The Stimulus

Official Newsletter of the New Zealand Brain Research Institute

New Zealand Brain Research Institute

Spring 2016 Edition

From Michael's Desk ...

It pays to be somewhat skeptical of media coverage of health research. Science generally proceeds by a series of tiny advances in understanding and incremental improvements in techniques. More often than we like to admit, it also involves dead-ends and retreats from once-promising ideas. The media, however, have a tendency to almost always describe results as heralding revolutionary new treatments or cures.

Sometimes, though, the hype might be justified. A few months ago, a study was published in the journal 'Nature' showing for the first time that it might be possible to slow and even reverse the pathological brain changes due to Alzheimer's disease.

The researchers crafted an antibody (called aducanumab) to train the immune system to target and remove the amyloid plaques that build up in the brains of people with Alzheimer's disease. After a year, volunteers on higher doses of the antibody showed progressively less cognitive deterioration than those taking a placebo. It is not yet a cure, but does show for the first time the real possibility of slowing or even stopping the progression of symptoms.

Alzheimer's disease was first described in 1906. Dr Alois Alzheimer had been following the cognitive and social deterioration of a female patient for five years. He only published an account of her symptoms, however, once she had died and he was able to examine her brain at autopsy. Under a microscope, he could see unusual clumps (plaques) between her brain cells and 'tangles' within them. This allowed him to link her clinical symptoms to underlying pathological changes in the brain. Inspired by this, Friedrich Lewy, working in Alzheimer's lab, looked for similar changes in the brains of people who had died with Parkinson's disease. He found different globular lumps within their brain cells, which we now call Lewy bodies.

The close link between Alzheimer's and Parkinson's research has continued since. It took further decades to find out the structures of the proteins that form aggregations in the two diseases. Lewy bodies are formed of alpha synuclein, plaques are made up of beta amyloid, and tangles are built from the tau protein. In essence, these three proteins, which are normally soluble, start to mis-fold into insoluble lumps (a bit like how the runny proteins in an egg solidify when cooked). Traditionally, amyloid and tau were exclusively associated with Alzheimer's and alpha synuclein with Parkinson's.

Increasingly, though, we now realise that abnormalities in these proteins are shared, not only between these two diseases, but also many other neurodegenerative conditions. We still don't really know what role these various proteins play in neurodegeneration. Do they directly cause symptoms, or are they themselves just another sign of the underlying disease process?

CONTINUED OVERLEAF...

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NZBRI is a subsidiary of the Canterbury Medical Research Foundation

At the NZBRI, we are currently running a project with people with Parkinson's, using advanced nuclear medicine techniques to measure the amount of amyloid in the brain, and how it relates to the eventual onset of dementia. Like the aducanumab study, this requires a specifically-crafted tracer chemical which can reveal the presence of amyloid. The tracer is made early on Monday mornings in Melbourne, rushed to the airport, and must be used by the end of that afternoon in Christchurch, before its brief half-life expires. This cutting-edge project is allowing us to measure some of the Alzheimer-like changes that also occur in Parkinson's. Recently a new tracer has been developed that can allow the tau protein to be measured. With support from the Neurological Foundation, and some of our own funds donated to NZBRI, Christchurch will be one of the first centres in the world to apply it in people with Parkinson's. This is only possible with the support of Pacific Radiology Group, and their sophisticated PET (positron emission tomography) scanner at Southern Cross Hospital.

Until recently, it wasn't possible to measure these proteins until autopsy. Being able to do it while people are at earlier stages of the disease is a huge advance. A PET tracer for alpha synuclein does not yet exist, but when it is developed, we hope that Canterbury patients and researchers will again be at the forefront of using these revolutionary techniques.

(Sevigny et al., 2016: The antibody aducanumab reduces Aβ plaques in Alzheimer's disease. 'Nature', volume 537, issue 7618.)

Thank you John!

The August NZBRI Board meeting was the last one for John Bayley who stepped down as Chairman of the Board after twelve years of exemplary service to the Institute.

John was with us right from the beginning of the Institute's history and has steered the governance team over the early years of the development of the Van der Veer Institute for Parkinson's Research which, in 2011, was re-branded as the NZ Brain Research Institute.

John has witnessed the evolution of the Institute to where we are today as active members of the national "Brain CoRE" and with a wealth of internationally presented and published work in the area of brain health.

Thank you for all you have done for the Institute John and your dedication and passion for the cause of brain research in New Zealand.

Introducing the new Chair of the Board

Very ably stepping into John's shoes, is Dr Cheryl Doig, who joined the NZBRI Board early this year.

Cheryl is a leadership futurist and curator of leadership ideas. She follows leadership trends and research and translates these into practice, working internationally and virtually with organisations, business leaders and educators. Her passion is for challenging organisations to think differently in order to adapt to a changing future – to think beyond their current leadership realities, while still using the best of the past.

Cheryl has been a highly successful school principal, teaching fellow in Education Management, and school reviewer. As a principal, Cheryl led both Richmond and Fendalton schools to achieving national recognition for their standards of excellence in education, including being awarded Goodman Fielder School of the Year. Cheryl has also received a number of prestigious awards for leadership in education, including the Beeby Fellowship and the Woolf Fisher Fellowship.

Researcher Profile – Professor John Dalrymple Alford

Prof Dalrymple Alford is one of the team at the BRI working on Parkinson's Disease. His home institution is the University of Canterbury and we are very lucky to have his expertise in Psychology and Neuroscience at our disposal.

Here is what John has to say about his career to date and where he is going next.

I have always been interested in biology, but the interface between neurobiology, behaviour and the mind, has always been my main passion. I took a Joint Honours degree in Zoology and Psychology, followed by a PhD in neuroscience at Swansea University in Wales, UK. In particular, I wanted to learn how the environment influences both neurobiology and behaviour - they are inter-dependent. Genetics provide a blueprint, but the subtleties of human and even animal behaviour are molded by experience.

My current research is mostly extension of these interests. My main focus is to provide a better understanding of the impact of neurodegeneration and brain injury that causes either selective but severe memory loss or the more extensive loss of cognitive skills, that result in significantly decreased ability to cope with everyday life in people with degenerative disorders. That is, I primarily study Parkinson's disease, Alzheimer's disease, Korsakoff's syndrome and the interacting brain systems primarily associated with these brain disorders.

My primary goal, however, is to find ways in which the environment or neurobiology can be used as a tool to modify the impact of such brain injuries. For example, we have shown that environmental stimulation, in rats, can markedly reduce the impact of brain injuries that, like injuries occurring in humans, appear to produce permanent memory loss. This work sets the scene for studies to intervene in humans with memory loss.

Other work, in patients with Parkinson's disease, seeks to learn how physical and thinking exercises might slow down the negative effects of progressive brain degeneration that occurs in this disorder. We are also looking at both brain function and cognitive functions to learn how best to understand those patients at greatest risk of decline over time, so researchers can target more effectively, those people at greatest risk. Related work looks at whether genetic markers in people with Parkinson's disease will help in that regard.

Too often, we envisage the brain as a fixed entity once we have passed early childhood. Theories of brain function are generally based on a static view of brain function and over-rigid views of the role of individual brain regions. By contrast, a more flexible view of brain functions, extended across distributed and interacting networks in the brain, means we can take a more hopeful approach. We anticipate suitable interventions to improve brain circuitry to benefit even the injured or degenerating brain. We know that the neurobiology of the brain exhibits plasticity of structure and function - somehow, we need to harness that to our advantage for treatments of brain disorders.
Offsetting acute brain injury effects and slowing down the impact of neurodegeneration is a feasible goal, whereas better treatments that might prevent the onset of such disorders are still a more distant prospect.
One particular inspiration for me, was Professor Bruno Will, who worked at the University of Strasbourg in France. I undertook post-doctoral research with Bruno before coming to New Zealand. His research group was focused on different ways to improve "recovery of function after brain injury", which set the scene for such work in the future. His leadership of a collegial approach to science was a particular inspiration, Indeed, the excellent collegial approach to neuroscience at the New Zealand Brain Research Institute is one of the major reasons I enjoy working in Christchurch.

My advice to young researchers is that they should be flexible in their approach and ideas. They should focus on a particular question but be prepared to switch to different areas of expertise when the need arises. Seek collaboration rather than isolation. Connecting their research with patients and thinking of ways that might eventually benefit human health, even if they are interested in basic science, is a rewarding experience
- even if those benefits are often a long way in the future.

FBI Fundraising Swings into Action

The FBI committee is hosting their annual golf tournament at the Christchurch Golf Club on Friday 25th November. This event sells out within weeks and has become a highlight on the golfing calendar.

This year there will be 132 people donning their plus twos and Bob Charles shirts, setting a colourful scene for a wonderful day of golf. With the Christchurch Radiology Group, continuing to show their community spirit as Principal Sponsor, they're joined by more than a dozen businesses that sponsor holes and prizes to enable the Friends of the NZ Brain Institute to produce a stirling day.

KMPG took out the top prize last year and will be back to defend their title. This event raises a significant amount of money for neurological research at the NZBRI. With more than $3,500 in prizes up for grabs, we look forward to another stellar year for all.

Back by popular demand, after its inaugural show in 2016, is Opera meets Art 2017. The Opera Club enchanted the audience with well-known songs which rung out in the foyer of the Christchurch Art Gallery. The show sold out very quickly, we are expecting the same for the 2017 show on Saturday, April 1st 2017. Tickets will be available in the New Year at **www.cmrf.org.nz/events**. The night includes canapés from Lizzies Cuisine and fine wine thanks to Pegasus Bay. If you would like to be a part of the FBI fundraising activities, please contact **caroline@cmrf.org.nz** or **03 353 1245**

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Please note your last name and "donation" in the reference line and if you would like a receipt,
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