HEADLINES

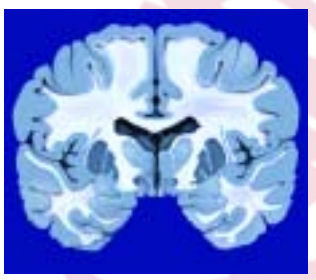
The Newsletter of the Neuroscience Institute of Schizophrenia and Allied Disorders. MARCH 2005.

Pinpointing where the damage is done

Widely reported in TV and print media, this NISAD breakthough has located some sources of impaired thinking in schizophrenia.

Studies have confirmed that the onset of schizophrenia is associated with a depletion of density in areas of the brain's grey matter (the cortex), where high-level processing is done, but how this depletion relates to the impaired thinking, paranoia, delusions and other symptoms of the illness has remained unknown.

Brain functions such as hearing, intellectual processing and vision are processed in different areas of the cortex, so the question to be answered was whether or not the symptoms of schizophrenia correspond to damaged areas of grey matter. That is, does an individual's particular symptoms of schizophrenia depend upon which areas of grey matter are most depleted?



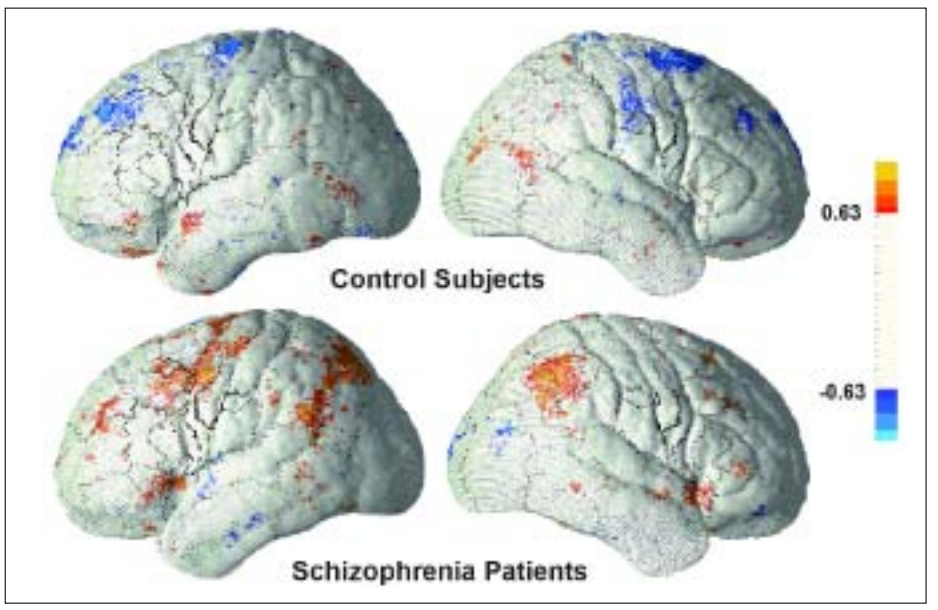
The highest density of neurons is concentrated in the 'grey matter' layer (the cortex) just under the folded surface of the brain.

The main difficulty of answering this question is that the billions of grey matter cells called the cortex are concentrated in a layer just under the surface of the brain, and the wrinkled surface of each brain is as subtly unique as the contours of each human face. This makes it difficult to be sure that a grey matter damage location observed in one brain is precisely identical to any other.

In collaboration with the Laboratory of Neuro Imaging at the University of California Los Angeles, the NISAD research team has now overcome this obstacle by adapting image processing software to warp individual brain images into a standardized anatomical format - allowing precise matching of cortex areas.

The NISAD team has applied this new imaging technology in a study* involving 10 male first-episode schizophrenia patients, and 10 age-matched male healthy control subjects.

The chief objective of the study was to show for the first time that areas of depleted grey matter density in schizophrenia-affected brains were directly involved in producing core deficits such as impaired thinking.



One set of many images from the NISAD study, the pairs of left and right hemispheres shown above are each a combined and averaged composite of fMRI data from all schizophrenia and control subjects - recorded as they performed a puzzle solving task. The orange/red markings in the schizophrenia brains show where reduced functionality corresponded with areas of depleted grey matter caused by the illness.

Functional Magnetic Resonance images (fMRI) of brain activity were taken as each of the subjects performed the same 'Tower of London' puzzle task, designed to become increasingly difficult. The resulting fMRI images of each subject were then processed to ensure that any point selected on the cortex of one brain corresponded in cortex functionality with the same point on other brains.

Further processing identified any grey matter deficits, as well as individual variations in brain activity caused by performing the puzzle task.

The images of all 10 schizophrenia subjects were then merged to create a single composite encompassing the averaged data from all subjects, and the same was done to all images from the healthy controls.

When compared, the composite images showed that schizophrenia subjects recorded less activity than controls in the brain areas affected by grey matter depletion.

The NISAD research team is now applying the analysis technique to hundreds of similar brain images from other studies.

*Rasser P, Johnston P, Lagopoulos J, Ward P, Schall U, Thienel R, Bender S, Toga A, Thompson P. Functional MRI BOLD response to Tower of London performance of first-episode schizophrenia patients using cortical pattern matching. *Neuroimage:* in press.

Thanks to the Big Hearts on Sydney's Building Sites

The Construction Forestry Mining Energy Union (CFMEU) and construction companies continued their tireless support for NISAD this summer with a spectacular display of giant banners at construction sites across Sydney.

The CFMEU's Andrew Ferguson, Brian Parker and Brian Fitzpatrick secured the banner locations, while Rebel Hanlan, Wayne Baxter, Dave Harwood and Daren Power hoisted them into position.

Construction companies and sites involved were St Hillers at Kings Cross, WestPoint at Scotts Church CBD, Bovis Lend Lease sites at Darling Park, Macarthur Shopping Complex and Penrith Plaza, Australand sites at Black Wattle Bay, Tempe, and Australia's Wonderland, Moonfair at George Street Broadway, AbiGroup at Maroubra Junction, Gammcon at Botany Rd Redfern, Multiplex at Oxford Street, Baulderstone Hornibrook sites at WestPoint Blacktown and Oxford Street, and John Holland Group at North West.

Special thanks also go to Awesome Screen Printing at Peakhurst for printing the banners.

Coinciding with the banner campaign, workers at the Bovis Lend Lease Macarthur Shopping Complex site have started a car park donation campaign similar to the highly successful Jackson's Landing project which raised over $100,000 last year.

Public response to the banner campaign has already delivered a surge of extra website hits and a number of new members to the NISAD Society.

If you would like to join, please log on to www.nisad.org.au

From NISAD's Executive Director Debbie Willcox:

A Great Start to 2005

The new year is shaping up to be a significant one for NISAD - with a big splash of TV and press media interest in our neuroimaging breakthrough (see front page), solid progress in our efforts to establish Australia's first University Chair in Schizophrenia Research, and many other signs that schizophrenia is at last getting the attention it deserves:

■ A place for the Chair

With the $500,000 contributed by NSW Health in March last year, NISAD has been in discussions with NSW universities and institutes in quest of the best home base for the new research centre which will support the Chair. The eminent scientist who will occupy the position has yet to be decided, but whoever is appointed will construct and direct a major new force in the fight against schizophrenia.

■ A brilliant bequest

NISAD was overwhelmed by the generosity of a recent donor, who bequeathed $100,000 to our research program in his Will. While this level of generosity is outstanding, it reminded us that people are often in a far better position to give through their Wills than to donate during their lifetimes. News of such intended bequests also allows NISAD to plan for the future, to more effectively mobilise research resources.

With this in mind, and in keeping with our public awareness work, we would be very happy to come and talk to community groups about the priceless benefits NISAD's work will deliver to so many people in the future.

In March and April we are meeting up with the Nepean and Auburn Probus groups to deliver this message.

So please do not hesitate to contact us if your organisation would also like to hear more about the impressive work coming out of our research team.

■ NHMRC ACCREDITATION

In recognition of NISAD's growth and increasing research outputs, the National Health and Medical Research Council has endorsed the Institute as an NHMRC Accredited Independent Research Institute.

The purpose of this Federal accreditation program is to recognise the high quality of research undertaken, and that the Institute has in place appropriate governance and operational procedures for management of public monies, and its eligibility for support from infrastructure funding.

There are only 11 such accredited institutes in NSW, and 30 nationwide.

■ A new face at NISAD

The Central Office staff are very happy to welcome Sharne Nicholls, who has joined the team as Executive Officer - an essential role in what is often a highly energised environment!

■ The Fellowship invites you

The Schizophrenia Fellowship NSW invites you to two important May events during Schizophrenia Awareness Week:

• **A Parliamentary Luncheon**, hosted by Judy Hopwood, MP. 17th May at NSW Parliament House, Macquarie Street, Sydney.

• **Symposium 2005 - 'Succeeding Together for Better Outcomes'**. 21st May, 8.30am - 5.30pm. Masonic Centre, Goulburn-Castlereagh Streets, Sydney.

For full details of both events, please call Sue Sacker or Myriam Marchand at The Fellowship on (02) 9879 2600.

The 500 x 700mm poster provides up-to-date information on the illness, emphasising the warning signs of onset which are so often mistaken by parents for adolescent behavioural changes. Delays in diagnosis and treatment in many cases account for habituation to symptoms, non-compliance with treatments, subsequent severity and duration of disability, and increased risk of suicide .

EARLY INTERVENTION POSTERS ON DISPLAY

Designed and produced by Alan Tunbridge, funded by NSW Health, and endorsed by the Schizophrenia Fellowship NSW, Australia's first medical information poster about schizophrenia is now on display in a wide variety of public venues throughout NSW.

Aimed at alerting family members to symptoms of onset, and featuring the contact number of the Area Mental Health Service where each poster is displayed, it is hoped that the campaign will increase numbers of schizophrenia onset cases receiving crucial early intervention treatment.

$2 Million for Bigger and Better Brain Banks

The National Health and Medical Research Council (NHMRC) has awarded a grant of $2 million for the development of a National Network of Brain Banks - to Prof. Clive Harper of the NSW Tissue Resource Centre, University of Sydney, and Assoc. Prof. Catriona McLean of the Mental Health Research Institute (Victoria).

The grant is applauded as further official recognition of the enormous potential of brain tissue research into mental illnesses, using emergent technologies.

Collection centres for brain tissue already exist in all States except NT, and each centre will receive funds from the NHMRC grant to enhance their facility, and to develop brain donor programs such as NISAD's 'Gift of Hope'.

An urgent need in all centres is for more trained personnel to interview donors on their medical, psychiatric and family histories so that donated tissue is 'well characterised' when collected after death. Brain tissue is an organic record of its owner's genetic predispositions and experiences, so the more information we know about the donor's life, the more valuable the tissue will become to research.

A NSW Tissue Resource Centre Research Officer prepares slices through the right and left hemisphere occipital lobes for neurobiological analysis. The 'grey matter' containing the greatest density of neurons can be seen as the darker layer beneath the folded outer surface of the brain.

Amanda North

NISAD has employed Amanda North to work as a research assistant at the NSW Tissue Resource Centre, to liaise with the Department of Forensic Medicine and the next of kin in coordinating tissue collection and categorisation details.

NISAD Chairman Peter Dempsey thanks all Golf Day participants.

GOLFERS SWING $32,000 FOR SCHIZOPHRENIA RESEARCH

Clyde Richards of Baulderstone Hornibrook, with the assistance of Tony Bleasdale, worked tirelessly to put together November's Baulderstone Hornibrook NISAD Charity Golf Day and Dinner - which scored a whopping $32,000 for schizophrenia research.

Over 30 companies entered their best four golfers in the competition, after which more guests assembled at the Camden Lakeside Country Club for the charity dinner and auction.

Peter Dempsey's team was overall winner - inspiring Deb Willcox and Lee Drury to start practicing their swings so they can give the gentlemen a run for their money at this year's Golf Day - scheduled for November.

Join the NISAD Society

If you have been following NISAD's progress for a while, and thinking about how you can help, joining the NISAD Society is the simplest way you can make a real contribution.

Members make quarterly payments of just $60 - automatically deducted from their credit card account - and receive a tax-deductible receipt mailed at the end of each financial year.

In return, you will receive an invitation to the October 'Cocktails & Consciousness' members' event, and to the annual 'Spark of Genius' Gala Dinner. Plus, of course, free copies of HeadLines - and the satisfaction of joining with other NISAD Society Members to create substantial funds for schizophrenia research.

To join a society that will make a real difference to the future world, just complete and return the form on the back of the enclosed letter.

Three new scanpath studies build from previous findings

■ Psychosis, cannabis and eye movement

Dr Carmel Loughland's work in eye movement studies in Australian schizophrenia research won her a grant from the US-based National Alliance for Research in Schizophrenia and Depression. With additional funding from NISAD, the Hunter Medical Research Institute and the University of Newcastle, Dr Loughland is now extending her research with a new investigation of scanpath abnormalities in schizophrenia patients and normal controls - but this time with the added factor of cannabis use.

The 1999 National Survey of Mental Health and Well-Being in Australia reported that among people with psychotic disorders 36 percent of males and 15 percent of females were long-term users of illicit drugs - with cannabis as the most commonly abused substance.

While it is well known that cannabis use exacerbates symptoms of schizophrenia, no studies have been done on the specific effects of such drug use upon face scanning/processing abnormalities, nor upon the poor interpersonal communication abilities associated with the illness.

Above: *Typical research results showing scanpath differences between a schizophrenia subject (left) and a healthy control (right) when viewing a face image.*

Left: *Dr Melissa Green (standing) and Dr Tamara Russell demonstrate the workings of the scanpath remedial program to a volunteer.*

Dr Loughland is now using NISAD's Schizophrenia Research Register to recruit schizophrenia patients and control subjects. Half of each group will be long-term cannabis users.

By comparing the scanpaths and facial expression recognition performance between cannabis users and non-users, Dr Loughland hopes to shed more light on the drug's cognitive effects, and on the deficits in interpersonal behaviour associated with such drug usage and schizophrenia.

■ Using scan path training to remedy emotion recognition deficits

NISAD is collaborating with the Macquarie Centre for Cognitive Science (MACCS) in a jointly funded investigation of how visual attention remediation strategies may be used as training aids for improving the social skills of schizophrenia patients.

The recent discovery of facial scanning abnormalities in schizophrenia has helped to explain why patients often misinterpret the emotional content of facial expressions, and are subsequently unable to respond appropriately in interpersonal communications.

These deficits in social perception and communication may be improved by training patients to 'normalise' their attention to the relevant features of facial expressions. That is, to deliberately attend to the features that most people would automatically attend to.

To explore this possibility, Dr Tamara Russell from the Institute of Psychiatry, London, has joined Dr Melissa Green at MACCS. The study will examine visual scan paths of schizophrenia patients before and after they receive a training package designed to remediate abnormal attention to faces.

40 subjects with a diagnosis of schizophrenia will be recruited. After an initial visual scan path assessment, each volunteer will undertake an intensive training program using both moving and still images of different facial expressions. If successful, the results from this study could form the basis for a new treatment intervention to improve many patients' emotion recognition and social communication skills.

■ What causes scanpath abnormalities?

The third study to build on NISAD's eye movement research findings will investigate the sources of eye movement abnormalities in schizophrenia subjects and their relatives, to define the effectiveness of remedial retraining. The Newcastle and MACCS teams will liaise in relation to this work.

Kathryn McCabe

To conduct this research, Kathryn McCabe has been awarded the Natasha Snow Postgraduate Scholarship for Schizophrenia Research - a 3-year stipend enabled by an *in memoriam* donation from Natasha Snow's family.

Kathryn will work with Dr Carmel Loughland at the University of Newcastle.

In Loving Memory of Natasha

Natasha Snow

NISAD was able to initiate another postgraduate scholarship at the University of Newcastle by an *in memoriam* donation from the family of Natasha Snow, who died in September 2003 at the age of 30, after a long struggle with schizophrenia.

The Snow family believe that helping to fund a young NISAD researcher is the most meaningful way to commemorate Natasha's life, and have contributed to funding the Natasha Snow Postgraduate Scholarship for Schizophrenia Research - a 3-year stipend.

The scholarship has been awarded to Kathryn McCabe, who will work with Dr Carmel Loughland at the University of Newcastle.

PPI: Testing the Brain's Security System

NISAD initiates new 'sensory gating' research at The Garvan

With $15,000 donated by the Baxter Charitable Foundation and $4,000 from the Alma Hazel Eddy Trust, new Prepulse Inhibition (PPI) research equipment has been purchased and installed in the Garvan Institute.

Although hallucinations and delusions are the most infamous symptoms of schizophrenia, the disease commonly involves more subtle impairments such as poor memory, attentional and learning problems, and disordered thought and speech. Some of these impairments may be caused by defects in the brain's ability to filter and categorise information - known as sensory 'gating'.

The 'gating' mechanism in the brain allows sequences of consecutive orderly thoughts to proceed by screening out any irrelevant other thoughts, memories and random associations which may happen to arise.

Modulations in 'gating' produce variations in the brain's excitation and inhibition processes which allow greater or lesser numbers of brain cells to communicate. Such variations govern whether the brain produces linear cognition, enhanced creative ideas, or disabling disordered thought and behaviour.

When this mechanism is disturbed by schizophrenia, it can make the 'gates' of the mind open too wide, allowing into consciousness a bewildering and chaotic mix of ideas and memories, as well as incidental impressions from the outside environment.

The startle response

One of the methods currently being used to investigate the 'gating' malfunction in schizophrenia is Prepulse Inhibition (PPI) - which measures the brain's 'startle response' to an auditory stimulus.

Earlier schizophrenia studies have shown that when research subjects equipped with earphones hear a soft sound (the prepulse) immediately followed by a loud sound, the brain suppresses its startle response to the loud sound by mobilising inhibitory processes. The degree of this suppression is taken as a measure of the brain's 'gating' mechanism, because it is the inhibitory processes which limit the spread of activation among brain cells.

Many studies have shown that schizophrenia subjects are less able to suppress the startle reflex, and that first degree relatives of patients also exhibit reduced PPI responses.

Interestingly, PPI is one of the few techniques that can be applied to animals as well as humans, therefore it is a very valuable tool for studying not only the neurobiology of schizophrenia, but its genetic origins.

Liesl Duffy

NISAD has now employed Liesl Duffy, based at the Garvan Institute, to apply the PPI technique together with a battery of other behavioural tests in transgenic animal models of schizophrenia.

NHMRC commits $700,000 to two new studies

Australia's Federal research funding body The National Health and Medical Research Council (NHMRC) has awarded grants to two NISAD supported studies.

Functional neuroimaging of prepulse inhibition in schizophrenia and Parkinson's disease

$440,625 has been awarded to investigators Ulrich Schall, Frini Karayanidis, Bill Budd, and Pat Johnston to investigate the mechanisms of sensory motor gating using the advanced brain imaging technology developed by the NISAD team at the University of Newcastle.

An integrated psychoacoustic and high-field fMRI study of auditory temporal processing dysfunction in schizophrenia

An NHMRC 'New Investigator Grant' of $302,250 has been awarded to NISAD scientist Bill Budd at the University of Newcastle to investigate auditory processing dysfunctions in schizophrenia, and whether these dysfunctions originate in the basic sensory regions of the brain stem rather than the cortex or higher function areas.

WHY I SUPPORT NISAD

AMP

Andrew Mohl

Managing Director and Chief Executive Officer, AMP Limited.
NISAD *Board member since 2002.*

Mental illness is a serious community issue, affecting a large number of the Australian population. It's also an issue which doesn't have a deep awareness or understanding from within the community. Schizophrenia, in particular, strikes so many young people at an age when all they should be thinking about is how to get through school or how to fund their backpacking overseas. I believe that funding research into schizophrenia is one way we can ensure that better treatments are developed and hopefully maybe even find a way of preventing it.

My involvement with NISAD is on a personal level. This is my commitment to helping the community - to do something about an issue I feel strongly about and where I think I can make a difference.

AMP encourages its employees and financial planners to help others, and this is facilitated through a number of community programs and partnerships. It's important for companies to make a contribution to our community, to help people who are vulnerable and who need our support.

Whether it's a direct financial contribution, volunteering or fundraising by their employees, or even allowing the use of premises and facilities - all companies have something to offer not-for-profit groups.

Neuroscience Institute of Schizophrenia and Allied Disorders

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

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- *National Alliance for Research on Schizophrenia and Depression (USA)*
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NISAD IS SUPPORTED BY NSW HEALTH

Three New NISAD Scientists

Dr Sinthuja Sivagnanasundaram has been appointed a NISAD Senior Research Officer, based at the University of Sydney, to investigate the protein expression profiles in post mortem schizophrenia brain tissue using advanced proteomics techniques.

Dr Murray Cairns has been appointed NISAD Senior Research Officer, based at the University of Newcastle to investigate the genetics of schizophrenia using microarray analysis.

Dr Yean Yeow Tan has been appointed NISAD Research Officer based at the University of Wollongong. Dr Tan's research will use the NISAD Beta-Imager to investigate the role of neurotransmitters in schizophrenia.

PLUS SEVEN SUMMER STUDENT SCHOLARSHIPS

The following students were awarded NISAD Summer Student Scholarships in 2004 - 2005. These scholarships provide an introduction to schizophrenia research for young scientists:

Kevin Aquino
Brain Dynamics Centre, Westmead Hospital;

Natalie Beveridge
School of Biomedical Science, University of Newcastle;

Danielle Clark
Department of Pathology, University of Sydney

Madeleine Hinwood
School of Behavioural Science, University of Newcastle;

Gabrielle McQueen and **Kathleen Khoo**
Centre for Mental Health Studies, University of Newcastle;

Kelly Skilbeck
Department of Pharmacology, The University of Sydney.

NISAD Communications Director Alan Tunbridge with Dawn Tyack and other guests at the 'VineFire' event.

Hungerford Hill's 'VINEFIRE' raises $20,000

The Hungerford Hill winery in the Hunter Valley became a novel venue on 6 November for 250 guests attending the inaugural 'VINEFIRE' charity dinner - a festival based on the old French Bordeaux tradition of using vine clippings as barbeque fuel.

Several central office staff decided to buy tickets, and to accompany NISAD's speaker Prof. Vaughan Carr, and Lee Drury, who with the help of Kylie Teasdell of Hungerford Hill organised the silent auction, contributing to the $20,000 raised on the night.

Many thanks to all who supported the event through donating or purchasing the valuable auction prizes.

Special thanks to Hungerford Hill's owner James Kirby, and to the Hungerford Hill team for their strong support of NISAD. The good news is that 'VINEFIRE' has become an annual event, with NISAD as the official charity again this year.

Can YOUR workplace help NISAD?

Have the dark days of stigma about mental illness been left behind?

With the groundbreaking work of Australian Charities Fund, more and more companies are including NISAD in their workplace giving programs. ABN AMRO led the charge, with IAG and now Deutsche Bank including NISAD in their workplace giving newsletters and regular donation programs - and thereby making a real difference to the progress of research.

No matter what the size of your company, please create an opportunity for NISAD to be included on its list of charities. Every dollar raised helps us bring the cure for schizophrenia one step closer.

Please call Lee Drury on (02) 9295 8362 for any information you need.

To include yourself on the mailing list to receive free HeadLines, call (02) 9295 8407.
Visit the NISAD website at 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.

NISAD Schizophrenia Research
SPARE A THOUGHT. FIND A CURE.