Brain Health Research Centre

Te Pokapū Rakahau Hauora Hinekaro

Newsletter August 2015

For regular updates visit our website: otago.ac.nz/bhrc

University of Otago
Te Whare Wānanga o Otāgo
New Zealand

IN THIS ISSUE

Brain in Brief

Drugs and Addiction

Nerve cells in the brain communicate with each other by releasing tiny amounts of a chemical messenger called a neurotransmitter. Many drugs of abuse act by hijacking this messenger system to artificially and directly activate the parts of our brain that produce feelings of pleasure and 'need'. These brain areas normally exist to ensure that we indulge in behaviour that ensures our survival, for example, eating and drinking.

When these systems are repeatedly 'hijacked', the brain circuits underlying our behaviour are changed so that we come to crave the 'artificial' message over the real one.

Current brain research aims to understand how these brain changes occur and how they might be prevented or even remodelled, back into their natural state.

Our brains reaction to motivation and reward

Professor Lique Coolen

Professor Lique Coolen, from the University of Mississippi Medical Centre, was our guest speaker at our BHRC Conference on 4 June. Prof Coolen explained that natural rewards, such as drinking when you recognise you are thirsty, elevated your dopamine levels in the reward part of your brain (or mesolimbic pathway) and reinforced the behaviour leading to the reward.

Drugs of abuse act on the mesolimbic pathway with greater efficiency, increasing dopamine transmission more effectively than natural rewards. This over-stimulation feeds the addict's compulsion to abuse drugs. In addition, the process of addiction physically changed the brain, affecting areas critical to judgement, decision making, learning and memory and behaviour control.

Addiction is the compulsive seeking and taking of drugs despite the adverse consequences. People had different addiction thresholds based on their genetic makeup and their psychological and family backgrounds. While the initial decision to take drugs was usually a voluntary conscious decision, once the addiction took over, a person's ability to exert self-control was impaired.

Prof Coolen told the audience that addiction was a life-long condition involving craving and the risk of relapse. People thought of addiction as a lack of will-power, but it was actually a chronic and relapsing brain disease. Recovery was often a long-term process requiring repeated treatments.

Neuroscience is searching for better treatments, such as anti-craving compounds, for addiction treatment.

New test being developed to check effectiveness of anxiety drugs

Professor Neil McNaughton

BHRC researcher Professor Neil McNaughton spoke earlier this year about his research on anxiety. He explained how anxiety differs from simple phobias by describing how you may sometimes approach the threat in anxiety, rather than avoiding it as you would with a phobia. Medications that inhibit anxiety, such as benzodiazepine, target general anxiety disorders, however, the effects of the drug in the brain are widespread and we need to understand what specific brain areas and mechanisms might be critical to their action. Professor McNaughton highlighted a brain rhythm known as theta activity that occurs in the hippocampus. He suggested that when you reduce theta activity in this area, as anxiolytic drugs do, you change the way other brain areas are modulated.

Professor McNaughton investigated a "goal-conflict" paradigm with human subjects and saw that a particular balance of approach and avoidance produces a conflict within the brain. He found that when participants take anti-anxiety drugs there is a reduction in the conflict observed and this is reflected by changes in the theta brain rhythm. These findings suggest that the goal-conflict paradigm, and the theta response to it, can be used by researchers to quickly test the effects of novel anti-anxiety drugs in a way that will predict their effectiveness against actual anxiety disorders.

News in brief

Australasian sharing of ideas for PhD students

Every year twelve young PhD students from around Australasia are chosen to attend a three week intensive course on North Stradbroke Island, Queensland. This programme focuses on rigorous training in the theory and practice of neurophysiology and fluorescence imaging. This latter technique uses the phenomenon that certain materials emit energy detectable as visible light when excited with the light of a specific wavelength.

This year two BHRC students Laura Boddington (Anatomy) and Anurag Singh (Psychology) attended. Anurag described attending as "life changing", and said the course was a "complete package for learning, fun and building relations with eminent scientists across the world".

Laura Boddington and Anurag Singh

Update on intrepid Pacific Crest Trail hiker

Dr Julie Lawrence has now raised $855 for Alzheimers Research at our centre. Weather conditions, bush fires and an injury have meant that Julie has had to come off the trail. Julie's last post on her blog showed the emotions she has felt during this trek. "…had X-rays which show I have a hairline fracture of my heel and this will mean eight weeks rest. Therefore, my hike is over and I'm going home. I don't need to write how I am feeling right now – so many emotions are running through me."

We thank Julie for making the BHRC part of her journey.

Tinnitus Fellowship Awarded

BHRC researcher Dr Yiwen Zheng has been awarded a two-year $200,000 Jean Cathie Research Fellowship for her project *Selective activation of GABAergic neurons to treat tinnitus.*

Tinnitus, commonly know as ringing in the ears, affects 15-20% of New Zealanders, with 1% of those severely affected. Chronic tinnitus is a debilitating condition that significantly reduces the quality of life in individuals affected and presents a considerable socioeconomic impact to society.

Student success

Laura Boddington was awarded the prize for the top 'Go-tech' oral presentation at the inaugural Stroke Rehab conference in Christchurch for the presentation of her PhD work, May 2015.

Help us **to help you**

The Brain Health Research Centre has over 200 researchers all based in Dunedin. Supporting our researchers keeps your donation in Otago and helps our team continue their work. There is so much about the brain that we are still finding out. Your donation helps us unlock those mysteries.

Yes, I would like to support the Brain Health Research Centre

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Thank you for generously supporting the Brain Health Research Centre

Protecting the heart from the brain

We don't often think about the links between our brain and our heart, but BHRC Master's student Dominic McCann has spent the past two years studying how to protect the heart during epileptic seizures.

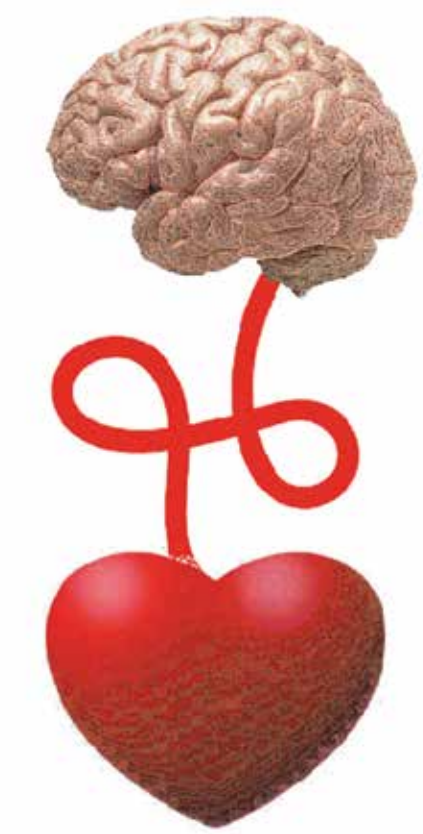
The excessive electrical impulses generated in the brain during an epileptic seizure cause widespread effects throughout the body, causing twitches or convulsions, raising blood pressure and causing tachycardia (abnormally rapid heart rate). Tachycardia can cause structural damage to the heart over time, increasing the risk of developing arrhythmias and even death. While intense seizures can appear to be over within minutes with the person regaining consciousness, cardiac damage can still be occurring over the following hours and days.

Dominic, working in Associate Professor Ivan Sammut's lab with Dr Morgayn Read and Dr Joanne Harrison, and with Rebecca Millen in the Department of Pharmacology & Toxicology, studied two different drugs to see if either could control heart rate and reduce cardiac injury in severe epilepsy. One was a beta-blocker and the other a calcium channel blocker. Treatment with both drugs was studied at two different time points, as a pre-seizure treatment, and as a rescue intervention treatment during seizure.

Dominic discovered that when the beta-blocker was given as a pre-treatment, it completely prevented tachycardia and reduced cardiac structural damage. "Also, we didn't expect this, but pre-treatment with the beta-blocker has a neurological affect because it reduced seizure behaviours and activity in the brain."

The blood brain barrier is thought to breakdown during seizures possibly allowing some of the beta-blocker to impact on beta receptors in the hippocampus of the brain. The group also hypothesised that normalising the heart rate allowed normal oxygenated blood flow to the brain alleviating some of the effects of seizure activity.

While the calcium channel blocker also provided cardiac protection it was not as profound. When the drugs were administered as an intervention during the seizure period, the beta-blocker again showed "amazing results" returning heart rate to baseline after five minutes; "without any drug treatment the heart rate would still be elevated three hours after the onset of seizure, and potentially not return to baseline even 24 hours later," Dominic said. While was not as potent, the calcium channel blocker did normalise heart rate back to base line one to two hours later. Dominic says his research could have a profound clinical effect for people with epilepsy who are drug-resistant, which is about 30% of epileptics. Further clinical trials are needed in order to determine the effectiveness or therapeutic value of the beta-blocker as an intervention measure in status epilepticus patients.



Message from our Director

Professor David Bilkey

Hello and thanks for your interest in our centre. It's been an exciting few months with more to come. June kicked off with our annual conference. This event showcases some of the interesting research that is being conducted within the BHRC and more broadly. Topics ranged from exercise to epilepsy. A particular pleasure was seeing some of our graduate students present a three minute talk on their thesis topics. This was a great way to pique interest in the audience and stimulate later discussion. A further highlight was the public lecture by Professor Lique Coolen who talked about the brain mechanisms that underlie reward and addiction. She had a great turnout for the event, particularly given that it coincided with Dunedin's heaviest rainfall in decades. Thanks to everyone who braved the weather!

The theme of addiction is an important one, as this disorder has a huge impact on the health and wealth of the addicted, their families and loved ones. Drug and alcohol addiction has been estimated to cost New Zealand more than $7 billion annually. Solving the problem is not simply a matter of 'will' on behalf of the addicted. Brain research shows that repeated exposure to drugs of abuse actually changes the circuitry underlying our response to drug-related stimuli. We need to have a better understanding of how these brain changes alter our behaviour. I am pleased to say that researchers within the BHRC are working on these kinds of questions right now. This newsletter includes more information about addiction in our 'Brain in Brief' section. I am hoping this will become a regular item. The BHRC has also put together an interesting group to speak on drug addiction in Queenstown on 2nd September. Further details are in this newsletter. We look forward to seeing some of you there.

What's coming up?

QUEENSTOWN

The Brain on Drugs – Wednesday 2 September Queenstown Memorial Centre, 5.15 - 6.30pm. Three of our researchers will take part in the new outreach programme; **Question it; the world of science comes to Queenstown**, an entire week of science-related programmes.

From chocolate to opioids, therapies to addictions, how does the brain respond? Professor Brian Hyland will talk about reward pathways. What is it that makes us want to eat chocolate and what does that do to the brain? Dr Shakila Rizwan will discuss her research on finding ways to absorb therapeutic drugs into the brain more easily. Associate Professor Christine Jasoni will discuss the impact of drug use during pregnancy and the effects on the developing fetus's brain and subsequent mental health. There will be time for questions. We hope to see you there. Gold coin donation at the door.

Please register at: QuestionIt@catalystnz.org or call Jane at the BHRC 03 479 4066. A full list of Question it events can be found on our website: otago.ac.nz/bhrc/news/otago116434.html

DUNEDIN

The brain agencies network in Dunedin is hosting two professional development sessions for health professionals in October and November. Both events will have BHRC researchers as guest speakers in their area of expertise:

Brain Health Forum on Memory Monday 5 October 5.30pm Community House, Moray Place Dunedin. Cost $10 includes light tea.
Speaker Dr Margaret Ryan

Brain Health Forum on Pain Monday 2 November 5.30pm Community House, Moray Place Dunedin. Cost $10 including light tea
Speaker Dr Louise Parr Brownlie.

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Bright young minds

BHRC researcher celebrates Early Career Award


Dr Karl Iremonger

Dr Karl Iremonger has won one of five Otago Early Career Awards for Distinction in Research for 2015. His work is looking at a part of the brain called the paraventricular nucleus, which is part of the hypothalamus. Karl's work is looking at how neurons inside the paraventricular nucleus are activated by different types of stress.

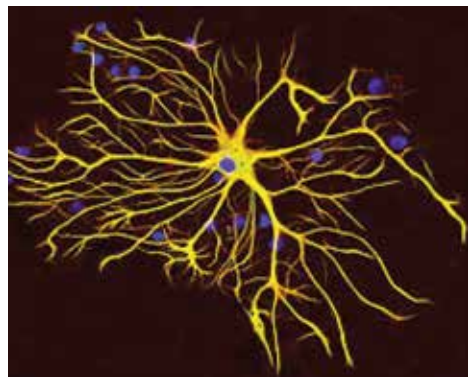
The Early Career Awards for Distinction in Research were introduced in 2004 to recognise and nurture the University's most promising early career researchers. Each recipient will receive $5000 to support their research and scholarly development.

Recipients also become members of the University's O-Zone Group of early-to-mid-career researchers. O-Zone undertakes activities to promote interdisciplinary thinking and collaborations and to present a positive, clear, innovative, and independent voice for research within the University and beyond.

Last year Dr Iremonger was awarded the Prime Minister's MacDiarmid Emerging Scientist Prize as well as the Sir Charles Hercus Fellowship and a Marsden Fast Start grant.

Young researcher excels

BHRC post-doctoral fellow, Dr Owen Jones continues to excel. Owen won the Otago Medical School Research Society's 2015 Research Staff Speaker Award this month. In our last newsletter we mentioned Owen had won our own Young Investigator's award and this new honour has followed in quick succession. The Centre is proud of the work our young researchers are undertaking.


Magnified image of astrocyte

Owen's winning talk; *Astrocytes regulate synaptic plasticity in the hippocampus* focused on the way Astrocytes (Star Cells) regulate the ability of the brains electro-transmitters to increase and decrease activity in the hippocampus. His research focused on a novel role of specific glial (glue) cells previously considered passive, in supporting elements of the central nervous system.

The talk focused on a model in which strong activity in the hippocampus can dampen down the ability of neurons (nerve cells) to strengthen their connections with one and another. This reduction in the plasticity of these connections (synapses) could be a means of avoiding pathologically high levels of activity. Intriguingly, blocking the activity of astrocytes, a type of glial cell, allowed synaptic connections to strengthen as normal. This suggests that astrocytes are recruited following strong neuronal activity and respond by restricting the activity of nearby neurons. These findings add to a growing repertoire of functions fulfilled by astrocytes. "Far from being passive, astrocytes actively respond to neuronal activity and appear to be a "star player" in maintaining healthy brain function," Dr Jones said.