

The stigma, misery and mystery surrounding schizophrenia in particular and mental illness in general is being uniquely addressed by Sydney University researchers, while a new play at the Seymour Centre explores the personal impact on one sufferer's family. **Caroline Baum** reports

cover story

A mother and son in conversation. The usual banter and collisions between a middle-aged parent and an adolescent male. Except, as the dialogue between Sue and Simon progresses, it becomes obvious that something is not quite right. One of these people is a little off balance. There are signs of a disturbance that might be cause for concern.

It's a scenario that some will recognise when they attend a performance of *Inside Out*, an award-winning new play by Mary Rachel Brown at the Seymour Centre in May. Subtitled "*When you think you know someone*", this brisk, unsentimental, often funny play delicately exposes the early warning signs that baffle so many parents before a diagnosis of psychiatric illness labels their child as suffering from schizophrenia.

But while the play offers both entertainment and insight, real-life dramatic breakthroughs are happening elsewhere throughout the Sydney University campus in the search to find a cure for schizophrenia.

The former Bonds Clothing headquarters in Camperdown, which lay dormant and filthy with pigeon droppings for years, is the unlikely nerve centre for one of Sydney University's most dynamic and ambitious developments, the Brain and Mind Research Institute, where research into the causes of schizophrenia is shedding light on this much misunderstood condition.

This flagship institute is the product of former Vice Chancellor Gavin Brown's and Professor Maxwell Bennett's vision. Now converted into a laboratory housing thousand of rats, mice and zebra fish (apparently the best species to use for observing cell migration as one can see straight through them) and offices on five floors in Mallett Street, the building is at the heart of an ever-expanding site. Currently spread over 15,000m², the Institute's footprint will grow with the launch of a new building opening in June 2009 dedicated to adolescence, combining community outreach programs - including ambulatory care for sufferers of autism, ADHD and brain tumours - with molecular biology research facilities. Next will come a research hospital, the first on any university campus devoted to psychoses and neurological disorders, including multiple sclerosis.

*When
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LIES OF



Established in 2003, the Brain and Mind Research Institute (BMRI) is unique, a world-first hub for neuroscience and the investigation of psychological and neurological disorders. Some critics believe that schizophrenia has long played poor cousin to mood disorders when it comes to research in Sydney, lacking high-profile academic champions to further research - unlike Melbourne, which is recognised internationally for its pioneering work. But the BRMI is changing all that.

Its philosophy is that few medical discoveries are made in isolation and that new and effective solutions require collaboration, a clear common purpose and an active dialogue with the wider community.

At the helm of the BMRI is Professor Ian Hickie, former director of the Beyond Blue Institute, an

THE MIND



organisation dedicated to a better understanding of the causes of depression.

“There is now increased recognition of how common schizophrenia and other neurological disorders are and how much they cost the community and the public health system,” says Professor Hickie.

“Traditionally, research in universities in this area was a very low priority because of social stigma and because of a lack of accessible organs to examine. But a change in public attitudes, together with a technological revolution

in genetic and imaging, has changed all that.

“Gavin Brown picked up on this as a hot issue and pursued it,” Hickie explains. “Until then, the University had over 60 disparate groups working on brain science, but none of them were coordinated and focused. Now they are combined and interdisciplinary. We have been able to attract international funding for our research and there are over one hundred people at the BMRI now on competitive research grants, about half of which are tied up with mental health problems.”

Professor Hickie is a passionate and persuasive advocate of early intervention in schizophrenia.

“All too often it is dealt with after 20 years of symptoms, but we should be tackling it in the teen years, when there is a significant change in frontal lobe development,” he says.

Professor Maxwell Bennett (DSc '77), the sprightly 70-year-old Director of Science at the BMRI, cups a reproduction of the human brain in one hand and explains:

“You are born with a third of your synaptic connections in place in the brain. Then, in the first ten years of your life, you make new connections at the rate of half a million every second, night and day for 10 years.”

During adolescence, says Professor Bennett, these are pruned back. The brain loses a third of those connections by the age of 20 due to environmental factors and for increased efficiency when it comes to higher cognitive learning. “Later, between the ages of 20 and 70, nothing much happens,” he says.

“In sufferers of schizophrenia, we see accelerated synaptic regression,” says Bennett. “Instead of losing a third of these connections, they lose another 30 per cent – a total of 60 per cent. We can see that thanks to the latest technology such as non-invasive neuro-imaging, but we still have no clear idea why, although we suspect it has something to do with a hormone group called glucocorticoids, produced by the adrenals, the hypothalamus and the pituitary gland, which disrupt the synapses by stressing certain molecular properties.”

Professor Bennett is in charge of the neurobiology laboratory looking into the molecular mechanisms underlying synaptic transmission in the nervous system. The lab is currently placing special emphasis on synaptic plasticity, the brain’s remarkable ability to alter the structure of its circuitry (a discovery that has particularly attracted the attention of baby boomers keen to stave off Alzheimer’s and other degenerative diseases with new brain exercises and techniques).

“Once we understand the normal process of synaptic regression and its molecular, chemical drivers, we may be able to manipulate that through the use of second generation anti-psychotic drugs to slow down the process in schizophrenia sufferers,” says Professor Hickie. Professor Bennett cites the encouragingly positive results from clozapine, a well known but controversial antipsychotic drug, which some doctors are wary of because of significant risk factors.

Tracy Mann and Lindsay Farris in *Inside Out*. Photo: courtesy CDP

Over in Concord, Professor Tim Lambert is at the frontline of clinical outreach in charge of schizophrenia treatment and outcomes. Since 2008 the Concord Hospital Centre for Mental Health has operated a 170-bed facility. Its mission is a multi-pronged strategy covering the much-neglected physical health of sufferers, relapse prevention and treatment resistance.

The facts that Professor Lambert is dealing with are stark. Despite advances in treatment, the longevity of schizophrenia sufferers is going backwards. "They lose 25 years of life on average, mainly due to premature cardiovascular disease," says Lambert. "Moreover, the quality of physical care that schizophrenia sufferers receive is appalling. Our research shows that they are rarely checked for diabetes, blood pressure or cancer and that mental illness is a real barrier to getting standard medical care. Our centre now provides a cardiologist and an endocrinologist to help integrate physical and mental health."

Professor Lambert has forged international links with other centres of clinical research, making Concord the



first in a global network with future links in Barcelona, Munich and New York coming on-stream by 2010. "These will be centres of excellence to develop improved clinical services, teaching and training in relation to detection and management of schizophrenia," he explains. "We will be training local people and offering fellowship for local doctors who want to get involved in our programs."

Across town at the Royal North Shore Hospital, SAM spoke with Dr Carissa Coulston (MPsych '98 PhD '06) who completed her PhD in 2006 in Psychological Medicine, examining the neuropsychology of cannabis and other substance use in schizophrenia. Her groundbreaking research found that for some individuals with schizophrenia, cannabis use can improve cognitive functions such as attention, speed of information processing, and planning and organisation.

"Our clinical sample of 60 males with schizophrenia

and a control group of 17 healthy males were recruited through hospitals and community mental health centres in the Northern Sydney and Mid-Western Area Health Services," explains Dr Coulston. "The individuals with schizophrenia varied in terms of frequency and recency of cannabis use. They had to meet criteria of being psychiatrically stable at the time of assessment. All were taking antipsychotic medication in order to manage their illness. My results found that relatively frequent and recent cannabis use was associated with better cognitive performance, but that does not mean I would advocate it as a treatment for all individuals with schizophrenia."

Cannabis has already been found to alleviate symptoms in sufferers of Multiple Sclerosis and other neurological conditions, but Dr Coulston is the one of the first to publish research suggesting it may be of some benefit to sufferers of schizophrenia. Earlier research had shown a now widely accepted view of a causal link between cannabis use and the onset of psychotic episodes in those with a genetic predisposition to the disorder.

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At Westmead Children's Hospital another branch of investigation is being conducted through the University's Brain Dynamic Centre in partnership with the Westmead Millennium Institute. Created in 2001, the centre now has 60 staff, engaged in a holistic, pioneering project of integrative neuroscience under the direction of Lea Williams, Professor of Cognitive Neuropsychiatry.

The multi-disciplinary approach involves a synthesis of information drawn from all modalities – clinical, genetic, etc – to create a unique library of raw data, stored in one place. Thanks to ever-improving information technology capabilities, this material can be accessed and cross-referenced by international researchers, allowing them to decode information that is no longer held separately, divided by old rivalries and feuds between the world of psychology and psychiatry.

"It has taken the blinkers off," says Professor Williams, who declares herself to be "excited by the fact that for the

Above left: Ian Hickie
Above right: Maxwell Bennett

first time, we can pull all the evidence together, forming a much more comprehensive and complex picture and making the detective work much more thorough.”

One of the revelations this approach has already revealed is the identification of poor synchrony.

“In a healthy person, the brain synchronises information every few milliseconds to integrate perception, cognition and emotion like a perfectly calibrated watch,” says Williams. “The brain of someone with schizophrenia does not do this, it is out of whack, causing it to make random associations and to have no ability to contextualise things such as random sounds. Now we have to work out how that links up with everything else we can observe and find the cause.”

(Adding to the notion of the perfectly calibrated timepiece, Tim Lambert comments that research in chronobiology indicates that people with schizophrenia also have defective circadian rhythms as part of a genetic fault.)

While investigation continues in departments of psychology, psychiatry and medicine within Sydney



hospitals, other University departments are also engaged in furthering a better understanding of schizophrenia from the perspective of another discipline.

The Faculty of Education and Social Work’s Agi O’Hara (BA ’90) trains future social workers in how to provide effective services to better support sufferers.

“We look for practical solutions, how to work with people who suffer from the illness, their families and their friends,” Dr O’Hara says. “There are lots of personal anecdotes in our discussion as it is quite common for students to know someone who is a sufferer. We’ve had students who have been sufferers themselves who have provided us with very valuable insight into strategies that have proved helpful to them and we collate all that information so that it is available to each new group of students entering the department.”

Some of the negative perceptions and myths associated with the illness are reinforced by the media, says O’Hara.

“Media stories are problematic because they misrepresent the truth. For example, the focus is

generally on the small minority who harm others, ignoring the reality that people with schizophrenia are much more likely to harm themselves. And, contrary to popular belief, many people don’t hear voices. There is a wide spectrum of symptoms.”

Attending a reading of *Inside Out*, O’Hara was struck by how authentic Sue’s slow realisation of Simon’s problem was.

“Too often, the early warning signs are ignored as typical adolescent behaviour. What I think *Inside Out* captures so well is that the illness develops gradually, and that there are small clues that should ring alarm bells for us. Diagnosis happens way down the track. We need greater awareness in schools and we need to normalise the condition a bit more, to eliminate the stigma.”

In her teaching Dr O’Hara tries to introduce her students to the way other cultures perceive the condition.

“In some cultures, sufferers would be thought of as shamans. The illness is not pathologised in the same way, the sufferer is not shunned or ostracised. Research shows that the way one responds to the condition can



The multi-disciplinary approach involves a synthesis of information

affect whether a sufferer will have a relapse or not; criticism can trigger an episode as it creates stress.” Families need to learn how to back off and resist responses that, despite their best intentions, appear critical or smothering, she explains.

“We also discuss why some people choose to go off their medication because of side effects and that it is important for family members not to judge them for doing this.” **SAM**

Inside Out plays at the Seymour Centre, May 13-30: for tickets: www.seymour.usyd.edu.au. Dr Agi O’Hara will conduct a 45-minute discussion forum after the performance on 14 May. For further information: a.ohara@edfac.usyd.edu.au

Special offer for alumni at this performance: tickets \$32 (normally \$45), to include a drink and canapes before the performance and the opportunity to meet the cast afterwards. Check eSydney and the website.

Above left: Carissa Coulston.
Above right: Agi O’Hara. All photos Karl Schwerdtfeger