

HEADLINES

Neuroscience Institute of Schizophrenia and Allied Disorders. SEPT 2006



Dr Cynthia Shannon Weickert with her twin brother David.

Introducing Australia's first Chair of Schizophrenia Research

“ This is a story of the Shannon twins born in September in San Angelo, Texas in the sixties. The boy and girl twin were healthy, happy and well-loved as children, until adolescence hit.

As teens, one twin embraced life and socialized and dated; the other twin embraced solitude and withdrew from friends. Both twins started college. One twin made the deans list, the other dropped out. One twin listened to rock music; the other twin heard unpleasant voices. One twin continued college; the other twin entered a mental institution with the subsequent diagnosis of schizophrenia. One twin suffered from adverse reactions to antipsychotic medication, the other twin suffered too. One twin decided something more must be done for people with this horrible disease, and she dedicated her life to this pursuit. ”

Dr. Cynthia Shannon Weickert NISAD Chair of Schizophrenia Research

After a national and international search for the best candidate, NISAD is delighted that Dr. Cynthia (Cyndi) Shannon Weickert has accepted the appointment as Australia's first Chair of Schizophrenia Research. Cyndi graduated with a BA in Biology and Psychology, earned a Ph.D in Biomedical Science, trained in the Neuropathology of Schizophrenia, and became Chief of the MiNDS Unit at the National Institute of Health in Washington DC. She will commence her position as NISAD Chair of Schizophrenia Research in December 2006 – a position created by NISAD in partnership with the University of NSW,

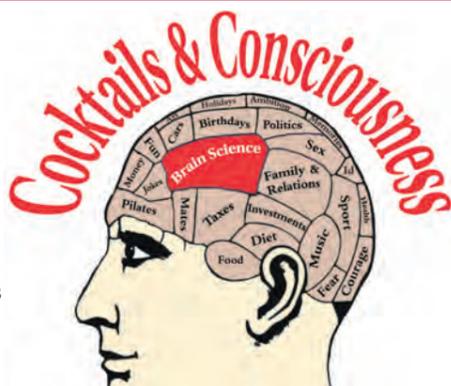
and the Prince of Wales Medical Research Institute.

Cyndi's research is focused on determining how normal brain development gets derailed by schizophrenia. She has published several landmark findings which have shifted the attention of worldwide research onto the role of growth factors and hormones in the development of the illness.

Cyndi brings not only her expertise, but also her passion to Sydney this summer, and she shares in the hope of all NISAD supporters for better treatment for all who suffer from schizophrenia, including her twin brother, David.

A Dramatic Event for NISAD Society Members

Cocktails & Consciousness will happen on 25 October. Society Members have been invited to enjoy a live performance excerpt from the new play 'One in a Hundred' about schizophrenia onset, followed by a lively discussion by a distinguished panel. Members donate \$60 per quarter. To join and receive an invitation, please call (02) 9295 8407.



PRATT FOUNDATION TAKES NISAD NATIONWIDE



BRISBANE

- University of Queensland
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ORANGE

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\$1.4 million moves Australian schizophrenia research up to a new national level

Back in 1996 when NISAD began operations, the first task was to establish the infrastructure which would enable research to take place in NSW. It took about 5 years to get a register of research participants, a brain donor program, a DNA bank and a 'virtual' brain bank up and running. Supported by these programs, the number of NISAD's published scientific papers has risen from 5 to 50 per year since 2000.

It was this exponential increase in productivity and the infrastructure foundation in NSW which helped to win NISAD an award of \$1.75 million from the National Health and Medical Research Council (NHMRC) to develop similar linked infrastructures in other States - creating an Australian Schizophrenia Research Bank (ASRB).

However, the NHMRC funding was sufficient only for the development of NSW, Queensland and WA, meaning that Victoria – the second most populous State in the country – could not be included.

While laying the foundations for the ASRB, NISAD successfully approached the Pratt Foundation (one of the largest private sources of philanthropy – established by Richard and Jean Pratt in 1978) to provide funding to include Victoria and to support

the national structure. The Pratt award of \$1.4 million will ensure that the ASRB becomes a truly national resource.

The national quest to find the genes of schizophrenia

With a fund of over \$3 million, NISAD is now starting its 5-year task of setting up the national network via affiliated mental health centres in Brisbane, Sydney, Newcastle, Orange, Melbourne and Perth. The ASRB will recruit 2,000 people with schizophrenia and 2,000 controls, and obtain brain scans, blood samples and detailed clinical information from these volunteers. The scans will be processed to provide information on brain structure; the blood samples used to produce individual genetic profiles and cell lines, and the clinical information to compile dossiers of personal and family health history. All data will then be cross referenced and linked by a specially developed software grid.

The finished database will be the biggest of its kind in the world and, once made available, be of enormous ongoing value to Australian and international scientists searching for the genetic bases of schizophrenia.

Singleton Ogilvy & Mather masterminds national ASRB campaign – pro bono

Mobilised by John Singleton AO, one of Australia's biggest marketing services groups, Singleton Ogilvy & Mather, is creating a national advertising campaign to raise awareness of the Australian Schizophrenia Research Bank, and to attract volunteers from all across the country. The campaign is scheduled to launch in March next year.

Meanwhile, NISAD has recruited the first ASRB employee, Rebecca Wilson – based at the University of Sydney.

For details about volunteering for ASRB, call toll free on 1800 639 295 or visit the NISAD web site www.nisad.org.au



Rebecca Wilson – first ASRB Clinical Assessment Officer.

NISAD Welcomes 'Cyndi'

The appointment of Australia's first University Chair of Schizophrenia Research marks the establishment of a new research centre in NSW. But even more importantly, it marks the official recognition by Government and academic authorities of the urgent need to find an answer to the illness, and of the ability of current research to do so.

The personal story of Dr Cynthia (Cyndi) Shannon Weickert, our new Chair, adds a very special dimension to her commitment to schizophrenia research. Together with our partners the University of NSW and the Prince of Wales Medical Research Institute, we look forward to Cyndi's arrival in late November as the beginning of a dynamic new force in the fight against schizophrenia.

AMP Hosts Business Leaders Lunch

Once again, AMP generously hosted our annual sponsors and supporters lunch in their Board Dining Room overlooking Circular Quay. This year the proceedings were entitled '10 Years On - Business Leaders Lunch', and NISAD's first decade was commemorated with an overview of progress by our Scientific Director Prof. Vaughan Carr, and by the well-deserved appointment of Don McDonald as a 'Life Governor' of the Institute. Many thanks to our speakers Andrew Mohl - CEO AMP, and the Hon. Cherie Burton MP - Minister for Housing and Minister Assisting the Minister for Health (Mental Health). Thanks also to Andrew Ferguson - State Secretary, Construction Forestry Mining Energy Union (NSW), and to all other sponsors and supporters who attended.

Paint a Rainbow

Thanks to the Premier Morris Iemma's strong commitment to NISAD, our work was introduced to the Paint a Rainbow Foundation. The foundation's Chairman, Pat Sergi AOM, and committee are tireless fundraisers. NISAD was awarded a grant of \$65,000 - which I gratefully accepted at the Foundation's 'Dancing With The Charities' event on 23 June. I would also like to acknowledge a few of the many celebrities who support the Foundation: Maria Venuti, Glen Wheeler, Vic Larusso and Jane Fleming. Thank you.



'Stuck' by Matthew Dysart (1964-1999).

Art of Schizophrenia

The biggest ever exhibition of art by people living with schizophrenia was launched at Campbelltown Arts Centre on 1 September. 'For Matthew and Others - Journeys with Schizophrenia' showcases the impacts of the illness on individuals,



At the 'Business Leaders Lunch' L-R: Andrew Mohl, Don McDonald, Peter Maher, Cherie Burton, Vaughan Carr.



Vaughan Carr reviews ten years of NISAD progress at the 'Business Leaders Lunch'.



NISAD's Debbie Willcox accepts a big cheque from Morris Iemma and Pat Sergi of 'Paint a Rainbow Foundation'.



Debbie celebrates the receipt of \$65,000 from members of Paint a Rainbow's 'Italian Committee'.

families and society through paintings, films, music, poetry and performance.

Much more than an art show, the exhibition will be presented at a range of Sydney venues until 22 October, before moving down to Melbourne. Full details of this groundbreaking initiative are available from the Campbelltown Arts Centre website at <http://tinyurl.com/gdmf5>

Ernst & Young

Many thanks to Graeme McKenzie, Partner, and to Ernst & Young for undertaking *pro bono* services as NISAD's accountants. Ernst & Young are world leaders in financial services and we look forward to working with them.

Ramsay Health Care

Ramsay Health Care is Australia's largest private hospital group, operating over 70 health care facilities throughout Australia for more than 40 years. NISAD is proud to announce that Ramsay Health Care has become a NISAD Partner with funding of \$50,000. Ramsay's Chief Operating Officer Christopher Rex is further cementing Ramsay's commitment by joining the NISAD Board.

Fellowship Funding

Special thanks to Mrs Margaret Sainsworth, who has funded NISAD's new Research Fellowship in Epigenetics (see back page).

Fast tracking Beta meds

NISAD's Beta Imager at Wollongong is helping to cut years off the timeline to new treatments.

While the new 'atypical' antipsychotics have proved to be more effective than old style meds, they are still far from perfect. There remains an urgent need to discover additional ways of reducing the symptoms of schizophrenia, and to move towards treatments which restore normal brain function, not just suppress symptoms.

Current antipsychotics modulate the brain's dopamine activity by blocking the relevant receptors on the surface of brain cells. This blockade causes cells to produce more receptors, thus modulating dopamine neurotransmission. Increasing research evidence suggests that another class of receptor, the muscarinic cholinergic receptor, may be treated in a similar way to upregulate the brain's acetylcholine activity.

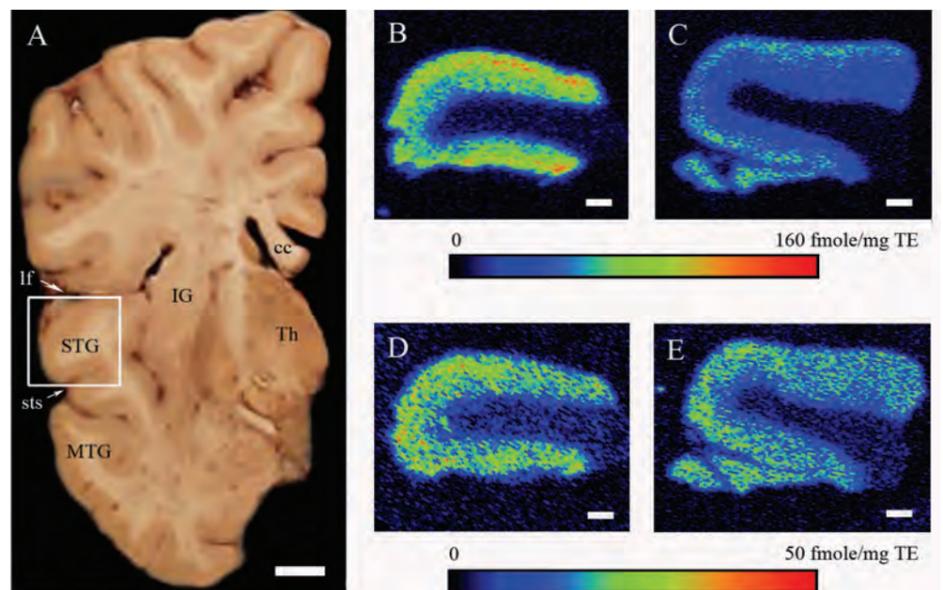
Postmortem brain tissue studies such as those now underway at the University of Wollongong have shown that numbers of specific muscarinic receptors are significantly less than normal in the brains of people with schizophrenia. Moreover,



Prof. Xu-Feng Huang and NISAD PhD Scholar Kelly Newell in the Beta-imaging lab at the University of Wollongong.

drugs have been synthesised which partially blockade these receptors, with beneficial effects.

The study featured below focussed on the superior temporal gyrus (STG) brain area because it is known to be involved in the pathology of schizophrenia - particularly in auditory hallucinations (hearing voices). The study found that there were up to 48 per cent less muscarinic receptors in the STG of schizophrenia brains than in healthy brains. Increasing evidence suggests that muscarinic-based medications could be of enormous value in the treatment of schizophrenia. In this and other vital research efforts, NISAD's Beta Imager is enabling results that used to take months to be achieved in hours.



A recent example of the research results* achieved by the Beta Imager, the above images show A: a section of post mortem brain tissue with the superior temporal gyrus (STG) area indicated by the white square. B: the density of M1/4 muscarinic receptors in the STG of a control subject (indicated by yellow/red colouring). C: M1/4 muscarinic density in the STG of a schizophrenia subject. D and E: similar differences found in M2/4 muscarinic receptors.

Beta funding for schizophrenia research

The NISAD-initiated campaign to raise \$200,000 for a Beta Imager was supported by Wollongong City Council and many Illawarra-based companies and the community. Their efforts came to fruition in 2003 with the installation of the only Beta Imager in the Southern Hemisphere at the NISAD research centre in the University of Wollongong.

The presence of the machine has had a dramatic impact on Australia's fight against schizophrenia, and placed the university in the front line of research. The number of schizophrenia researchers has tripled, and funding for the university's Neurobiology Research Centre for Metabolic and Psychiatric Disorders has risen from \$382,000 in the period 1998 - 2001 to \$2.1 million during 2002 - 2005.

"We really want to thank everyone who supported the fund-raising campaign, and let them know that they have made a major contribution in a very difficult area of research - looking at what happens in the human brain," said Prof. Xu-Feng Huang, the Centre's Director.

Prof. Huang and his NISAD team are researching various neurochemicals in

brain tissue - comparing levels found in schizophrenia affected brains with those found in brains unaffected by the illness. The aim is to develop new medications, and to overcome the side effects of current medications - which include the high incidence of obesity among patients.

"The Beta Imager makes our research so much quicker, giving results in a matter of hours where previously we would have had to wait three months," said Prof. Huang. "This enormous time saving allows us to explore and test our ideas more creatively, knowing that we will very quickly find out whether we are on the right track or not."

A NISAD-supported PhD scholar at the centre, Kelly Newell, said, "We're getting a lot of results, and people are really taking notice. Recently our group gave 10 presentations to 700 attendees at the Australian Neuroscience Conference in Sydney - our largest number of presentations at a neuroscience conference."

*Deng C, Huang XF Decreased density of muscarinic receptors in the superior temporal gyrus in schizophrenia. *Journal of Neuroscience Research* 2005; 81: 883-890.

What causes the side effects?

While the Wollongong team's research is pointing to a promising potential new source of schizophrenia medications, other NISAD researchers at the Garvan Institute and the University of Sydney have completed a series of studies into the side effects of current front line medications.

Extrapyramidal symptoms (EPS) such as involuntary movements and tremors are often a neurological side effect of antipsychotic medication. Many people who take 'typical' antipsychotics experience some form of EPS, and it has been estimated that more than 70 per cent of patients discontinue treatment because of these side effects. While new 'atypical' antipsychotics appear to carry less risk of EPS, they have been associated with obesity and diabetes.

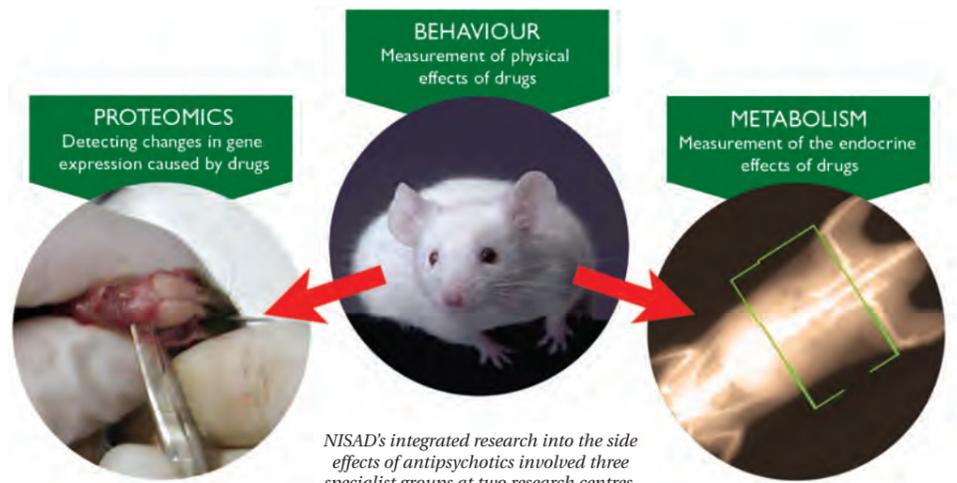
NISAD researchers at the Garvan Institute and the University of Sydney devised a three-stage collaborative project, using laboratory animals to investigate the causes of EPS and other side effects. In the first stage of the study¹ at the Garvan Institute, rats were divided into four groups. The first group received no treatment; the second received a neutral solution; the third received regular doses of a 'typical' antipsychotic, and the fourth group received regular doses of an

'atypical' antipsychotic.

Over 28 days of treatment, the team observed the behaviour of these animals and found that both groups of drug-treated rats exhibited EPS-like symptoms, diminished activity, impaired working memory, and increased anxiety. These effects were more pronounced in the 'typical-treated' animals, suggesting that these differences in the behavioural profile were likely due to the unique receptor activation of the 'typical' antipsychotic.

In the second stage of the study², the brains from the 'atypical'-treated rats and those treated with a neutral solution were analysed using proteomic methods by NISAD's team at the University of Sydney. Analysis of proteins in mental health research is considered important because proteins are the building blocks of the brain, and the types and numbers of them present in individual brains indicate the activity of the specific genes which design them.

The University of Sydney team found that 31 proteins had changed in the brain tissue of the 'atypical' rats compared to the neutral group (the 'typical' group is currently being tested), and that the types of these proteins indicated that the 'atypical' treatment had triggered cellular



metabolic dysfunction and oxidative stress, which may be the causes of EPS and other side effects.

The third stage of the study³ investigated the obesity and diabetes aspect of side effects by recruiting the expertise of the Neuroscience Research Group of the Garvan Institute. This team studied the effects of both antipsychotic-treated rat groups, and found no increase in food intake, body weight or adipose tissue. However, the 'typical' group showed increased insulin levels, and the 'atypical' group showed increased serum glucagon (glucose) levels – indicating that both antipsychotics had caused a distinct diabetes-related metabolic effect.

This type of integrated research

provides us with the best chance of finding the answers to schizophrenia. The study has provided the scientific community with an animal model of antipsychotic drugs in action, which will be valuable to future investigations of side effects and better medications.

1. Karl T, Duffy L, O'Brien E, Matsumoto I, Dedova I. Behavioural effects of chronic haloperidol and risperidone treatment in rats. *Behavioural Brain Research* 2006; 171, 286-294.
2. O'Brien E, Dedova I, Duffy L, Karl T, Matsumoto I. Effects of chronic risperidone treatment on the striatal protein in rats. *Brain Research* (in press).
3. Lin E, Lee N, Slack K, Karl T, Duffy L, O'Brien E, Matsumoto I, Dedova I, Herzog H, Sainsbury A. Distinct endocrine effects of chronic haloperidol or risperidone administration in male rats. *Neuropharmacology* (in press).

Ten Years On NISAD Research 1996 - 2006

Up to the early 1990s, there was little schizophrenia research being undertaken in NSW. The few investigators involved were poorly resourced, and had minimal access to research infrastructure. All this started to change in 1991 when Dr Stanley Catts led a group of scientists, clinicians and concerned parent-carers to propose the formation of an institute dedicated to developing world-class standards of schizophrenia research in NSW. With the backing of key groups such as the Schizophrenia Fellowship of NSW, the NSW Labor Council and the Construction Forestry Mining Energy Union, NISAD presented a strong case for State Government support, which was ultimately awarded by the NSW Labor Party upon winning office in 1995.

Critically, these early years of development also forged firm partnerships between the consumers/carers and the research community, and vital accord between neuroscientists and clinicians regarding the structure of the Institute. An innovative "institute without walls" structure was adopted to provide infrastructure and support, and to enhance networking and collaboration between existing NSW centres. The plan was to avoid the expense of a separate 'bricks and mortar' institute and to utilise the human and technical resources of existing NSW facilities.

The first years of operations were focussed on establishing the necessary infrastructure. The **NISAD Schizophrenia Research Register**: a database of patients and family members willing to participate in research; the **NSW Tissue Resource Centre**: a 'bank' of postmortem brains; the **'Gift of Hope' Brain Donor Program**: allowing people to authorize post-mortem donations; the **Hunter DNA Bank**: a database of the DNA profiles of schizophrenia patients, their families and others, and the **NISAD Virtual Brain Bank**: a library of MRI brain scans from people with schizophrenia at various stages of their illness. These NSW research facilities have since been so successful in supporting world-class research that NISAD was successful in attracting NHMRC and Pratt Foundation funding in 2006 to expand elements of them into a national facility called the Australian Schizophrenia Research Bank (ASRB - see front page) – in collaboration with researchers from Queensland, Western Australia and Victoria.

As such infrastructures came 'online', NISAD was able to initiate and/or support increasing numbers of research studies, as well as to engage in national and international collaborations. Under the successive Scientific Directorships of Professors Stan Catts, Philip Ward and Vaughan Carr, the Institute and its affiliated scientists have been awarded over \$15 million in external grant funding, supporting original research producing 140 published scientific papers and 400 presentations at national and international scientific conferences.

The 'hands on' laboratory work that produces such papers is often carried out by research higher degree students (e.g. Honours, Masters, PhD) studying to become the senior scientists of the future. To nurture such researchers, and to attract the best minds into schizophrenia research, NISAD has to date provided support to around 75 students, 35 of whom have already achieved their degrees.

What are the most significant discoveries NISAD has made in its first decade?

Despite the time and resources expended on creating essential infrastructure, NISAD and affiliated scientists have played a vital role in many recent findings of Australian schizophrenia research. A few highlights of these include:

- **Using a new fMRI brain scanning technique to demonstrate, for the first time, a correlation between areas of reduced regional cortical thickness and impaired brain function in first-episode schizophrenia;**
- **Identifying differences in the brain's auditory processing (known as mismatch negativity), which has been proposed as a biological marker of vulnerability to schizophrenia;**
- **Using a new computer-based remediation tool to demonstrate improved recognition of facial expressions of emotion in schizophrenia, with increased visual attention to important facial features, suggesting the utility of computer training tools in remediation of facial emotion recognition impairments;**
- **Discovery that blood lymphocytes can be used to identify distinct gene expression profiles within schizophrenia, which may be useful in the development of a biological basis for diagnosis and subtype classification for the disorder;**
- **Discovery of similar patterns of reduced brain activation in first episode schizophrenia patients and chronic cannabis users during performance of a planning task, suggesting the possibility of a shared pathology in these conditions;**
- **Demonstrating similar, but attenuated, restricted visual scanpaths in response to facial emotions in first degree biological relatives of schizophrenia patients, providing evidence that visual scanpath dysfunction may be a trait marker in familial transmission of schizophrenia.**

In addition to cutting-edge research results, NISAD has established Australia's first University Chair of Schizophrenia Research - in partnership with the University of New South Wales and the Prince of Wales Medical Research Institute (see front page). On the public awareness front, NISAD has designed and produced Australia's first schizophrenia early intervention poster - which was distributed nationwide with the assistance of the Mental Illness Fellowship of Australia.

There is genuine optimism within the world-wide research community that we now have the techniques and knowledge to achieve significant breakthroughs in regards to the treatment and prevention of this devastating disease. Ten years on*, all NISAD contributors and supporters can feel proud of the achievements made to date. The institute has played a major role in creating a vibrant, multidisciplinary network of over 120 Australian clinicians and neuroscientists who are actively collaborating on a range of schizophrenia research initiatives. With an increasing national collaborative research focus, together with the commencement of the NISAD Chair of Schizophrenia Research, NISAD remains committed to its vision of finding the means to prevent and cure schizophrenia.

*Draganic D, Catts S, Carr V. The Neuroscience Institute of Schizophrenia and Allied Disorders (NISAD): 10 years of Australia's first 'virtual research institute'. *Australian and New Zealand Journal of Psychiatry* (in press).
Copies of this detailed overview of NISAD's history and research findings, can be requested from NISAD.

The M.C. Ainsworth Research Fellowship in Epigenetics

A powerful new addition to NISAD's research program

Epigenetics is an emergent field of research arising from the last decade's flood of information about genes. It focuses on the chemical 'switches' which turn genes on and off, and how these switches may be affected by their molecular environment and factors such as nutrition or stressful experience.

The view of schizophrenia as a genetic predisposition triggered by environmental effects is still widely held, but has now broadened to encompass proteomics (the study of how genes produce the proteins which may alter organic functions) and epigenetics (the study of factors which may alter genetic expression and change the amount of proteins produced).

To establish a focus in this emerging field, we are extremely grateful for the generosity of Mrs Margarete Ainsworth, one of NISAD's loyal sponsors who has



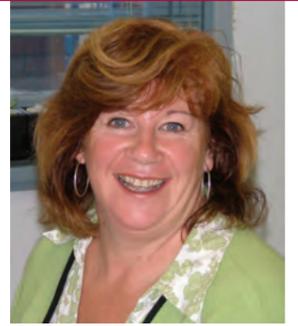
Dr Murray Cairns, awarded the M.C. Ainsworth Research Fellowship in Epigenetics.

extended her financial commitment to create NISAD's first ever targeted postdoctoral fellowship. Located at the University of Newcastle, Dr Murray Cairns will take up the M.C. Ainsworth Research Fellowship in Epigenetics, a four year commitment, which adds a vital new force to the Institute's ongoing research effort.

.....Profile of a NISAD Scientist.....

Dr Carmel Loughland

Senior Research Fellow,
Manager of Australian Schizophrenia Research Bank



I have worked for NISAD for 10 years, primarily in the development of large scale schizophrenia research infrastructure resources such as the Australian Schizophrenia Research Bank (ASRB), the NISAD Schizophrenia Research Register (NSRR) and the Hunter DNA Bank. I currently manage all three resources but also oversee a program of research at the Centre for Mental Health Studies, University of Newcastle, where I have an Eye Movement Laboratory and conduct research investigating social cognition and face processing deficits in people with schizophrenia.

What does NISAD mean to you? The strength in numbers gained by all the researchers and bright minds focused on a single purpose - to cure schizophrenia. It is both awesome and humbling to be a part of that focus.

What got you interested in researching schizophrenia? Before NISAD, I worked for a few years in womens health and ran programs providing support for women with schizophrenia who had recently become mothers. I had little experience working with people with mental illness at that time and I was struck by the enormous difficulties many of these women experienced, even with doing simple things in life like interacting meaningfully with their baby. This work kicked off my interest in schizophrenia, and face processing research, in particular.

What is the most difficult thing about your work? Currently, my most challenging role is overseeing the establishment of the Australian Schizophrenia Research Bank (ASRB) and rolling it out across six Australian sites (Sydney, Newcastle, Orange, Brisbane, Melbourne and Perth) to develop a national resource that can be accessed by Australian researchers investigating the genetic factors underlying schizophrenia. The ASRB will collect and cross-reference clinical, neuropsychological, MRI brain scan and genetic data in 2,000 people with schizophrenia and 2,000 healthy controls.

If you were not a scientist, what would you be doing? This is very difficult to answer as I am doing exactly what I love to do - working with people and conducting research in schizophrenia. However, if for some reason I could no longer be a researcher then I would probably escape the city and make a tree change. I grew up in the country and still have a passion for living on the land and growing my own food.

What do you do when not researching? My partner Ian and I have been renovating our old 1930's home for more than five years. It is a labour of love and we have managed to do much of it ourselves - mostly on weekends.

How can YOU help NISAD?

The not-for-profit sector is increasingly competitive with more than 700,000 organisations listed in Australia. In this environment NISAD must constantly explore new ways of building sustainable growth for schizophrenia research.

A recent trend is the level of decision-making being delegated to employees. The top-down approach to 'giving' is fading, and employees are being encouraged to nominate preferred charities for corporate support. This new approach presents a great opportunity for NISAD's individual supporters, and NISAD stands ready to provide any help you need to profile NISAD in your workplace, and to obtain your organisation's support for the Institute. NISAD is also looking to build meaningful partnerships with organisations, and are now able to offer corporations opportunities to build their corporate image, reward staff and entertain clients. 'Cocktails and Consciousness' and 'Spark of Genius' are two such examples.

To our current supporters, we will shortly make contact with you to share in some new opportunities.



Ramsay Health Care's Chief Operating Officer and new NISAD Board Member Christopher Rex (right) and Group Corporate Services Manager Paul Fitzmaurice (left) promote NISAD during the Sydney Harbour Bridge Run on 17 September.

Note for your diary: Spark of Genius 2007 will held at Sydney Town Hall on Friday, 18 May!

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