Prevention is better than cure

Neuroscientists Associate Professor James McAuley and Dr Sylvia Gustin are seeking to improve understanding of the development and maintenance of chronic pain, and ultimately change the lives of those affected by it.

Associate Professor James McAuley
Dr Sylvia Gustin

Could you introduce your respective backgrounds?

SG: For the past 20 years I have been using brain imaging techniques and psychological assessment to investigate the central and psychological circuits underlying chronic pain in humans. I have experience in the use of many brain imaging techniques, such as magnetoencephalography and functional, structural and biochemical magnetic resonance imaging. I have practised as a psychologist focusing on the management of chronic pain. My aim is to increase our understanding of the development and maintenance of chronic pain, in particular psychological and central components and their association with each other. And most importantly to develop and evaluate novel interventions that target these factors to produce pain relief.

JA: I have been researching back pain for 15 years, since I completed my PhD at Brunel University in the UK, and immigrated to Australia. Initially my research focused on investigating evidence - practice gaps in the management of low back pain; testing commonly used interventions such as spinal manipulative therapy, different types of exercise therapy, or simple analgesia. More recently, and in collaboration with Dr Gustin, my research has been directed towards developing and testing new interventions for low back pain that aim to prevent, and more effectively manage, chronic low back pain. These interventions focus on normalising sensory input and processing in the brain, which we have shown is disrupted when people experience pain.

What do you find most interesting about research on chronic pain?

SG: I find it fascinating that our brain is critical in the development and maintenance of chronic pain rather than the periphery, for example hand, face and legs, where the experience of chronic pain is associated. My vision is to change the lives of people with chronic pain through the development of new therapies that can provide pain relief via our primary source of pain: the human brain.

JA: My team has developed a simple five-item clinical tool, MYBACK, which provides a risk score or probability, that a person who has recent low back pain will develop chronic low back pain. We are using this tool to identify patients at a high risk of poor outcome. We have developed new interventions for this group of patients that aim to prevent them from developing chronic low back pain. We are testing these interventions in randomised controlled trials.

How are you translating the knowledge gained through your fundamental research into innovative treatment?

JA: We have shown, in a series of randomised controlled trials, that the current approach to low back pain isn't effective; most common interventions such as exercise, spinal manipulative therapy or simple analgesic medicines only produce small reductions in pain or disability. Our team is at the forefront of developing a brand new approach, which aims to help the millions of people who struggle daily with low back pain. For example, we can now identify people with acute low back pain who are at high risk of developing chronic low back pain. We have shown that these people have disrupted sensory processing, which can manifest as an attentional bias towards perceived environmental threats and poor sleep quality. We are testing whether if we intervene early to normalise these brain functions, using specially designed psychological or pharmacological interventions, we can stop these people developing chronic low back pain.

What is next for your research?

SG: We will develop clinically accessible and inexpensive hardware by which our novel and innovative treatment regimes, including EEG-NFB (electroencephalography based neurofeedback), can be widely implemented, thus every chronic pain sufferer has the chance of being treated.

JA: I hope in the future we have truly effective interventions for chronic pain that will involve normalising brain function through combining novel pharmacological management with contemporary physical and psychological interventions.
Chronic pain is a significant problem on a global scale. The Global Burden of Disease study has consistently ranked low back pain over the last 10 years, as the single largest cause of disability worldwide. In the US, the costs of low back pain are rising more rapidly than for any other health condition, making it now the equal second most expensive condition. In Australia, the annual costs of chronic pain are AU$34.3 billion each year and economic modelling indicates these costs will more than triple by 2030. However, no effective treatment has been found that benefits the majority of individuals, and most available treatments have significant side-effects or serious risks.

Associate Professor James McAuley and Dr Sylvia Gustin are developing innovative treatments for chronic pain, with a specific focus on low back pain. They are co-directors of the Centre for Pain Research, Education and Management (PREM) at Neuroscience Research Australia (NeuRA) and the University of New South Wales (UNSW), Australia. McAuley is a psychologist and senior scientist at NeuRA and Associate Professor at UNSW, while Gustin is the AI & Val Rosenstrauss Fellow, senior neuroscientist and psychologist at NeuRA and Head of the Pain Imaging Laboratory (PIL) at UNSW. ‘Low back pain is very common and can be highly distressing for those suffering from it and their families. Despite billions of dollars worth of research over 30 years, we still do not know why some people do not recover and develop chronic low back pain. Although there are many interventions for patients with chronic low back pain, even the most effective only offer limited pain relief and a truly effective solution is not yet available,’ highlights McAuley. ‘Why do we not have effective interventions? What aspect of low back pain should treatments target to obtain pain relief? How can we best stop people with low back pain from developing chronic low back pain? These questions fascinate me, they underpin my interest in low back pain and keep me coming in to work each morning.’

**NOVEL TREATMENTS**

Four key research streams at the Centre for PREM at NeuRA are fundamental research, translational research, implementation and education. ‘Through new discoveries into the development and maintenance of chronic pain (fundamental research) we are developing novel innovative treatments to stop or reverse the effects of the chronic condition, for example changes in neuroplasticity (translational research),’ explains McAuley. ‘A success in implementation depends on consistent knowledge flow from research to practice and policy. We founded the Centre for Pain Research, Education and Management (PREM) at NeuRA to ensure fast implementation of our novel evidence-based chronic pain interventions through individual and group sessions and educational seminars (implementation and education).’

Three key projects are underway at the Centre. First, McAuley and Gustin are working with Edel O’Hagan and Dr Markus Huebscher on SLEEPAIN, which is investigating the positive effects of medication, usually used to treat sleep issues, on back pain. The goal is to ascertain whether improving sleep has a knock-on effect in terms of improving pain in people who have a new onset of pain in their low back.

Second, RESOLVE, which, in addition to McAuley, involves Professor Ben Wand, Professor Lorimer Moseley, Matthew Bagg, O’Hagan and Dr Huebscher, is exploring whether treatment programmes that target the function of the brain, as well as the back, are effective in reducing pain for people with long term or chronic low back pain. To do this, the researchers are conducting a randomised clinical trial, funded by the Australian government (NHMRC).

Third, McAuley is working again with Moseley and Huebscher, in addition to Dr Adrian Traeger, Dr Hopin Lee and Dr Ian Skinner, on PREVENT, a large, government-funded (NHMRC) clinical trial that aims to help people recover early from their low back pain. This trial is evaluating the efficacy of a promising new psychoeducative intervention that has been designed to prevent the development of chronic low back pain. If successful, McAuley and Gustin hope that the results of these trials will lead to changes in the way that low back pain is managed.
TARGETING THALAMIC AND MEDIAL PREFRONTAL CORTEX CHANGES

The team is already making headway in its work, as Gustin explains: ‘Our research has identified biochemical, structural and functional alterations within the medial prefrontal cortex and the thalamus, that are now known to play a key role in the generation of chronic pain,’ she explains. ‘We identified medial prefrontal and thalamic ‘biomarkers’ of chronic neuropathic pain and delivered the thalamocortical model for the generation and maintenance of chronic neuropathic pain. Our model hypotheses that a loss of cortically projecting ventral posterior thalamic neurons, results in disruption of normal thalamocortical rhythm. It is this disruption of thalamocortical rhythm that results in ongoing pain; making this dysrhythmia a potential target for intervention.’ The researchers have developed a new approach that targets these thalamic and medial prefrontal changes to ultimately treat chronic pain. Their intention is to modulate these changes via electroencephalography (EEG) based neurofeedback in a new study and they hope this will lead to significant pain reduction. ‘EEG based neurofeedback teaches individuals to gain control over their brain activity in a way that reduces their pain,’ highlights Gustin.

NEW APPROACHES

The researchers are developing and testing new treatment approaches that focus on the brain, particularly how the brain processes sensory information. ‘We have shown that brain function is disrupted in people with chronic pain, and this can lead to structural changes in circumscribed brain areas such as the thalamus and the medial prefrontal cortex,’ McAuley explains. ‘Our new treatment approach is to target this area of the brain using a combination of physical and pharmacological methods.’

In addition to important progress in identifying the critical role of the thalamus in the development and maintenance of chronic neuropathic pain, Gustin was the first to measure γ-aminobutyric acid (GABA), an inhibitory neurotransmitter, in the thalamus in people with chronic pain. She also showed, for the first time, that time decreased blood flow within the thalamic reticular nucleus in patients with chronic neuropathic pain.

UNRAVELLING MECHANISMS

Looking ahead, the team is keen to see the fruits of their labour, as McAuley highlights: ‘I think that the next 10 years will see major changes in the management of painful conditions. We are on the cusp of a new evidence-based treatment paradigm that focuses on changing the way the brain produces pain, and in what circumstances it does so,’ he states. ‘At the Centre for Pain Research, Education and Management, myself and Dr Gustin have developed a pioneering research programme to develop interventions that target brain function so that our brains respond normally to threats, which reduces pain and allows people with chronic pain to recover. Extensive research has shown these innovative interventions to be very promising and definitive trials are now underway. Early positive results suggest that targeting the brain is the new frontier of chronic pain management.’

The researchers hope that new advances in brain imaging techniques will enable them to unravel the mechanisms underlying the transformation from acute to chronic pain, to ultimately stop acute pain before it becomes chronic.

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Having completed a Bachelor, Master’s and PhD in Psychology (2006) at the Institute of Medical Psychology & Behavioural Neurobiology, University of Tuebingen, Germany, Dr Sylvia Gustin is currently working in Sydney at the School of Psychology, University of New South Wales (UNSW) and Neuroscience Research Australia (NeuRA). She is the Head of the UNSW Pain Imaging Laboratory (PIL) and co-leads the Centre for Pain Research, Education and Management (PREM).

Having completed his PhD at Brunel University, UK in 2002, Associate Professor James McAuley immigrated to Australia in 2004 to take up a postdoc at the University of Sydney. In 2010, he moved to NeuRA, where he has a current appointment as a Senior Research Scientist and an A/Prof appointment in the School of Medical Sciences, UNSW. He co-leads the PREM.