HEADLINES
SCHIZOPHRENIA RESEARCH INSTITUTE MARCH 2007

A New Name and Logo for a New Era of Research

The Neuroscience Institute of Schizophrenia and Allied Disorders (NISAD) has changed its name to the **Schizophrenia Research Institute.**

It is now ten years since the Institute commenced operations as a largely NSW-based research centre. Thanks to the NSW State Government, and our sponsors' support, the organisation has grown to include over 175 clinicians and scientists collaborating on a range of research initiatives.

In 2006 the Institute initiated the $3 million Australian Schizophrenia Research Bank (ASRB - see below), and the recruitment of Prof. Cyndi Shannon Weickert to take up the position of Australia's first Professor of Schizophrenia Research (see page 3).

These important milestones have helped to position Australia to take a leading role in schizophrenia research internationally and have provided the incentive for the name change. With *pro bono* assistance from Singleton, Ogilvy & Mather, Schizophrenia Research Institute will become our new name from March 2007.

The name change clearly identifies the Institute's focus, and the new logo reflects the nationwide problem of schizophrenia, as well as the increasing national collaborative research focus.

We hope you as a valued supporter approve of the new name and HeadLines format. All our different activities will be retitled to conform with the new branding, and their expansion will mean that new treatments and a means of prevention will be discovered sooner rather than later.

BIG NAMES GET BEHIND THE BIG RESEARCH BANK

Following on from the support of the Pratt Foundation, which has allowed the Australian Schizophrenia Research Bank (ASRB) to expand to include Victoria as well as NSW, Queensland and Western Australia, other major corporations have joined the battle against schizophrenia.


John Singleton

With support from John Singleton, the award winning marketing services group Singleton Ogilvy & Mather and production company Plush Films have created a *pro bono* recruitment campaign to attract volunteers to the ASRB.

To be nationally launched in May, the campaign will include TV, radio, print and other media, and will be the biggest ever Australian appeal for schizophrenia research.

Matthew Cullen, Co-President of Australia's leading specialist call centre, McKesson Pacific, has also donated support to manage the responses to the appeal.

The aim of the Australian Schizophrenia Research Bank's five-year project is to recruit 2,000 people with schizophrenia and 2,000 controls, and to obtain brain scans, genetic profiles and detailed individual information - all of which will be cross referenced to become the biggest schizophrenia research database of its type in the world.

For details about volunteering for the ASRB, call 1800 639 295, or visit the website at: www.schizophreniaresearch.org.au

Sydney Town Hall glows red for Spark of Genius.

Book your table now for Spark of Genius '07

Andrew Denton said that Spark of Genius '06 was the best event he'd been to. He's hoping to see you at Spark of Genius '07.

On Friday 18th May 2007 yet again Sydney Town Hall will blaze a brilliant red to mark our truly inspirational event. A night where around 600 business leaders, major corporations, senior Government Ministers and passionate individuals unite to celebrate what makes us uniquely human - our minds.

To raise funds for the Institute's research each $5,000 'Genius Table' will be hosted by a 'Spark of Genius'. Perhaps your table may be hosted by Allan Moss AO, Justice Michael Kirby AC CMG, Doug Walters, Bill Granger, John Symond AM, Jonathan Coleman, Tony Bilson, Richard Pratt AC, Jeanne Pratt AC, Mikey Robbins, or maybe even Andrew Denton.

The funds raised from the event are vital to our research. So make a powerful statement of your support by gathering together your friends and colleagues or your company to invest in a 'Genius Table'.

We can assure you that the event will live in the hearts and minds of your guests forever. Book Now!

SPARK OF GENIUS
Sydney Town Hall. Friday 18 May.
Reservations: (02) 9295 8407.
www.schizophreniaresearch.org.au

Cocktails & Consciousness

Very special thanks to actors Jennifer Hagan and Lindsey Farris for their gripping performance of an excerpt from the new play '1 in 100' at our 'Cocktails & Consciousness' event in October. Written by Mary Rachel Brown and directed by Carol Woodrow, the play explores the impact of schizophrenia onset on a mother and son. There were many in the audience with personal experience of that situation, and the general view was that the play got as close as possible to showing what the real thing was like. If you would like to see the play in its full stage version, please see the ad above.

Christmas Appeal

The Institute's Ambassador Angela Greensill made a valuable contribution to the 'Cocktails & Consciousness' discussion panel, and later wrote about her personal experience of schizophrenia in the 2006 Christmas Appeal. The appeal was for donations to our genetic research programs, and Angela's letter has raised more than $20,000 for this vital branch of research. Many thanks to Angela, and to all HeadLines readers who donated.

Actors Jennifer Hagan and Lindsey Farris.

Scientists Honoured

Three Schizophrenia Research Institute scientific employees received awards in late 2006. Scientific Director Prof. Vaughan Carr was awarded the Founders Medal at the 2006 Australasian Society for Psychiatric Research (ASPR) conference. This highly prestigious award, voted on by peers, is presented to persons who, over their entire careers, have made a contribution of significance to psychiatric research. Prof. Carr's acceptance speech focused on the need for multi-disciplinary lines of research to combat schizophrenia.

Nina Sundqvist was awarded the Schizophrenia Fellowship Researcher Award at the ASPR conference for her presentation on work at the NSW Tissue Resource Centre.

The Hunter Medical Research Institute's award for Early Career Research was presented to Dr Carmel Loughland. This award supports the continuing work of a promising researcher in the early stage of their career.

Prof. Clive Harper, the Director of the NSW Tissue Resource Centre and long-time supporter and affiliate of the Institute, received an AM (Member of the Order of Australia) for service to medicine in neuroscience.

Actors Jennifer Hagan and Lindsey Farris keep the 'Cocktails & Consciousness' audience spellbound.

Dr Martin Cohen explains some biological causes of the schizophrenia onset drama. L-R: Pru Goward, Prof. Vaughan Carr, Angela Greensill, Sheryl Taylor, Alex Rivers, Dr Martin Cohen, Carol Woodrow.

The Drama of Schizophrenia

Held in the Galleria of The Garvan Institute in October, the 2006 'Cocktails & Consciousness' event presented an early release performance from the new play '1 in 100' by Griffin Award winner Mary Rachel Brown. This true-to-life portrait of a mother and son coping bravely with schizophrenia onset was superbly portrayed by Jennifer Hagan and Lindsey Farris. After the performance, a panel took the stage to discuss the issues dramatised in the play, with Prof. Vaughan Carr and Dr Martin Cohen providing insights into the biology of the mind, and how it can go dramatically wrong. Sheryl Taylor (former award-winning Channel Nine Health Reporter) led the lively debate, with Angela Greensill providing her first-hand experience of what onset is really like. Our warm thanks to all sponsors (noted on the back page) and participants. Once again, 'Cocktails & Consciousness' provided a unique experience for around 200 Institute Society members and their guests. To find out how to become a member yourself, simply call (02) 9295 8407.

Psychosis Research Goes to Canberra

Prof. Stanley Catts with Rob Knowles, National Chairman of Mental Illness Fellowship of Australia will co-chair the APRN Steering Committee

(L-R): Andrew Laming MP, Prof. Vaughan Carr, Prof. Stanley Catts, Rob Knowles and facilitator Sheryl Taylor at the APRN launch.

A major step towards a cure for schizophrenia and bipolar disorder was taken on November 28 at Parliament House, Canberra, with the official launch of the Australian Psychosis Research Network (APRN).

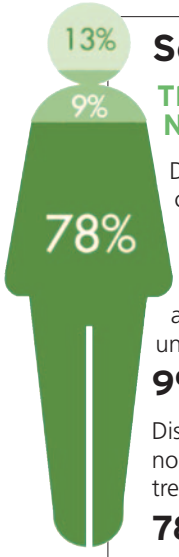
In what is a world first, Australia has taken the lead in psychosis research, with a huge national team of medical researchers and psychiatrists planning to collaborate and integrate currently separate fields of research in the development of a nationwide research program.

Hosted by the Federal parliamentary group the Parliamentary Friends of Schizophrenia, the launch was attended by an impressive line up of senior researchers from across Australia, as well as consumer advocates and business/community leaders.

APRN acknowledges Australian Public Affairs who provided support in bringing APRN before Federal parliament.

Further details regarding the Canberra Summit and a list of research institute participants are available from the website at www.aprn.net.au

APRN
collaborate | consolidate | cure



Schizophrenia:

The Urgent Need for New Treatments

Disability averted by current treatments:

13%

Additional disability averted if services had unlimited funding:

9%

Disability for which there is no current effective treatment:

78%

Adapted from Andrews et al. 2003 Br J Psychiatry 183, 427-435

Schizophrenia Research Institute is just one of the many research centres participating in the APRN national project.

Building Australia's first Chair of Schizophrenia Research

Prof. Shannon Weickert prepares to investigate the role of hormones in schizophrenia.

While her laboratory at the Prince of Wales Medical Research Institute is being completed, Prof. Shannon Weickert is preparing a major study of the role of estrogen in schizophrenia.

Since the 1990s, many studies have raised interesting questions regarding the hormonal aspects of the illness. Why do almost all onsets occur in puberty? Why does gender influence symptoms? Why are testosterone levels lower in male schizophrenia patients? Why do female patients relapse when estrogen levels are low, and improve when levels are high?

Prof. Shannon Weickert was among the first researchers to link the estrogen receptor gene (ESR1) with the diagnosis of schizophrenia in both males and females. The goal of her new hormone research program is to identify ESR1 genotypes that are related to psychosis and cognitive impairments in schizophrenia, and to develop a hormone intervention therapy.

The role of the neuregulin gene in brain development

Dr Shannon Weickert's second research target is the neuregulin gene (NRG1) and its role in brain development. The NRG1 gene has been linked to schizophrenia in populations all over the world, and is known to regulate the migration of neurons from central brain areas to form the adult cortex. Therefore any abnormality of NRG1 expression could result in 'arrested development' of the cortex.

Prof. Shannon Weickert and colleagues have previously found that NRG1 and its major receptor ErbB4 is abnormally expressed in the frontal cortex of schizophrenia patients. Her new team will use a combination of post mortem brain tissue, DNA analysis, and cell cultures to determine how the NRG1 abnormalities may lead to altered brain development.

A room with a view - to better treatment. Prof. Shannon Weickert surveys the construction site of her new laboratory at the Prince of Wales Medical Research Institute.

Cannabis, Schizophrenia and Mice

Finding a link between genetic and environmental risk factors

According to the neurodevelopmental theory of schizophrenia now being widely tested by researchers, the illness is caused by abnormalities in the brain's biochemistry and structure which occur during the development from childhood to adult, and these abnormalities can arise due to an interaction between genetic and environmental risk factors for schizophrenia.

One of the environmental factors believed to increase risk of schizophrenia is heavy cannabis use – particularly when such usage occurs during adolescence. One of the genes thought to be involved in the development of schizophrenia is called neuregulin 1 (Nrg1), which plays an important role in the development of the nervous system, and which is found to be altered in people with the illness.

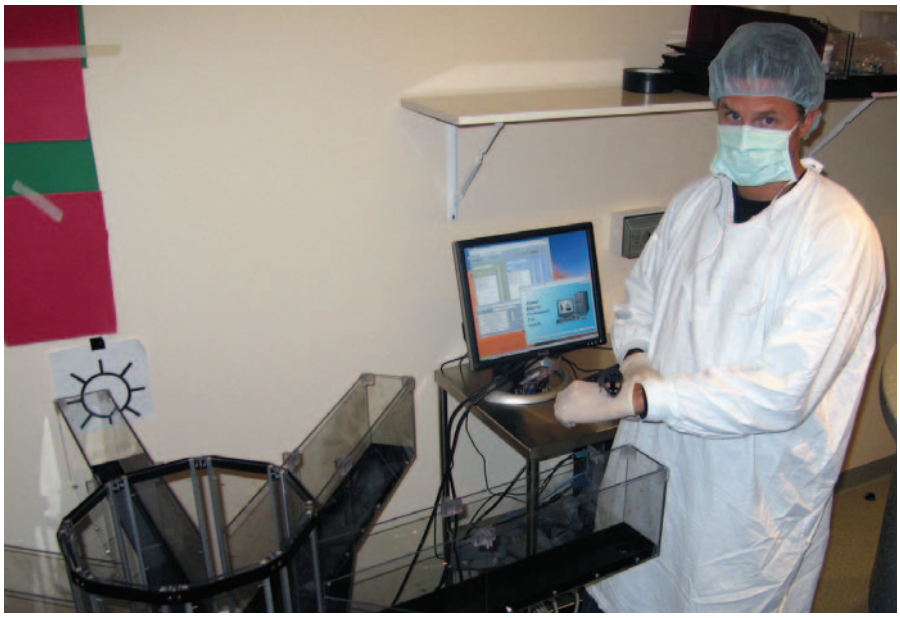
What would happen if we brought these two factors together? Would we be able to observe an obvious connection between the environmental risk of cannabis and the genetic risk of Nrg1?

Schizophrenia Research Institute researcher Dr Tim Karl and his team at The Garvan Institute decided to find out. Genetically modified 'knockout' mice were obtained in which the Nrg1 gene had been rendered inactive. Doses of tetrahydrocannabinol (THC), the main psychotropic agent in cannabis, were given to the knockout mice and to a similar number of unaltered mice. Then both groups were tested on a range of schizophrenia-related behaviours measuring the effects of the drug on movement, explorative behaviour, learning, memory and anxiety.

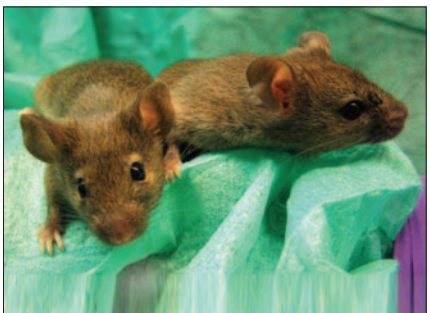
The test results indicated that the knockout mice were more sensitive to the general effects of THC in an array of different behaviours. This increased sensitivity to THC suggests that there may be a link between genetic background and cannabis use.

However, as this study used a one-off dose of THC, and susceptibility to the illness is associated with long-term cannabis use, further studies involving Nrg1 knockout mice and extended THC dosage are required to achieve deeper insight into the effects of cannabis abuse on schizophrenia.

Boucher AA, Arnold JC, Duffy L, Schofield PR, Micheau J, Karl T. Heterozygous neuregulin 1 mice are more sensitive to the behavioural effects of tetrahydrocannabinol. *Psychopharmacology* (in press).



Dr Tim Karl about to introduce a knockout mouse into the maze to study changes in explorative behaviour, learning and memory. The symbols stuck on the wall help the mice to orientate themselves in the maze.



HOW TO MAKE A 'KNOCKOUT' MOUSE

A knockout mouse is a mouse which has had one or more of its genes made inactive by genetic modification. As mouse genes are very similar to human genes, such mice are a vital part of research into the role played by specific genes in human illnesses.

Knocking out the activity of a gene provides information about what that gene normally does.

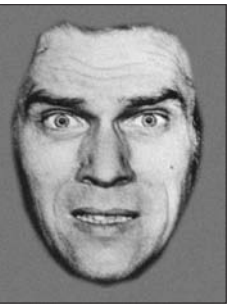
The gene to be knocked out is extracted from a laboratory-stored mouse DNA molecule called a plasmid, then altered to make it inactive. Then stem cells are taken from a mouse embryo, and the altered DNA introduced to them. Some of the stem cells will incorporate the altered DNA to replace their original DNA, and these are introduced into embryos which are implanted into female mice. By cross-breeding the resulting offspring with other altered mice, a new breed of mouse is created which will feature the altered 'knocked out' gene.

Such breeds – each featuring a different knocked out gene – are invaluable for research into different kinds of cancers, obesity, heart disease, diabetes, arthritis, substance abuse, and Parkinson's disease, as well as mental illnesses. Knockout mice also offer a biological context in which drugs and other therapies can be developed and tested.

Schizophrenia and Social Dysfunction

Investigating the tendency to misinterpret social situations

"This is a story of man who had recently bought a new car. The man is walking back to his car across the parking lot. From a distance, he can see some kids around his car - he sees one of them holding one of the car's hubcaps. He yells at the kids and they run into a nearby forest waving the hubcaps in their hands. Now that he is close to his car he can see that it is certainly missing its hubcaps."



Subjects were asked to identify the emotion of a facial expression after reading a short description of a social situation. The results showed how schizophrenia subjects are less able to consider social situations when judging others' emotions.

Many studies have demonstrated poor facial expression recognition in schizophrenia. This may contribute to the poor social functioning that is symptomatic of the illness, affecting the ability to engage in social relationships, attend to self-care, maintain employment, and participate in recreational or community activities.

One of the factors implicated in misinterpreting facial emotions is the abnormally restricted scan path used by schizophrenia patients when viewing a face. Interestingly, this restricted scan path is often evident in close relatives of patients, indicating how the genetic sources of schizophrenia may affect the cognitive functions of otherwise healthy brains.

Another factor affecting the social-cognitive difficulties of people with schizophrenia involves the capacity to appreciate the situational context of a person's behaviour in order to correctly interpret their emotions. Deficits in context processing are a pervasive feature of schizophrenia that may impact negatively on social cognition and social functioning.

With this in mind, Dr Melissa Green at the Macquarie Centre for Cognitive Science devised a study to investigate the ability of schizophrenia patients, recruited from the Schizophrenia Research Register, to use information about social context when judging the meaning of emotional facial expressions.

A standardised set of face images expressing 'basic' emotions (such as anger, fear, sadness, surprise) were each preceded with a short 'social situation' story that differed in emotional content from the face with which it was paired.

Subjects were required to read the story aloud, and then a face image was shown on a computer screen; the subject was asked to select which emotion was expressed in the face by pressing a button on a keyboard. In this way, a sequence of 28 different story+face sets were completed by each participant.

The results showed that while the control subjects tended to judge each facial emotion in the context of the situation cued by its story, the schizophrenia subjects were less able to use the story as a guide to judging the emotion.

Interestingly, the schizophrenia subjects' impaired ability to process the context of the face emotion was most apparent when identifying negative or threat-related expressions, such as anger, fear or sadness. This suggests that context processing deficits in schizophrenia may be implicated in the misperception of threat associated with paranoia, as demonstrated in Dr Green's previous research.

Green MJ, Waldren JH, Coltheart M. Emotional context processing is impaired in schizophrenia. *Cognitive Neuropsychiatry* (in press).

Dr Melissa Green monitors a volunteer's interpretation of emotional context.

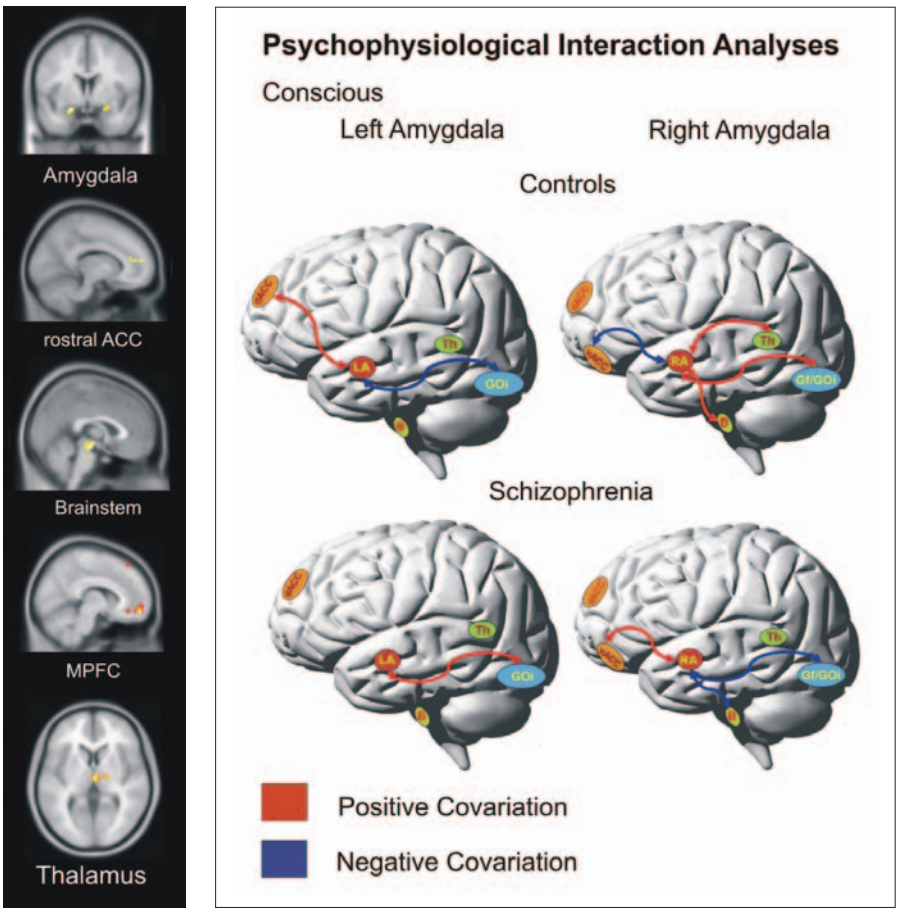
Scan path tracking device

Improving emotion recognition in people with schizophrenia

Dr Melissa Green was also involved in earlier studies at the Macquarie Centre for Cognitive Science, which trained schizophrenia patients to compensate for facial scanning deficits. An expansion of this study has now commenced, using the Micro-Expression Training Tools (METT) to improve emotion recognition, and thus social and vocational skills in schizophrenia patients. To volunteer for the study, please contact Dr Pamela Marsh on (02) 9850 6769.

Images of Emotional Disconnection

How do you feel when the part of the brain that tells you what to feel is out of order ?

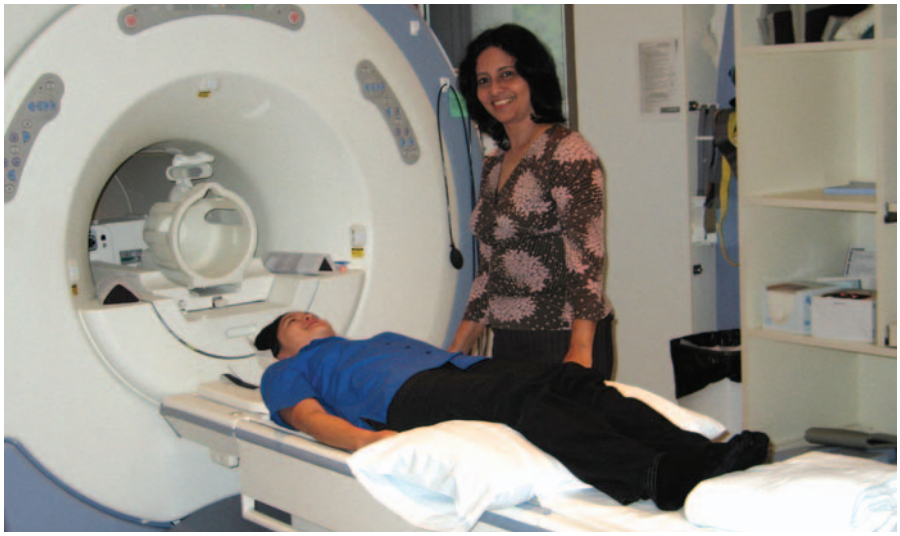


Black strip above: A selection of fMRI images from the study showing activity in various brain areas while subjects viewed fearful or neutral face images. Main image above: Results after fMRI images from schizophrenia subjects and controls were processed to define differences in signaling between the amygdala (LA and RA) and other brain areas.

It is now well established that schizophrenia causes disruption in the way different areas of the brain communicate with each other, and the disruption between the 'thinking' area of the prefrontal cortex and the 'feeling' area of the amygdala has come under special scrutiny. It is thought that neural disconnections between these two and other areas account for many of the disabilities associated with the illness.

Dr Melissa Green's team (see page 5) investigated an aspect of this disruption using face images, stories and questionnaires. Dr Pritha Das and colleagues at the Brain Dynamics Centre, Westmead, have used face images and functional magnetic resonance imaging (fMRI) to take pictures of the disruption in progress.

14 first episode schizophrenia patients and 14 healthy controls (average age 20-23 years) viewed alternate fearful and neutral face images while their brain activity was monitored via fMRI. The study was divided into two sections: 'conscious' and 'nonconscious'. In the 'conscious' section subjects viewed both neutral and fearful face images for half a second. In the 'nonconscious' section, the fearful face images were flashed on screen for 16 milliseconds, forming a subliminal impression.



Dr Pritha Das helps a volunteer in one of the MRI facilities at Westmead Hospital.

A special software program was then used to process the fMRI data to detect differences between the brain responses of schizophrenia subjects and controls. The results showed for the first time that schizophrenia causes a reversal of the normal pattern of connectivity between the amygdala and the prefrontal cortex, the brainstem and the visual cortex.

In lay terms, this reversal of connectivity between the feeling and thinking centres of the brain may be the root cause of the emotional alienation and social dysfunction symptomatic of schizophrenia.

Dr Das is preparing a further study which will use other emotional stimuli to add to the results from this valuable research method.

Das P, Kemp AH, Flynn G, Harris AWF, Liddell BJ, Whitford TJ, Peduto A, Gordon E, Williams LM. Functional disconnections in the direct and indirect amygdala pathways for fear processing in schizophrenia. *Schizophrenia Research* (in press).

The VCFS Risk of Schizophrenia

Velo-cardio-facial syndrome (VCFS) is a genetic disorder affecting 1 in 5,000 children. Sufferers are often born with cardiac defects, may have a cleft palate, and commonly experience learning difficulties. They also have a 30 per cent chance of developing schizophrenia.

Dr Linda Campbell

It is known that VCFS is caused by a deletion at the long arm of chromosome 22, so an investigation of this genetic abnormality is considered to be potentially very valuable to schizophrenia research.

Dr Linda Campbell from the University of Newcastle's Centre for Brain and Mental Health Research was awarded research fellowships from the National Health & Medical Research Council and the Hunter Medical Research Institute (sponsored by Port Waratah Coal) for a three year study of the link between VCFS and schizophrenia. She will recruit 40 people with VCFS and 20 of their siblings.

Schizophrenia Research Institute will provide further support for this study by making available the infrastructure associated with the Australian Schizophrenia Research Bank. The information being gathered by Dr Campbell will contribute an important subset to the ASRB database, particularly in relation to the genetics of schizophrenia.

For further information about this study please contact Dr Linda Campbell on (02) 4924 6648.

Schizophrenia in Sri Lanka

One of the problems of schizophrenia research is the difficulty of recruiting subjects who have never been treated with anti-psychotic medication. While medications can help manage symptoms, it is often difficult to distinguish between the changes they make and those caused by the illness.

Dr Nishantha Kumarasinghe

Schizophrenia Research Institute is supporting a study which offers a valuable chance to investigate the illness in its 'natural state' - via a collaboration between the University of Sri Jeyawardenepura in Colombo, Sri Lanka, and the University of Newcastle.

15 untreated Sri Lankan schizophrenia subjects will participate in a study which will obtain genetic profiles before and after antipsychotic treatment, and MRI brain scans after treatment. The results will provide valuable information regarding genetic and brain structural changes caused by the illness and by medication. This data will also be incorporated into the Australian Schizophrenia Research Bank.

Schizophrenia Research Institute PhD Scholar Dr Nishantha Kumarasinghe is currently collecting the data in Columbo, after receiving training in required methodology at the University of Newcastle.

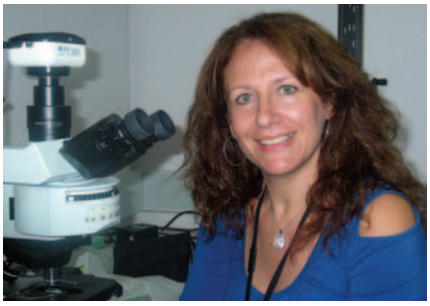
The Cannabis Question

Despite many targeted studies over the last decade, there remains much that is not understood about the connection between cannabis use and the onset of psychosis in adolescence.

More information about the mechanism of the brain's cannabinoid receptor system could lead to the development of treatments to neutralise or reduce any psychosis causing effects of such drug abuse, as well as shed light on the neuronal functions whose disturbances result in the disorganised thinking, attention deficits, memory and language problems that characterise schizophrenia.

With this in mind, Dr Katerina Zavitsanou has been granted a three year Senior Fellowship valued at $450,000 by Australian Nuclear Science and Technology Organisation (ANSTO) for an investigation of the chronic effects of cannabis on the neurotransmitter systems in the brains of adult and adolescent rats.

The aim is to produce an animal model of long-term cannabis abuse, and to examine its cellular effects using the cutting-edge molecular imaging (PET/SPECT) facilities of ANSTO.



Dr Katerina Zavitsanou

Schizophrenia Research Institute

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Lee Drury, the Institute's Manager of Corporate and Community Partnerships.

You can make a real difference by:

- Making a personal donation, better still, set up a regular donation.
- Giving generously to our PhD Scholarship and Christmas appeals.
- Joining the 'Schizophrenia Research Institute Society', a regular way to invest in our research and meet with other likeminded individuals.
- Leaving a gift in your Will.
- Registering to be an 'Institute Volunteer'.
- Becoming an Individual Sponsor.
- Investing in a table at 'Spark of Genius'.

Empower others to make a real difference

The Institute needs new partnerships, sponsors and workplace giving programs. Please help by introducing the Schizophrenia Research Institute to any organisations you belong to.

To discuss, please contact Lee Drury on (02) 9295 8362 or send an email to: l.drury@schizophreniaresearch.org.au

Please help by completing and mailing this donation form to Schizophrenia Research Institute, 384 Victoria Street, Darlinghurst, NSW 2010, or by faxing to (02) 9295 8415, or simply call (02) 9295 8407.

Name:_____ Address:_____ Postcode:_____

☐ Cheque enclosed (made out to Schizophrenia Research Institute): $_____

☐ Please debit my credit card: $_____ ☐ Bankcard ☐ MasterCard ☐ Visa ☐ Amex

Card No:_____ Cardholder's Name:_____

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SCHIZOPHRENIA RESEARCH INSTITUTE