

Brains trust

Unlocking the secrets of the mind

By capitalising on its strengths in the brain sciences — neuroscience, psychiatry, psychology and neurology — UNSW is making its mark on the next great frontier of medical research. By Susi Hamilton.



Britta Campion

Understanding how and why the brain functions, and malfunctions, remains one of life's great mysteries.

The emerging area of brain science is applying different approaches to tackling some of the most devastating conditions affecting humanity – from Alzheimer's disease and depression through to memory loss and other neurological diseases.

Over the past few months some of the University's leading researchers have made international headlines with their studies in the field. Head of Psychiatry in the Faculty of Medicine, Professor Philip Mitchell, is convener of Brain Sciences UNSW, a network established last year to facilitate multidisciplinary research opportunities.

It brings together experts in neuroscience, psychiatry, psychology and neurology.

"There is a palpable excitement about the neurosciences at the moment and we are at the forefront of that," says Professor Mitchell. "Brain Sciences UNSW capitalises on the existing research strengths of the University and affiliated institutes into disorders such as schizophrenia, anxiety, depression, bipolar disorder and Alzheimer's disease.

"What's driving us is an awareness of the arbitrariness of the boundaries. Increasingly, the major breakthroughs will be where the edges of disciplines overlap," he says.

And the work of the network is already making its mark, with a major study published in this month's *British Journal of Psychiatry*,

From left: Kay Wilhelm, Peter Schofield, Philip Mitchell and Gordon Parker

showing a genetic link to depression.

According to the 25-year study, more than a fifth of the population has a genetic predisposition to depression following exposure to multiple stressful life events. It found that people with a "stress-sensitive" form of a serotonin transporter gene are more than twice as likely to suffer from major depression than those with a "stress-resistant" form of the gene.

Professor Mitchell, one of several co-authors, says it's a very significant finding. "It proves that both nature and nurture are important in

depression. You can't have one without the other."

The study is based on the DNA samples and life histories of a group of 128 school teachers who graduated in 1978. Lead author Associate Professor Kay Wilhelm, of St Vincent's Hospital, established the cohort with Scientia Professor Gordon Parker, Executive Director of the Black Dog Institute. "We've been catching up with the group every five years since, to see if there has been any onset of depression with any major life events," says Professor Wilhelm.

Professor Peter Schofield, Director of the Prince of Wales Medical Research Institute (POWMRI), says there is an 80 percent chance that those with a genetic predisposition will become depressed if there are three or more negative life events in a year.

"This contrasts with some people who have a genetic resilience against depression. Even in similar situations, there's only a 30 percent chance of them becoming depressed," he explains. The majority of the population – 53 percent – are somewhere between these two groups.

Of the 128 study participants, 42 percent met criteria for major lifetime depression, says Professor Wilhelm. "We already had a chart for each individual's life events and whether or not they had a depressive episode. Now the genetic tests back that up."

She says the research has some major implications for prevention and treatment. "Perhaps you could reduce the likelihood of depression among those with the vulnerable genotype, by training them up in terms of improving their coping styles and stress responses."

Drug-free treatment for depression

Senior Research Fellow in the School of Psychiatry, Dr Colleen Loo, hopes that her work will help those suffering from debilitating depression without the use of anti-depressants.

Dr Loo and her team have just finished a trial using repetitive transcranial magnetic stimulation (rTMS) with dramatic results. Using a simple coil held to the patient's head, the technique stimulates the brain through highly intensive magnetic fields. "These produce small currents in an area of the brain which has been shown to be underactive in depressed people," explains Dr Loo, who is based at the Black Dog Institute.

"We've found that people who have a chemical depression are mostly happy with the results. It's non-invasive, patients don't have to be admitted to hospital and each session only takes 30 minutes," she says.

The technique has been used for decades,

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Other co-authors of the NHMRC-funded research, *Life events, first depression onset and the serotonin transporter gene*, are Heather Niven, Adam Finch, Lucinda Wedgwood, Anna Scimone and Ian Blair.

Brain Sciences UNSW has also been successful in attracting high-profile international researchers and winning much sought after funding bids.

Just four months after its launch, UNSW and POWMRI secured the right to establish Australia's first Professorial Chair of Schizophrenia Research. With support from NSW Health and the Board of the Neuroscience Institute of Schizophrenia and Allied Disorders (NISAD), \$8 million will be invested over the next five years to establish a joint program. The appointment to the Chair is expected to be announced shortly.

Another coup for the research network was the appointment of Australian biochemist Professor Lindy Rae as the inaugural NewSouth Global Professor in Brain Sciences. Professor Rae is internationally recognised for her expertise in magnetic resonance.

One of her current projects is looking at the drug commonly known as GBH. Previously used in medical practice, it is now popular on the party scene, with sometimes fatal consequences. "While it was used as an anaesthetic in the past, we don't really know how it is operating on a neurochemical level. We hope our work will unravel that," says Professor Rae, who is based at POWMRI.

She will also be collaborating with Associate Professor Rick Richardson from the School of

Psychology to find out more about another drug, DCS, and its effect on the brain.

"DCS has been used for around 30 years to treat tuberculosis," says Professor Richardson. "Now there's increasing evidence that it can benefit those who are suffering from anxiety too."

He is currently working on human trials to see if the drug helps with social phobias and other anxieties such as post-traumatic stress disorder. "The key thing about this drug is that it works on a receptor in the brain which is crucial in learning and memory," says Professor Richardson. "So it needs to be administered with some sort of 'learning' component in therapy. Currently, that's through exposure to what the subjects fear, in controlled circumstances."

The Head of the School of Psychology, Professor Peter Lovibond, says collaborations such as this have been made possible by Brain Sciences UNSW. "What psychology brings to the area is a sophisticated functional analysis of what the brain does," he says. "You can then discover the neural mechanisms that underpin particular functions, such as memory, attention or emotion. If you have a poor theoretical model, you can't interpret your neural data. We need to further understand both normal and abnormal brain functioning."

The quest for healthy ageing

One hundred years after the first description of Alzheimer's disease, a comprehensive global assessment of the prevalence of this and other forms of dementia has been published in *The Lancet*.

UNSW Professor Henry Brodaty, an international expert in psychogeriatrics, is one of the paper's authors.

The study predicts that the number of people affected by dementia will double every 20 years to more than 81 million by 2040. (This assumes there are no changes to mortality and any effective prevention strategies or curative treatments.)

"Our research found that 24.3 million people currently have dementia," says Professor Brodaty. "There is one new case every seven seconds, which equates to 4.6 million new cases of dementia every year."

While most people with dementia live in developing countries, the rates of increase are not uniform. "Developed regions start from a high base, but will experience a moderate to proportionate increase in the coming decades. The rate of increase is predicted to be three to four times higher in developing countries," Professor Brodaty says.

According to the paper, by 2040 there will be three times more people living with dementia in China and Western Pacific countries than in Western Europe.

Meanwhile, Professor Brodaty and a team of UNSW researchers led by Professor Perminder Sachdev, together with Tony Broe and Brian Draper, have received a \$5 million NHMRC grant to study healthy ageing. The five-year study will examine how lifestyle, social interaction, diet, exercise and other factors influence the way people age, both physically and mentally.

Use it or lose it

People who undertake complex mental activity across their lives almost halve their risk of developing dementia, according to UNSW research.

The study, published in *Psychological Medicine*, is the first comprehensive review of the research in the field of brain reserve. “Until now there have been mixed messages about the role of education, occupation, IQ and mentally stimulating leisure activities, in preventing cognitive decline,” says lead author, Dr Michael Valenzuela, from the School of Psychiatry.

“Now the results are much clearer. It’s a case of ‘use it or lose it,’” he says. “If you increase your brain reserve over your lifetime, you seem to lessen the risk of Alzheimer’s and other neurodegenerative diseases.”

The paper, co-authored by Professor Sachdev, also from the School of Psychiatry, integrates data from 29,000 individuals across 22 international studies. A key finding is that individuals with high brain reserve have a 46 percent decreased risk of dementia, compared to those with low brain reserve.

All the studies agreed that mentally stimulating leisure activities, even later in life, are associated with a protective effect, says Dr



Courtesy Matthew Johnstone, / Had a Black Dog

This research proves that both nature and nurture are important in depression. You can't have one without the other

Valenzuela. “This suggests that brain reserve is not a static property, nor that it is determined by early life experiences such as level of education, socioeconomic deprivation or poor nutrition. It is never too late to build brain reserve.”

Bipolar risk gene found

A risk gene for bipolar disorder has been discovered by a team including researchers from UNSW and the Garvan Institute of Medical Research.

The study, published in *Molecular Psychiatry*, found those who have a particular form of the gene are twice as likely to develop the disorder. “This research could help with better diagnosis of the condition and may also allow for new treatments,” says co-author Professor Mitchell.

Bipolar disorder, which is also known as manic-depressive illness, affects two people in every 100. “Apart from lithium, which a significant number of patients cannot tolerate, the currently available medicines are not specific for the condition. The identification of this gene could allow for the development of targeted medicines,” he says.

The researchers are the first to use such a multifaceted approach to identify a bipolar risk gene, explains Professor Peter Schofield, who led the team at the Garvan Institute of Medical Research, before moving to the POWMRI. “We used a number of families, unrelated patients and therapeutic drug models. Each of these led us to the same gene, called F-A-T 1.”

The team included researchers from Macquarie University, NISAD, the University of Wales, Cardiff and the Black Dog Institute at the Prince of Wales Hospital. The lead author on the paper, Dr Ian Blair, of the Garvan Institute of Medical Research, is also a UNSW conjoint senior lecturer. ■

The inaugural symposium of Brain Sciences UNSW will be held next month.

Robotic hand control

A unique collaboration on robotic control systems could eventually benefit people with artificial limbs.

“Prosthetic and robotic hands are notoriously clumsy and unforgiving,” says UNSW Senior Research Fellow, Dr Michael Breakspear. “Researchers are hoping to design a new generation of robotic control systems based on the principles of the human brain.”

With that in mind, Dr Breakspear is bringing together several very different research streams – neuroscience, mathematics, engineering, psychology and robotics.

An important first step is to look at how the brain and hand interact. “I became interested in doing experiments which relate to simple

movements of the hand because of the link with depression,” says Dr Breakspear, who is based at the Black Dog Institute.

“Voluntary and involuntary movements can be markedly affected in severe depression. In some cases people find it very difficult to initiate movements, such as getting out of bed. At other times, people get very agitated, so they get involuntary movements.”

Electrophysiology and functional neuroimaging experiments will enable the team to establish how the neural pathways are disturbed during that process. This preliminary stage of the project could also shed light on other neurological disorders such as schizophrenia, bipolar disorder, epilepsy, Parkinson’s disease and dementia, he says. ■