruth Empson	Associate Professor	University of Otago	Principal Investigator
Leigh Hale	Professor	University of Otago	Principal Investigator
Stephanie Hughes	Dr	University of Otago	Principal Investigator
Steve Kerr	Associate Professor	University of Otago	Principal Investigator
Ping Liu	Associate Professor	University of Otago	Principal Investigator
Liana Machado	Dr	University of Otago	Principal Investigator
Tracy Melzer	Dr	University of Otago	Principal Investigator
Pauline Norris	Professor	University of Otago	Principal Investigator
Louise Parr-Brownlie	Dr	University of Otago	Principal Investigator
Richie Poulton	Professor	University of Otago	Principal Investigator
Holger Regenbrecht	Associate Professor	University of Otago	Principal Investigator
Ted Ruffman	Professor	University of Otago	Principal Investigator
Paul Smith	Professor	University of Otago	Principal Investigator
Warren Tate	Professor	University of Otago	Principal Investigator
Ian Tucker	Professor	University of Otago	Principal Investigator
Joanna Williams	Dr	University of Otago	Principal Investigator
Yiwen Zheng	Dr	University of Otago	Principal Investigator
John Dalrymple-Alford	Professor	University of Canterbury	Principal Investigator
Tim David	Professor	University of Canterbury	Principal Investigator

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Richard Roxburgh	Dr	Auckland District Health Board	Principal Investigator
Suzanne Barker-Collo	Associate Professor	University of Auckland	Associate Investigator
Melanie Cheung	Dr	University of Auckland	Associate Investigator
Michelle Glass	Associate Professor	University of Auckland	Associate Investigator
Cris Print	Associate Professor	University of Auckland	Associate Investigator
Ben Thompson	Associate Professor	University of Auckland	Associate Investigator
Srdjan Vlajkovic	Associate Professor	University of Auckland	Associate Investigator
Henry Waldvogel	Associate Professor	University of Auckland	Associate Investigator
Rita Krishnamurthi	Dr	Auckland University of Technology	Associate Investigator
Michael Black	Associate Professor	University of Otago	Associate Investigator
Jon Shemmell	Dr	University of Otago	Associate Investigator
Reremoana Theodore	Dr	University of Otago	Associate Investigator
Ed Mee	Dr	Auckland District Health Board	Associate Investigator
Barry Snow	Associate Professor	Auckland District Health Board	Associate Investigator
Phil Wood	Dr	Auckland District Health Board	Associate Investigator
Gary Cheung	Dr	Auckland District Health Board	Associate Investigator
Ari Bok	Dr	Auckland District Health Board	Associate Investigator
Arjan Scheepens	Dr	Plant and Food Research	Associate Investigator

OUR STUDENTS

STUDENT NAME	LEVEL OF STUDY	UNIVERSITY	GRADUATE DESTINATION
Rehab Alkhater	Doctoral Degree	University of Auckland	Continuing Study
Wojciech Ambroziak	Doctoral Degree	University of Auckland	Continuing Study
Christine Arasaratnam	Doctoral Degree	University of Auckland	Continuing Study
*Ashleigh Baker	Doctoral Degree	University of Auckland	Continuing Study
Brittney Black	Doctoral Degree	University of Auckland	Continuing Study
*Beatriz Calvo-Florez	Doctoral Degree	University of Auckland	Continuing study
Hao Chang	Doctoral Degree	University of Auckland	Completed; Employed in NZ other
Amy Chapman	Doctoral Degree	University of Auckland	Continuing Study
Sam Dodd	Other	University of Auckland	Completed; Further study in NZ
Nicole Edwards	Other	University of Auckland	Continuing Study
Dawei Fan	Doctoral Degree	University of Auckland	Continuing Study
Matthew Fields	Other	University of Auckland	Completed; Unknown
Christine Fok	Other	University of Auckland	Continuing Study
Lyres Freeth	Other	University of Auckland	Completed; unknown
Tessa Fuhrer	Other	University of Auckland	Completed; Further study in NZ
William Fulton	Other	University of Auckland	Completed; Unknown
Tina Gao	Doctoral Degree	University of Auckland	Continuing Study
Bonnie Gardner	Doctoral Degree	University of Auckland	Completed; Employed overseas
*Nethra Ganesh	Doctoral Degree	University of Auckland	Continuing Study
Mandana Ghodratipour	Doctoral Degree	University of Auckland	Continuing Study
Charlotte Gordon	Other	University of Auckland	Continuing Study
Karan Govindpani	Doctoral Degree	University of Auckland	Continuing Study
Andrea Greenwood	Doctoral Degree	University of Auckland	Continuing Study
Guile Haldankar	Other	University of Auckland	Continuing Study
Victoria Hawkins	Other	University of Auckland	Continuing Study
Ghaz Jabur	Doctoral Degree	University of Auckland	Continuing Study
Rashika Karunasinghe	Doctoral Degree	University of Auckland	Completed; Employed in NZ other
Becky Lakadia	Doctoral Degree	University of Auckland	Continuing Study
Shelly Lin	Doctoral Degree	University of Auckland	Continuing Study
Rui Liu	Doctoral Degree	University of Auckland	Continuing Study

NAME	LEVEL OF STUDY	UNIVERSITY	GRADUATE DESTINATION
Emma McCafferty	Other	University of Auckland	Completed; Further study in NZ
Alana McCambridge	Doctoral Degree	University of Auckland	Continuing Study
Hayley MacDonald	Doctoral Degree	University of Auckland	Continuing Study
Marama MacDonald	Doctoral Degree	University of Auckland	Completed; Employed in NZ in Māori organisation
Gagandeep Mallah	Doctoral Degree	University of Auckland	Completed; Employed oversease
Nicole McKay	Doctoral Degree	University of Auckland	Continuing Study
*Natasha McKean	Doctoral Degree	University of Auckland	Continuing Study
Lakshini Mendis	Doctoral Degree	University of Auckland	Completed; Employed in NZ other
Abby Metson	Other	University of Auckland	Completed; Unknown
Katey Mitchelson	Doctoral Degree	University of Auckland	Continuing Study
Nisa Mohan	Doctoral Degree	University of Auckland	Continuing Study
Clarrence Molinyawe	Other	University of Auckland	Continuing Study
*Ruth Monk	Doctoral Degree	University of Auckland	Continuing Study
Ronan Mooney	Doctoral Degree	University of Auckland	Continuing Study
Janitha Mudannayeke	Doctoral Degree	University of Auckland	Completed; Employed Overseas
Helen Murray	Doctoral Degree	University of Auckland	Continuing Study
Samantha Murray	Doctoral Degree	University of Auckland	Continuing Study
*Jin Ng	Doctoral Degree	University of Auckland	Continuing Study
Thulani Palpagama	Other	University of Auckland	Completed; Further Study in NZ
Mahhdvi Pandya	Other	University of Auckland	Completed; Further Study in NZ
Rebecca Playne	Doctoral Degree	University of Auckland	Continuing Study
Guy Purcell	Other	University of Auckland	Continuing Study
Keith Runnalls	Doctoral Degree	University of Auckland	Completed; Unknown
Justin Rustenhoven	Doctoral Degree	University of Auckland	Continuing Study
Natalia Samorow	Doctoral Degree	University of Auckland	Continuing Study
*Phil Sanders	Doctoral Degree	University of Auckland	Continuing Study
Patrick Schweder	Doctoral Degree	University of Auckland	Continuing Study
Hanwant Shekawhat	Other	University of Auckland	Continuing Study
Marie-Claire Smith	Doctoral Degree	University of Auckland	Continuing Study
Leon Smyth	Doctoral Degree	University of Auckland	Continuing Study
Jennifer (Junru) Song	Doctoral Degree	University of Auckland	Continuing Study
*Meg Spriggs	Doctoral Degree	University of Auckland	Continuing Study
*Molly Swanson	Doctoral Degree	University of Auckland	Continuing Study
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*Kathryn Todd	Doctoral Degree	University of Auckland	Continuing Study
Clinton Turner	Doctoral Degree	University of Auckland	Continuing Study
Kate van Riegle West	Doctoral Degree	University of Auckland	Continuing Study
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Kyla Yamsuan	Other	University of Auckland	Continuing Study
David Yates	Other	University of Auckland	Continuing Study
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Halina Kalaga	Doctoral Degree	AUT University	Continuing study
Susan Mahon	Doctoral Degree	AUT University	Continuing study
Soheila Mohammadyari	Doctoral Degree	AUT University	Continuing Study
Caroline Stretton	Doctoral Degree	AUT University	Continuing Study
Bronwyn Tunnage	Doctoral Degree	AUT University	Continuing study

NAME	LEVEL OF STUDY	UNIVERSITY	GRADUATE DESTINATION
Claudia Zagreanu	Doctoral Degree	AUT University	Continuing study
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Mustafa Almuqbel	Doctoral Degree	University of Otago	Continuing Study
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Laura Boddington	Doctoral Degree	University of Otago	Continuing Study
Allyson Calder	Doctoral Degree	University of Otago	Continuing Study
Niamh Cameron	Other	University of Otago	Continuing Study
Stella Cameron	Doctoral Degree	University of Otago	Continuing Study
Polly Chen	Doctoral Degree	University of Otago	Completed; Employed Overseas
Jody Cicolini	Doctoral Degree	University of Otago	Continuing Study
Megan Elder	Doctoral Degree	University of Otago	Continuing Study
Simon Feng	Doctoral Degree	University of Otago	Continuing Study
*Timothy Galt	Other	University of Otago	Continuing Study
Anthony Garvey	Doctoral Degree	University of Otago	Continuing Study
Manju Gayarathny	Doctoral Degree	University of Otago	Continuing Study
*Hayley Guiney	Doctoral Degree	University of Otago	Continuing Study
*Chris Heinrich	Doctoral Degree	University of Otago	Continuing Study
Joshua Houlton	Other	University of Otago	Continuing Study
Roanne Hurley	Doctoral Degree	University of Otago	Continuing Study
Mohamed Fasil Ibrahim	Doctoral Degree	University of Otago	Continuing Study
*Sharon Jay	Other	University of Otago	Continuing Study
Javier Jimenez-Martin	Doctoral Degree	University of Otago	Continuing Study
Abby Johnson	Other	University of Otago	Completed; Unknown
Nick Lawson	Other	University of Otago	Completed; Unknown
Louisa (Joyce) Lim	Other	University of Otago	Continuing Study
Natalie Matheson	Doctoral Degree	University of Otago	Continuing Study
*Rosie Melchers	Other	University of Otago	Continuing Study
Stephanie Mercer	Doctoral Degree	University of Otago	Continuing Study
Normala Mesbah	Doctoral Degree	University of Otago	Continuing Study
James Miller	Other	University of Otago	Continuing Study
Jodi Morrissey	Doctoral Degree	University of Otago	Continuing Study
Himang Mujoo	Doctoral Degree	University of Otago	Completed; Employed in NZ other
Nikita Potemkin	Other	University of Otago	Continuing Study
Emmet Power	Doctoral Degree	University of Otago	Continuing Study
Leena Shoemaker	Doctoral Degree	University of Otago	Continuing Study
Anurag Singh	Doctoral Degree	University of Otago	Continuing Study
Lucy Stiles	Doctoral Degree	University of Otago	Continuing Study
Matt Sykes	Doctoral Degree	University of Otago	Continuing Study
Valerie Tan	Doctoral Degree	University of Otago	Completed; Employed in NZ other
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Lisa Zhou	Doctoral Degree	University of Otago	Continuing Study
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*Sophie Barnett	Doctoral Degree	University of Canterbury	Continuing Study
Christine de Lancea	Doctoral Degree	University of Canterbury	Completed; Other
Fraser Doake	Other	University of Canterbury	Completed; Further Study in NZ
Katharina Dormanns	Doctoral Degree	University of Canterbury	Completed; Employed Overseas
Beth Elias	Other	University of Canterbury	Continuing Study
Jeremy Goh	Doctoral Degree	University of Canterbury	Continuing Study
*Michelle Goodman	Doctoral Degree	University of Canterbury	Continuing Study
Jenny Hamilton	Doctoral Degree	University of Canterbury	Continuing Study
Kyla Horne (nee Wood)	Doctoral Degree	University of Canterbury	Continuing Study
Guneet Kaur	Other	University of Canterbury	Completed; Employed Overseas
*Allanah Kenny	Doctoral Degree	University of Canterbury	Continuing Study
Siobhan Lockie	Other	University of Canterbury	Continuing Study
Shaun London	Other	University of Canterbury	Completed; Unknown

NAME	LEVEL OF STUDY	UNIVERSITY	GRADUATE DESTINATION
Morgan McPhail	Other	University of Canterbury	Completed; Unknown
Elshin Mathias	Doctoral Degree	University of Canterbury	Continuing Study
Meisha Nicolson	Other	University of Canterbury	Completed; Employed in NZ other
Jaijus Pallippadan Johny	Doctoral Degree	University of Canterbury	Completed; Employed in NZ other
Brook Perry	Doctoral Degree	University of Canterbury	Continuing Study
Emma Peterson	Other	University of Canterbury	Continuing Study
Susan Rapley	Doctoral Degree	University of Canterbury	Continuing Study
Jamie Small	Other	University of Canterbury	Continuing Study
Megan Stark	Other	University of Canterbury	Completed; Employed in NZ other
Mildred Tan	Other	University of Canterbury	Continuing Study
Sivaporn Tasananukorn	Other	University of Canterbury	Continuing Study
Tim Van Ginkel	Doctoral Degree	University of Canterbury	Continuing Study

*Directly funded by BRNZ

RESEARCH OUTPUTS

PATENTS GRANTED

1. Connor, B., Maucksch, C., and Dottori, M. "Cell Reprogramming." Publication no. WO 2011/096825 A1.

PATENTS FILED

1. Ethris GmbH and Connor, B. "Enhanced cell reprogramming by mRNA." Application no. EP 151 73409.
2. La Flamme, A.C., Connor, B., and O'Sullivan, D. "Methods and compositions for treatment of multiple sclerosis." Application no. PCT/US11/42244.
3. Reynolds, J. N. J., Tan, E. W., Hyland, B. I., Jameson, G. N. L., Myint, M. A. M., and Wickens, J. R. "Acoustic driven drug delivery systems." 2016 PCT Patent Application No. PCT/NZ2016/050130; Australian priority date 21 August 2015, AU 2015903387.
4. Turuwhenua, J. and Thompson, B. "Stimulus and eye tracking." Application no. NZ 727 230.

SPINOUTS

1. Searchfield, G. "TinnitusTunes (www.tinnitustunes.com)". An online tinnitus clinical resource -(subscription based).

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1. Abouzayd, M., Smith, P.F., Moreau, S., & Hitier, M. (2016) What vestibular tests to choose in symptomatic patients after a cochlear implant? A systematic review and meta-analysis. *Archives of Oto-Rhino-Laryngology*, EPUB ahead of print.
2. Ackerley, S.J., Byblow, W.D., Barber, P.A., MacDonald, H., McIntyre-Robinson, A., & Stinear, C.M. (2016) Primed Physical Therapy Enhances Recovery of Upper Limb Function in Chronic Stroke Patients. *Neurorehabilitation and Neural Repair*, 30(4), 339-48.
3. Addis, D.R., Hach, S., & Tippett, L.J. (2016) Do strategic processes contribute to the specificity of future simulation in depression? *British Journal of Clinical Psychology*, 55(2), 167-186.
4. Addis, D.R., Pan, L., Musicaro, R., & Schacter, D.L. (2016) Divergent thinking and constructing episodic simulations. *Memory*, 24(1), 89-97.
5. Aitken, P., Benoit, A., Zheng, Y., Philoxene, B., Le Gall, A., Denise, P., Besnard, S., & Smith, P.F. (2016) Hippocampal and striatal M1-muscarinic acetylcholine receptors are down-regulated following bilateral vestibular loss in rats. *Hippocampus*, EPUB ahead of Print.
6. Alamri, Y., Vogel, R., MacAskill, M., & Anderson, T. (2016) Plasma exosome concentration may correlate with cognitive impairment in Parkinson's disease. *Alzheimer's & Dementia*, 4, 107-108.
7. Almuqbel, M., Melzer, T.R., Myall, D.J., MacAskill, M.R., Pitcher, T.L., Livingston, L., Wood, K.L., Keenan, R.J., Dalrymple-Alford, J.C., & Anderson, T.J. (2016) Metabolite ratios in the posterior cingulate cortex do not track cognitive decline in Parkinson's disease in a clinical setting. *Parkinsonism & Related Disorders*, 22, 54-61.
8. Alshaer, A., Regenbrecht, H., & O'Hare, D. (2016) Immersion factors affecting perception and behaviour in a virtual reality power wheelchair simulator. *Applied Ergonomics*, 58, 1-12.
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BOOK CHAPTERS

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CONFERENCE PROCEEDINGS

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OUR PARTNERS

- The University of Auckland
- University of Otago
- University of Canterbury
- AUT University

OUR COLLABORATORS

- Plant and Food Research
- Canterbury District Health Board
- Counties Manukau District Health Board
- Auckland District Health Board
- Southern District Health Board
- Waitemata District Health Board
- Neurological Foundation of New Zealand
- MedTech Centre of Research Excellence
- Alzheimer's New Zealand

2016 RESEARCH HIGHLIGHTS

175 JOURNAL ARTICLES

04 PATENT APPLICATIONS

01 PATENT GRANTED

$30+ MIL EXTERNAL FUNDING

88 RESEARCH GRANTS

FINANCIAL REPORT 2016

FUNDING SUMMARY FOR THE YEAR ENDED 31 DECEMBER 2016

FUNDING RECEIVED	2016
Tertiary Education Commission grant	$4,972,000
Total Funding received	**$4,972,000**

EXPENDITURE[2]	2016
Salaries	$1,982,000
Overheads	$2,062,000
Project costs	$1,016,000
Postgraduate students	$429,000
Travel	$205,000
Extraordinary Expenditure[3]	$64,000
Subcontractors[4]	$41,000
Total Expenses	**$5,798,000**

NET SURPLUS/(DEFICIT)[5]	-$826,000

*All amounts are shown exclusive of Goods and Service tax (GST)

NOTES

1. This financial report is for the period 1st January to 31st December 2016. This report only contains details of funding and expenditure relating to the CoRE grant that the Centre receives from the Tertiary Education Commission. It does not contain details of philanthropic funding, or operating funding to Centre investigators from other funding agencies.
2. This funding summary details funding received and funds distributed to collaborative partners of the CoRE.
3. The extraordinary expenditure budget is for board and science meeting expenses.
4. 2016 costs include funding paid for clinical tenths.
5. In 2015 BRNZ carried forward a net surplus of 1,684. This surplus has been added to BRNZ's 2016 income to fund the CoRE's research programme in 2016. BRNZ therefore has a net surplus of 858 that will be carried forward into 2017 to fund future expenditure of the CoRE.

TABLE OF STATISTICS

BROAD CATEGORY	DETAILED CATEGORY	YR 2
VALUE OF CORE FUNDING FROM TEC ($M)		**$4,972**
FTES BY CATEGORY	Principal investigators	3.58
	Associate investigators	.03
	Postdoctoral fellows	7.13
	Research technicians	6.5
	Administrative/support	2.3
	Research students	148.7
	Total	**168.24**
HEADCOUNTS BY CATEGORY	Principal investigators	52
	Associate investigators	17
	Postdoctoral fellows	60
	Research technicians	45
	Administrative/support	11
	Research students	154
	Total	**339**
PEER REVIEWED RESEARCH OUTPUTS BY TYPE	Books	0
	Book chapters	8
	Journal articles	175
	Conference papers	75
	Other	0
	Total	
VALUE OF EXTERNAL RESEARCH CONTRACTS AWARDED BY SOURCE	Vote Science and Innovation contestable funds	$1,222,000
	Other NZ Government	$77,000
	Domestic – private sector funding	$206,000
	Overseas	$1,023,000
	Other	
	Total	**$2,528,000**
COMMERCIAL ACTIVITIES	Number of licenses	0
	Income from licenses	0
	Patent applications	4
	Patents granted	1
	Invention disclosures	0
	Number of new spinouts	1
	Capitalisation value of spinouts	0
STUDENTS STUDYING AT CORE BY LEVEL	Doctoral degree	109
	Other	45
	Total	**154**
NUMBER OF STUDENTS COMPLETING QUALIFICATIONS BY LEVEL	Doctoral degree	21
	Other	19
	Total	**40**
IMMEDIATE POST-STUDY GRADUATE DESTINATIONS	Further study in NZ	8
	Further study overseas	1
	Employed in NZ	16
	Employed overseas	6
	Unknown	8
	Other	1
	Total	**40**

YOUR BRAIN. OUR MINDS.

Brain Research
NEW ZEALAND
Rangahau Roro Aotearoa