“That was the best event I’ve ever been to!” Andrew Denton

‘Spark of Genius’ raises $250,000 for research

It is difficult to imagine that a more eclectic assembly of talent has ever gathered together in Sydney.

At 7pm on Friday 24 March, 42 remarkable individuals and over 50 of Australia’s leading corporations joined together with the Governor of NSW and 600 guests at Sydney Town Hall to focus on the importance of research into schizophrenia.

With Macquarie Bank Foundation as principal partner and Adam Spencer as MC, the event was staged as a celebration of the creativity and achievements of the human mind - in aid of those whose abilities in such areas are diminished by mental illness.

St. George Bank provided an electronic bidding system for auction items donated by the 42 ‘genii’ - many of whom are represented by ICMI Speakers and Entertainers.

Major partner smart Australia donated a brand new ‘smart farfour’ car for which guests competed by buying keys. Special thanks also to InterContinental Sydney for demonstrating their world class hospitality to our Sparks of Genius.

For a comprehensive list of corporates, organisations and individuals who made it all possible, please see back page.

With such tremendous support, ‘Spark of Genius’ is now set to become a regular fixture on Sydney’s social calendar.

(A) A typical control subject’s triangular scan path of a face image compared to (B) a schizophrenia subject’s scan path.

(C) A schizophrenia subject’s scan path of an angry face before scan path training.

(D) The same subject’s improved scan path after training.

(Centre Picture) A study participant wearing the EYELINK II gaze monitoring system.

Images (C) and (D) courtesy of Paul Elman (www.emotionsrevealed.com).

Facial recognition computer software used around the world to train Customs Officers how to identify suspicious travelers has provided an exciting breakthrough in the treatment of one of the major impacts of schizophrenia.

Misinterpreting the emotions and facial expressions of others (eg. seeing anger where there is joy) is one of the most socially debilitating symptoms of schizophrenia - caused by an inability to read subtle facial signals, and associated with abnormal visual scanning of faces.

A pilot study by a NISAD-supported team at the Macquarie Centre for Cognitive Science, led by Dr Tamara Russell and Dr Melissa Green, used the Micro Expression Training Tool (METT) system to see if it could assist people with schizophrenia to become better at facial emotion recognition.

Dr Russell said the technology would provide a much-needed addition to what are currently limited treatments available to deal with the social problems associated with schizophrenia, which can make the difference between being able to work and being isolated. She explained that it has previously been demonstrated that people with schizophrenia severely restrict the amount of the face they scan leading to a misinterpretation of emotion.

“You and I scan a face in a triangle - looking at the eyes, nose and mouth and then process very quickly the information about that person’s expression”, Dr Russell said.

“People with schizophrenia generally can train people to overcome that hurdle,” she said.

continued on back page...
A FAT Chance of Becoming Manic-Depressive

First bipolar disorder risk gene found

NISAD's Dr Albert Chetcuti has collaborated on a study led by scientists at the Garvan Institute of Medical Research and the University of New South Wales, which has discovered the first risk gene specifically for bipolar disorder, also known as manic-depressive illness. The discovery has shown that people who have a particular form of this gene are twice as likely to develop the disease.

Dr Ian Blair, lead investigator of the study, says: “We are the first group in the world to take a multi-faceted approach to identify a bipolar risk gene - we used a number of families, unrelated patients, and therapeutic drug mouse models. Each of these three lines of investigation led us to a gene called FAT.”

“We know that the FAT gene codes for a protein that is involved in connecting brain cells together, what we need to do now is find out exactly how it contributes to the increased risk of bipolar disorder,” explained Dr Blair.

Bipolar disorder is a major psychiatric illness affecting around one person in every 50. Tragically, around one in six people suffering from the condition will ultimately attempt suicide. Mood-stabilising medications are typically prescribed to help control bipolar disorder. Lithium was the first mood-stabilising medication approved by the U.S. Food and Drug Administration (FDA) for treatment of mania. For decades it has been widely prescribed for treatment of bipolar disorder, yet no one knows for sure why it works.

Dr Blair’s research has raised the possibility that lithium exerts its therapeutic effect by altering FAT gene expression, as well as the expression of genes encoding FAT’s protein partners.

Lithium has a number of severe side effects that include tremor and weight gain. Kidney dysfunction may develop in a small proportion of patients when it is administered for long periods of time.

“Once we understand exactly what the FAT gene does, we will be able to develop better diagnostic tests for bipolar disorder. In the future, we hope our research will lead to new, targeted medicines specifically for bipolar disorder that don’t have the unpleasant side effects that lithium has”, said Dr Blair.

A highlight of the evening was the appointment of Angela Greensill as NISAD’s ambassador for Her Excellency Prof. Marie Bashir, Governor of NSW and NISAD Patron. Angela articulated the enormous talent and commitment that we have moved forward. Karen that we have moved forward.

Thanks again to Rotary for DNA Bank Support

The Australian Rotary Health Research Fund has provided second year funding for the NISAD-initiated Hunter DNA Bank for Schizophrenia and Allied Disorders. The existence of the DNA Bank played a vital role in obtaining the $1.75 million from the NHMRC to develop the new Australian Schizophrenia Research Bank (ASRB) - which will expand NISAD’s infrastructure elements into a nationwide resource.

Schizophrenia and Substance Use

Breaking the Cycle of Cigarette and Cannabis Smoking

People with schizophrenia have consistently been shown to have very high rates of cigarette smoking. Up to 88 percent of all patients smoke, as compared to 25 per cent of the general population. Some studies have linked this high rate to the clinical characteristics of schizophrenia, suggesting that the gene for the alpha 7-nicotinic receptor may play a role in the pathogenesis of the illness and may also be responsible for the heavy smoking among patients. However, as this high smoking rate represents a significant health and financial cost to patients, other studies are exploring ways to help them quit.

Supported by NISAD, one such study conducted at the Centre for Mental Health Studies (CMHS), University of Newcastle, recruited 248 regular smokers with a psychotic disorder into groups scheduled to participate in a 12 month intervention therapy program, and the other half in their usual care control program. The intervention program consisted of nicotine replacement therapy, plus motivational interviewing and cognitive-behaviour therapy (MI/CBT). The results showed that those patients who completed all sessions of the intervention program were 20 percent more likely to achieve abstinence or significant smoking reduction.

Quitting Street Drugs

A further study1 conducted at CMHS investigated whether an intervention program of motivational interviewing and cognitive-behaviour therapy was more effective than routine treatment in reducing cannabis, alcohol and/or amphetamine use. Similar to the smoking study, 160 substance using schizophrenia patients were divided into two groups, one of which received the 10-session MI/CBT intervention program. While some temporary benefits were noted during participation in the program, there were no differences in terms of frequency of drug use between the treated and untreated groups 12 months after the treatment. These results indicate that MI/CBT alone is ineffective in adding schizophrenia patients to the drug treatment system.


Australian Psychiatry Research Network

APRN, the national movement to establish an Australia wide program of clinical, neuroscience, and genetic research into the psychotic disorders, has launched a website explaining its proposals: www.aprn.net.au
Two Genetic Keys to Schizophrenia

1. Gene Profiling for Tailored Treatment

The symptoms of schizophrenia have long been separated into negative and positive types, and individual sufferers usually show a predominance of one type. Some patients, for example, show a diminution or loss of normal functions (negative symptoms), whereas others tend towards an excess or distortion of normal functions expressed in hallucinations and delusions (positive symptoms). Some scientists have proposed that a ‘disorganised’ or ‘cognitive’ type, indicating thought disorder, disorientation, and memory problems, be added as a third category - but this has yet to be generally accepted.

NISAD’s Nikolai Bowden and a team of Newcastle scientists designed a preliminary investigation to discover if an individual's schizophrenia type could be identified from a genetic profile obtained from a simple blood sample. 14 patients and 14 matched controls took part in the study, which identified 18 brain-related genes significantly altered by schizophrenia (Fig 1). When individual gene profiles were classified by age, distinct gene expression profiles for subgroups of schizophrenia were identified for the first time.

Such gene expression profiling from blood samples may in the future provide a template for individually ‘tailored’ treatments, and larger scale studies on the same lines may lead to a diagnostic tool to assess at-risk status in the early phases of the illness.

2. Genetic Abnormalities Found in the Amygdala

The amygdala is a part of the brain of special interest to schizophrenia researchers due to the key role it plays in emotion processing. While some studies have reported reduced tissue volumes and neural differences in the amygdala in schizophrenia, the genes involved in its dysfunction have yet to be identified.

Judith Weidenhofer and the NISAD affiliated team at the University of Newcastle examined gene expression in the amygdala of postmortem brain tissue of seven matched pairs of schizophrenia and normal control subjects.

Among other differences, genes involved in presynaptic function (Fig 2) were found to be consistently dysregulated in the schizophrenia samples.

These results are the first evidence that genes involved in presynaptic mechanisms in the amygdala are implicated in the pathophysiology of schizophrenia.

Why Proteomics is the New Buzzword in Worldwide Schizophrenia Research

The old idea that each of the human body's 30,000 genes produces a single protein which plays a role in biological construction has been discarded. Current evidence shows that thought life, when molecules are required, genes are transcribed first to the corresponding messenger ribonucleic acids (mRNAs), then translated to their protein counterpart - and that this process of transcription and translation is continually subject to modifications arising from genetic predispositions and environmental interactions. Thus it is now estimated that if the human genome contains 30,000 expressed genes, there may be the potential to express as many as one million different proteins - the building blocks of the body and brain.

The prospect of identifying what is termed an individual’s ‘proteome’ is daunting. Fortunately, the birth of ‘proteomics,’ an umbrella term encompassing the many tools available to investigate proteins expressed within cells, fluids, tissues or organisms, has made this task more manageable. These proteomic methods have the power to display and quantify the functional expression of genes, enabling the measurement of disease-associated or phenotypic changes in proteins.

Schizophrenia, with its early developmental and later degenerative/atrophic components, is a particularly complex disorder. We know that multiple, largely unidentified genetic and environmental risk factors interact to lead to disease and disease progression. However, the underlying functional changes at the cellular level remain unknown. This is where the strength of a proteomics approach lies, allowing researchers to identify, quantify and compare the levels of thousands of proteins in different brain areas.

42 protein differences detected in a schizophrenia ‘hot spot’

The brain area known as the anterior cingulate cortex (ACC) plays a fundamental role in cognition and attention, and has been a focus of neuroscience mental health research for some time. 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 a mental health ‘hot spot’ in the brain.

A NISAD-supported team at the University of Sydney has conducted the world’s first proteomic analysis of the ACC in schizophrenia, using post mortem tissue from 10 schizophrenia patients and 10 normal controls. The results have identified 42 proteins in the ACC which are differently expressed in schizophrenia, some of which exhibit a 200 percent greater abundance than normal.

The University of Sydney team were able to link all but two of the proteins to specific genes, and has classified them as affecting the synapses, neuronal signalling and other functions. Eight of the altered proteins are involved in energy metabolism within the brain.

Some of the identified proteins have previously been linked to schizophrenia in earlier studies. Others shed new light on the origins of the disease, and present new pieces to fit into the complex puzzle being completed by such research.

NISAD Scientists win NARSAD ‘Young Investigator Awards’

The US-based National Alliance for Research on Schizophrenia and Depression (NARSAD) is the largest non-government, donor-supported organization that distributes funds for brain disorder research.

The NARSAD Young Investigator Award Program offers up to US$30,000 a year for up to two years to enable promising investigators to either extend their research fellowship training or to begin careers as independent research faculty.

NISAD congratulates Dr Tim Karl and Dr Melissa Green as award winners in 2006. Based at the Garvan Institute, Tim Karl uses animal models to study the effects of genes on brain function and behaviour, and is currently applying this technique to clarify the role of the neuregulin and neuropeptide Y genes in schizophrenia.

At the Macquarie Centre for Cognitive Science Dr Melissa Green is working with Dr Tamara Russell on a training program to remedy abnormal facial emotion perception in people with schizophrenia - as detailed on the front page.


Profile of a NISAD Scientist

Sintha Sivagnanasundaram
Senior Research Officer, Discipline of Pathology, University of Sydney.

My current research focus is on applying a proteomics approach to identify molecular factors and consequently neural networks and pathways underlying schizophrenia pathogenesis. I am using the proteomics methodology to profile the brain proteins from the hippocampus, prefrontal cortex and corpus callosum to identify differences between post-mortem schizophrenia and control brains. These are areas of the brain that have shown structural and functional abnormalities in individuals with schizophrenia.

What does NISAD mean to you? NISAD is a collective group of highly enthusiastic people with a wide range of expertise and skills striving to unravel the complexities of schizophrenia in a collaborative manner. Hopefully within a few years NISAD will be marked as one of the important contributors to the advancement of schizophrenia research in the world.

What got you interested in researching schizophrenia? I was given a choice of two projects for my PhD, then I heard 'Genetics of schizophrenia' little did I know what I was getting myself into! The complexity of the disorder and the challenges it poses for a researcher has kept me hooked since then.

If you were not a scientist, what would you be doing? I would be exercising the creative and artistic side of my brain. It would be in the field of architecture or design, perhaps an interior designer.

What do you do when not researching? I have taken up rock climbing, which relieves the stress of research. Also I spend time socialising with family and friends and exploring Australia.

VINEFIRE to be lit for the first time

Thanks to James Kirby, Hungerford Hill's annual 'VineFire' event is to be dedicated to NISAD for the third year in succession. So don't miss this chance to take a break in the Hunter Valley and attend the unique black tie barbeque on 9 September '06 held among the giant vats of the HH winery. Contact the winery on (02) 4986 7666 for booking details.

YOUNG SCIENTIST SCHOLARSHIP(S)

Last year's End of Financial Year Appeal to HeadLines readers aimed at raising $30,000 to fund the first year of a 3-year schizophrenia research PhD scholarship. The response was the best ever recorded: $34,357!

After advertising and interviewing, we found we could only raise the $30,000 necessary to fund TWO scholarships, because both successful applicants were able to contribute partial funding from other university and government sources. So, thank you, HeadLines readers, for helping to start TWO new careers in mental health research!