

# HEADLINES

The Newsletter of the Neuroscience Institute of Schizophrenia and Allied Disorders. APRIL 2004.

## Morris Iemma pledges \$500,000 for Australia's First University Chair of Schizophrenia Research

*With \$500,000 for a University Chair and \$160,000 raised for research, NISAD's 'Spark of Genius' event was well named.*

More than 300 guests assembled at NSW Parliament House on 19 March to enjoy Andrew Denton's repartee, Wendy Harmer's wit, Ann Fulwood's presentation skills, and the company of many geniuses from times past.

In keeping with the event theme, 22 actors in full costume and make-up played the roles of famous people who suffered from mental illness. Guests were welcomed by Jackson Pollock, Beethoven and Vivien Leigh, and conversed with Virginia Woolf, Tennessee Williams, Isaac Newton, Abraham Lincoln and many others.

The bidding was enthusiastic for donated auction items ranging from a holiday in Greece to a training session in the RAAF's F111 fighter flight simulator. Pledged donations went to support the DNA Bank for Schizophrenia Research, a NISAD initiative dedicated to collecting DNA samples from patients and their relatives for use in investigating the genetic sources of the illness.

### New Recognition for Schizophrenia

In his keynote speech, NSW Minister for Health Morris Iemma announced a grant of \$500,000 towards founding a University Chair of Schizophrenia Research in NSW. NISAD will now attempt to raise the additional \$500,000 necessary to establish the position.

The first in Australia, such a Chair will establish a new source of research under the aegis of a NSW University, and will create a new national benchmark of priority for schizophrenia as a major disease.

### Don McDonald's Farewell

The black tie event also provided an ideal opportunity to honour Don McDonald on the occasion of his retirement. Don was interviewed on stage by Andrew Denton, and presented with a commemorative plaque in recognition of his inimitable role as NISAD's original and greatest advocate and fundraiser. As one of the founding NISAD Board members in 1996, and later as Director of the NISAD/NSW Health Partnership Project, Don has been personally responsible for raising over \$2 million in sponsorships and donations, as well as for lobbying government support, and significantly improving public awareness of schizophrenia.



Minister for Health Morris Iemma announces the good news for Australian schizophrenia research.



Andrew Denton looks on as Don McDonald receives a special plaque of appreciation from NISAD Founding Chairman Prof. Stan Catts.

### \$160,000 Thanks to NISAD's Supporters

Masterminded by NISAD's Lee Drury, with the assistance of Graziella Garrett, the 'Spark of Genius' event owes special thanks to Morris Iemma, Andrew Denton, Anne Fulwood, Telstra and 20 Telstra Friends, St. George Bank who supplied auction software and staff, Doug Hawkins of TUV, our auctioneer David Tapp, and to our cast of 20 actors. Many, many thanks to all who contributed significantly to create a truly 'sparkling' event in aid of NISAD. See the photos at <http://au.msnusers.com/sparkofgenius>



Wendy Harmer and Anne Fulwood relax at the Chairman's Table between duties.

## The Bank With Deposits Worth More Than Money

### Michael Costa opens Hunter DNA Bank for Schizophrenia Research

Possibly the most valuable bank in Australia was officially opened on 28 November at the John Hunter Hospital, Newcastle. A NISAD initiative, the Hunter DNA Bank for Schizophrenia and Allied Disorders is dedicated to collecting DNA samples from schizophrenia volunteers and their relatives for use in investigating the genetic causes of the illness.

While the risk for schizophrenia in the general population is 1 per cent, the risk for a child with a schizophrenia-affected parent is 10 per cent, even if the child is brought up by adoptive parents. It is believed that more than one inherited gene is responsible for the predisposition, which must be present for schizophrenia to occur. While it is believed that the predisposition is coupled with environmental stresses such as birth complications, drug abuse and urban living, the proportion of risk carried by the genetic vulnerability has been placed as high as 80 per cent.

Using the new 'gene-chip' technology, researchers will use the DNA Bank resource to test thousands of genes simultaneously, searching for the genetic 'signature' of schizophrenia that will aid diagnosis, help develop better treatments, and maybe lead to a cure. In opening the Brain Bank, Minister for the Hunter Michael Costa was joined by radio personality Craig Hamilton, who provided a blood sample.

The DNA Bank is co-supported by NISAD, the Hunter Medical Research Institute, the University of Newcastle and the Hunter Area Pathology Service.



Above: At the DNA Bank's opening on 28 November. L-R: Craig Hamilton, NISAD's Dr Paul Tooney, Prof. John Rostas, Prof. Rodney Scott, Minister for The Hunter Michael Costa, Prof. Mike Calford.

Left: Craig Hamilton does his bit for research by providing a blood sample on the spot.

# Exploring the Neural Geography of Emotional Response

## Two new studies shed light on the communication breakdowns of schizophrenia

One of the core characteristics of schizophrenia is the breakdown it causes in interpersonal communication, and many studies have indicated that this is due to a corresponding breakdown in the brain's ability to recognise and respond appropriately to the emotions of others.

Pursuing this line of research, NISAD affiliated scientist Prof. Lea Williams is extending her investigations into how schizophrenia affects emotion processing in the brain.

As reported in the January 2001 HeadLines, Prof. Williams and her team have confirmed that the illness causes a dysfunction of normal signalling between the brain's limbic system and frontal lobes. As the limbic system, including the amygdala, is responsible for emotionally interpreting received impressions, this dysfunction may produce difficulties in the interpretation of emotionally loaded information.

Prof. Williams and her collaborators have now completed two further studies; the first investigated how antipsychotic medication affects the perception of emotion; the second explored the role of limbic/frontal lobe dysfunction and arousal in producing the symptoms of paranoia in schizophrenia.

### The effects of medication on emotion processing

For the first study<sup>1</sup>, Prof. Williams and collaborators utilised visual scanpaths to assess the effects of antipsychotic medications.

Of 28 schizophrenia subjects, 15 were prescribed the atypical (newer) medication Risperidone, and 13 prescribed the older medication Haloperidol. A control group of healthy unmedicated subjects was also assessed.

Video-oculography technology was

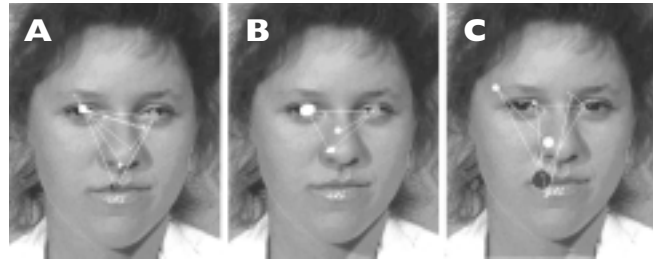
used to track eye movements of all subjects while viewing images of happy, sad and neutral facial expressions. All subjects were also tested on their ability to correctly identify the emotional content of the facial images shown.

Compared to the control group, both schizophrenia groups showed a general restriction of visual scanning, reflected in a pattern of shorter eye movements and fewer fixations of longer duration. However, the haloperidol and risperidone-treated groups differed in their ability to attend to specific features of the face (eyes, mouth). Haloperidol-treated subjects showed reduced fixation to the specific features of all expressions, in addition to restricted scanning. By contrast, risperidone-treated subjects were better at attending to these specific features and correspondingly better at recognising the expressions.

These findings indicate that atypical treatments such as Risperidone may aid the emotional function of people with schizophrenia. Given that we rely on facial emotions for our everyday interactions, the findings suggest that these treatments may modulate the ability to interpret and respond to the emotional content of interpersonal relations.

### The Sources of paranoia

Prof. Williams' second study<sup>2</sup> followed on from her earlier 2000 research, which used fMRI scans to reveal the brain activity of healthy and schizophrenia-affected subjects while they viewed alternate pictures of threat-related and neutral facial expressions. In the earlier study, while healthy subjects recorded strong activity in the limbic/amygdala areas when viewing threat-related images, schizophrenia subjects showed no activity here, but strong responses in the prefrontal



**The effects of medication.** Typical scanpaths of a neutral face: A - Unmedicated control subject without schizophrenia. B - Schizophrenia subject treated with Risperidone. C - Schizophrenia subject treated with Haloperidol.

'thinking' areas.

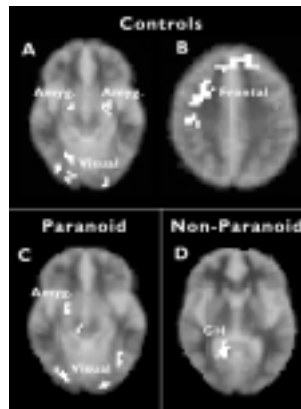
The new study was designed to discover whether this dysfunction of emotion processing in the brain was particularly evident in patients exhibiting paranoid symptoms, and also whether it was modulated by similar abnormalities in other 'body' arousal responses to emotional stimulation. Arousal responses were recorded via skin conductance

electrodes modified for the fMRI environment.

27 schizophrenia subjects (13 paranoid, 14 non-paranoid) participated, along with 22 healthy controls. As before, fMRI brain scans were recorded as subjects viewed alternating facial images expressing fear or neutral emotion. Simultaneously, the skin conductance electrodes placed on the fingers provided a measure of autonomic arousal.

The schizophrenia subjects produced more skin conductance arousal responses and less limbic/amygdala activity than the healthy subjects, and both these abnormalities were particularly pronounced in the subjects with paranoid schizophrenia.

These results suggest that while schizophrenia appears to increase the sensitivity and amplitude of instinctive or autonomic responses to emotional stimuli, it decreases the brain's ability to process such stimuli appropriately. In the case of threat or fear-related stimuli, the extreme sensitivity and the dysfunction of normal limbic/amygdala links to the prefrontal cognitive areas result in the cognitive misinterpretations typical of paranoia.



**Paranoia.** fMRI scans A-B show activity at different levels of the brain in normal controls when viewing a series of fear images (example left). Scans C-D pinpoint where brain activity is comparatively reduced in paranoid and non-paranoid schizophrenia subjects. Paranoid subjects showed reduced activity in the amygdala and visual areas, whereas non-paranoid schizophrenia subjects showed reduced activity only in the hippocampal gyrus area (GH).

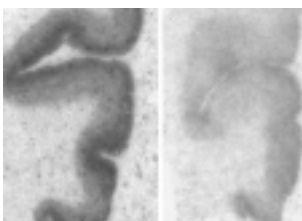
<sup>1</sup>Emotion perception in schizophrenia: an eye movement study comparing the effectiveness of risperidone vs. haloperidol. Published in *Psychiatry Research*, 2003.

<sup>2</sup>Dysregulation of arousal and amygdala-prefrontal systems in paranoid schizophrenia. Published in *American Journal of Psychiatry*, March 2004.

## Zeroing in on a Mental Health 'Black Spot'



The anterior cingulate cortex is a brain region strongly associated with the 'executive function' or decision-making role so commonly found to be affected in schizophrenia.



No differences were found in muscarinic receptor density in the anterior cingulate cortex of brain tissue from bipolar samples, major depression samples, and normal controls. Tissue from schizophrenia samples, however, contained 19-24% less muscarinic receptors than controls (left).

The brain area known as the anterior cingulate cortex (ACC) has been a focus of neuroscience mental health research for some time, and its dysfunction has been directly linked to disorders such as obsessive-compulsive, bipolar and post traumatic stress, as well as to depression, autism and schizophrenia. All evidence identifies the ACC as an 'accident black spot' in the brain's busy network of pathways.

In earlier studies, NISAD's Dr Katerina Zavitsanou at the University of Wollongong has detected increased numbers of cannabinoid and glutamate receptors, and decreased numbers of serotonin receptors in the ACC of post mortem brains from schizophrenia patients. Her recent research\* has focussed on muscarinic receptors in the ACC because these have been shown to play a role in depression and bipolar disorders. Are there abnormalities in these receptors in the ACC of schizophrenia affected brains as well?

To answer this question, Dr Zavitsanou obtained samples of the ACC from 60 postmortem brains: 15

schizophrenia, 15 bipolar, 15 depression, and 15 controls. A chemical process was used to label the muscarinic receptors in all samples, and the density of these receptors measured and compared across all samples.

No differences were found in the muscarinic receptor densities of bipolar and depression samples and controls, but the schizophrenia samples contained 19-24% less muscarinic receptors than controls.

As the ACC plays a fundamental role in cognition and attention, which are both disordered in schizophrenia, it is possible that the observed deficit in numbers of muscarinic receptors may combine with the earlier abnormalities found in other receptor levels as a cause of such disorders.

Further studies investigating the correlation between the altered receptor levels in the ACC brain region in schizophrenia are underway.

\*Receptors in the anterior cingulate cortex in schizophrenia, bipolar disorder, and major depression disorder. Published in *Neuropsychopharmacology*, vol 29, pg 619-625, 2004.

## Dr Tim Karl Joins the Team

The June 2003 HeadLines announced a \$240K grant from the Sylvia and Charles Viertel Charitable Foundation for the development of animal models aiding schizophrenia research. To expedite the research plan, Dr Tim Karl from the Hannover Medical School, Germany, has joined the NISAD team at The Garvan Institute as Research Officer under the supervision of Prof. Peter Schofield.



Dr Tim Karl

Dr Karl's experience in using animal behavioural techniques to study human psychiatric disorders such as depression and schizophrenia will be of great value.

The development and use of animal models in schizophrenia research is a collaborative project shared between NISAD and the Queensland Centre for Mental Health Research.



## FOUNDING SCIENTIFIC DIRECTOR STEPS DOWN

Prof. Philip Ward was a key figure among the original small group of scientists who were working hard for the NISAD cause long before the Institute's incorporation in 1996. He was appointed Scientific Director in 1998, and since then has been responsible for overseeing every aspect of the Institute's scientific expansion.

The figures over the period of Prof. Ward's Directorship speak for themselves: In 1998, NISAD encompassed 4 scientific employees, 1 post-graduate student, \$80,000 in research grants, and had published no scientific papers. This year, the totals have grown to 22 scientific employees and 33 supported students. Since 1998, NISAD has been involved in attracting \$9

million in research grants, and in the publication of 38 scientific papers related to schizophrenia research.

Having played a key role in establishing NISAD as a major Australian research organisation, Prof. Ward is stepping down from his Directorship to devote his attention to the several major research projects with which he is personally involved.

The appointment of NISAD Scientific Director has been accepted by another scientist with strong historical ties to the Institute. Professor Vaughan Carr is Director of Hunter Mental Health Services, and of the Centre for Mental Health Studies in Newcastle. He was founding Director of the Hunter Institute of Mental Health, and is a past



Prof. Philip Ward

President of the Australasian Society for Psychiatric Research. A recipient of the ASPR Organon Research Award, and the Novartis Oration Award, he has held a number of NH&MRC and other research grants, and has over 100



Prof. Vaughan Carr

publications in schizophrenia, early psychosis and other mental health research fields. NISAD welcomes an old friend and colleague in Prof. Carr, and looks forward to further advances under his experienced stewardship.

## Street Drugs and Schizophrenia

**Several NISAD studies are investigating why schizophrenia is so often associated with heavy usage of illicit drugs**

A number of recent surveys have indicated that 40-60% of people with schizophrenia have a history of heavy use of drugs such as cannabis, cocaine, amphetamines and heroin, as well as alcohol and tobacco. These drugs exacerbate the disabilities associated with the illness, and compound the already severe difficulties of treating it successfully.

Four NISAD-supported studies are now investigating the links between schizophrenia and drug abuse, using a variety of research methods:

### Is Drug Abuse 'Self Medication'?

In May 2003, Westfield Construction, contractors and workers commenced a campaign to raise \$75,000 for NISAD to fund a 3-year PhD scholarship for a



Aurelie Boucher

young scientist to investigate drug abuse in schizophrenia. The scholarship has been awarded to Ms Aurelie Boucher, who will come from Bordeaux in France to work on the study at the Garvan Institute of Medical Research under the supervision of NISAD-affiliated scientist Dr Bryce Vissel.

Dysfunctions of NMDA and dopamine receptors in the brain have long been suspected as a cause of schizophrenia, so Aurelie's study will investigate whether these dysfunctions are normalised by the effects of drugs such as cannabis and cocaine. If so, the case for drug abuse as 'self medication' in schizophrenia will be strengthened.

### Major Federal Funding for Cannabis Study

The National Health and Medical Research Council (NHMRC) has awarded \$365,000 to NISAD researchers including Vaughan Carr, Philip Ward, Ulrich Schall, Amanda Baker, Pat Johnston and Martin Cohen for an investigation into first-episode schizophrenia and cannabis use.

Twenty-five per cent of Australian adolescents use cannabis regularly. Long-term heavy usage can impair frontal brain functioning, affecting the capacities for attention, working memory, and concentration – all dysfunctions associated with schizophrenia's 'negative' symptoms.

Conducted in Newcastle and Sydney, the study will be the first to use the sophisticated Brain Atlas neuroimaging techniques to investigate how continuous heavy cannabis use affects the structure and function of the brain in adolescents without schizophrenia compared with brain changes associated with first-episode schizophrenia patients who do or do not use cannabis frequently.

Preliminary results from a pilot study have shown similar patterns of reduced brain activation in heavy cannabis users and patients with first-

episode schizophrenia, suggesting the possibility of common processes underlying these two conditions.

NISAD's Brain Atlas Initiative and collaborative link with Prof. Paul Thompson's group at the Laboratory of Neuroimaging, UCLA, was a vital ingredient in the successful application for NHMRC funding for this project.

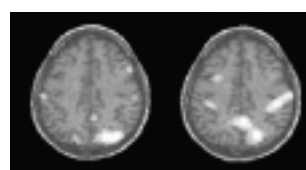
### How Does Cannabis Use Affect Medications?

Most current antipsychotic medications work by modulating dopamine in the brain, and schizophrenia-affected brains have abnormal numbers of dopamine receptors. The active substance in cannabis (tetrahydrocannabinol) works on cannabinoid receptors, and affects dopamine signalling in the prefrontal cortex. How this occurs, and what effects it has on the action of medications is being investigated by a NISAD-supported study conducted by Dr Fraser Ross and Dr Paul Tooney at the University of Newcastle.

### Memory, Cannabis and Schizophrenia

Cognitive impairments are among the most debilitating symptoms of schizophrenia, and of these verbal learning and recall show the greatest degree of impairment. Verbal learning and memory are also impaired by long term cannabis use in people who do not have schizophrenia. Does this similarity of symptoms indicate a similarity of brain dysfunction?

To investigate this, NISAD-affiliated scientist Dr Nadia Solowij and PhD



Early results from the NHMRC funded cannabis study show similar areas of reduced functionality in schizophrenia-affected brains (left) and long-term cannabis users' brains (right).

student Colleen Respondek from the University of Wollongong have commenced a study for which two groups of research subjects will be recruited, one with schizophrenia and one without. The schizophrenia group is composed of long-term heavy cannabis users, light cannabis users, and non-cannabis users. The second group is identical in its categories of cannabis use, but without schizophrenia.

fMRI brain scans will be taken of all subjects as they perform identical memory and recall tasks. These images will then be compared to discern significant differences in brain activity between groups, thereby clarifying any differences in the neurological effects on memory function of schizophrenia, cannabis use, and schizophrenia with cannabis use.

The cannabis study<sup>1</sup> is funded by the Clive and Vera Ramaciotti Foundation for Medical Research, with additional support from the Illawarra Institute for Mental Health and University of Wollongong. The schizophrenia component of the study<sup>2</sup> is supported by NISAD.

<sup>1</sup> Neurocognitive and biochemical correlates of memory impairment associated with long term heavy cannabis use.

<sup>2</sup> Functional magnetic resonance imaging of verbal learning and memory in schizophrenia patients with long term cannabis use.



Retta Andresen

recovery from schizophrenia, and the psychological processes involved.

## HOPE IS THE KEY TO REHABILITATION

The aim of study is to develop and test a model of the psychological processes of recovery. This will provide stronger empirical foundations for research, training and practice related to the emerging recovery movement in mental health.

Focussing on reports made by people with schizophrenia, the first stage of the study\* identified four key

factors in psychological recovery: (i) finding hope; (ii) re-establishment of identity; (iii) finding meaning in life; (iv) taking responsibility for recovery. Five stages were identified in this process: (I) moratorium; (ii) awareness; (iii) preparation; (iv) rebuilding; (v) growth.

Retta will now seek to recruit the help of 300 members of the NISAD Schizophrenia Research Register

(patients at all stages of recovery) via questionnaire to complete the model of recovery stages.

If you are a Register member and have been contacted about this project, your participation would be much appreciated.

\*The experience of recovery from schizophrenia: towards an empirically validated stage model. Australian and New Zealand Journal of Psychiatry 2003;37:586-594

## \$2 Million for the Brain Bank



Brain donor Gough Whitlam with Therese Garrick of the NSW Tissue Resource Centre.

Prof. Clive Harper, Director of the NSW Tissue Resource Centre (TRC), has received \$2.1 million from the US National Institutes of Health to further develop the brain bank which includes



Irina Dedova

NISAD's 'Gift of Hope' and the 'Using Our Brains' donor programs. Both programs seek pledged donations from people with and without illness.

"The only difference between donating your brain and your heart is that your brain will be used for research, and your heart given to someone who is extremely ill. The bottom line is that they will both save lives," said Prof. Harper.

Irina Dedova has been appointed by NISAD as TRC Coordinator responsible for the collection, storage and distribution of brain tissue, including that for the schizophrenia research program.

## Can You Help NISAD?

Public and official recognition that schizophrenia is the biggest single cause of lifelong disability starting in youth has made the illness a top priority for research. If you, or your company or organisation can help raise funds for NISAD's cause, please contact Lee Drury on 0421 068 430, or email [l.drury@nisad.org.au](mailto:l.drury@nisad.org.au)



Patron: Her Excellency, Professor Marie Bashir AO, Governor of NSW

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NISAD IS FUNDED BY NSW HEALTH



NISAD's Graham Shaw and Lee Drury (kneeling by the poster), Margrete Shaw (top row) and Elton Drury (bottom right) were overwhelmed with the generous support given by the Lidcombe CFMEU, and the students and parents of St. Ignatius College, Riverview.

## Thank You Holroyd CityFest 2004!

Many thanks to Mayor Malcolm Tullock, and the Holroyd CityFest 2004 Planning Committee for choosing NISAD as this year's official charity.

A team from the CFMEU, aided by their families, kicked the festival off with the NISAD float in the opening parade. Then came the 'Gold Coin' collection made by students of St. Ignatius' College, Riverview at the 'Jazz in the Gardens' event. The Hoyts

Charity Film Night, 'Big Night of Arab Shorts' raised more donations - bringing the total to \$2,300 during the festival, which ran from 12 to 19 March. The Lidcombe CFMEU branch added a further \$10,000 to the tally.

NISAD's Lee Drury was involved throughout. Her father Elton Drury, Graham and Margrete Shaw, and CFMEU members were most impressed by the interest shown in NISAD's cause.

## TMP/Hudson Bazaar Raises \$3,000

Each year, divisions of TMP/Hudson Global Resources choose a charity, and dedicate 4 weeks to internal fundraising. Last year NISAD was fortunate enough to be chosen by the Sales & Marketing division.

The highlight of the campaign was the "Hudson Bazaar" held in the Boardroom on 7 November. Over 100

staff enthusiastically participated in the live auction and 'Trash & Treasure' exchange. Combined with proceeds from the 'hand made' sausage roll morning teas, a grand total of \$3,000 was raised for the NISAD cause.

A big thank you to TMP/Hudson, and we hope you can do it all again for us this year!



As far as is known, NISAD's TV appeals for Schizophrenia Research Register volunteers (left) and brain donors (right) are the first of their kind in the world.



## NISAD's Unique Approach Pays Off

The idea of appealing to the general public for volunteer help for schizophrenia research was always shoved firmly into the 'too hard' basket - until NISAD's TV ads proved that it wasn't too hard at all.

Following the re-run on all Sydney channels last year of the Research Register TV appeal, memberships now number over 1,000. The more recently launched Brain Donor appeal has attracted a further 100 volunteers to join the 'Gift of Hope' program.

Designed and produced by NISAD Communications Director Alan Tunbridge, both campaigns achieved unprecedented results at minimal cost by utilising still photographs from photo libraries, discounted fees from voiceovers and video editing studios, and free Community Service Announcement (CSA) airtime. All channels were particularly generous in occasionally airing both CSAs at peak viewing times.

Many thanks to all contributors!

**To include yourself on the mailing list to receive free HeadLines, call (02) 9295 8407. Visit the NISAD website at [www.nisad.org.au](http://www.nisad.org.au)**

HeadLines is written, designed and produced by NISAD Communications Director Alan Tunbridge. The opinions expressed in HeadLines do not necessarily represent the views of all NISAD's participating scientists.

