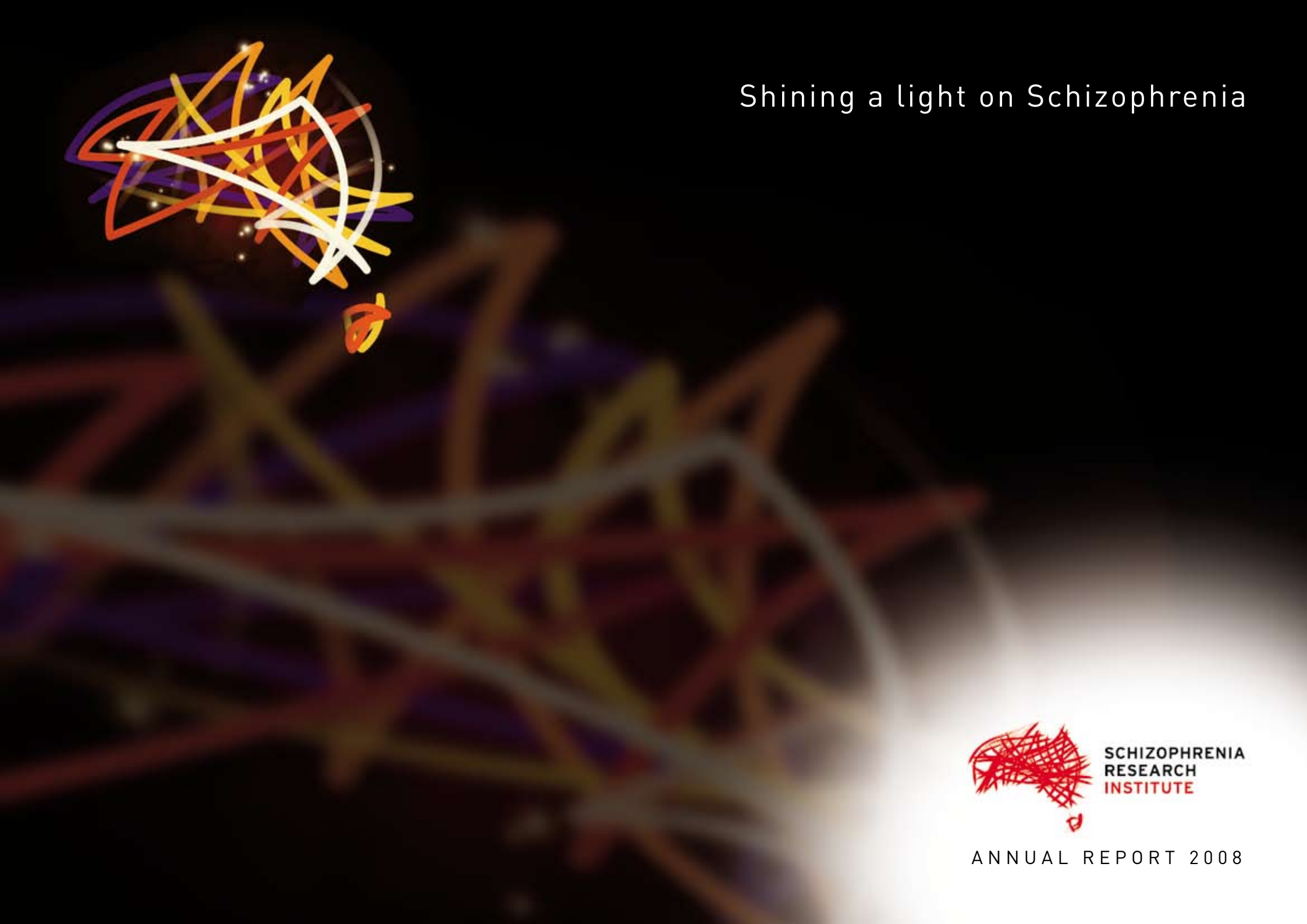


Shining a light on Schizophrenia

SCHIZOPHRENIA
RESEARCH
INSTITUTE

ANNUAL REPORT 2008

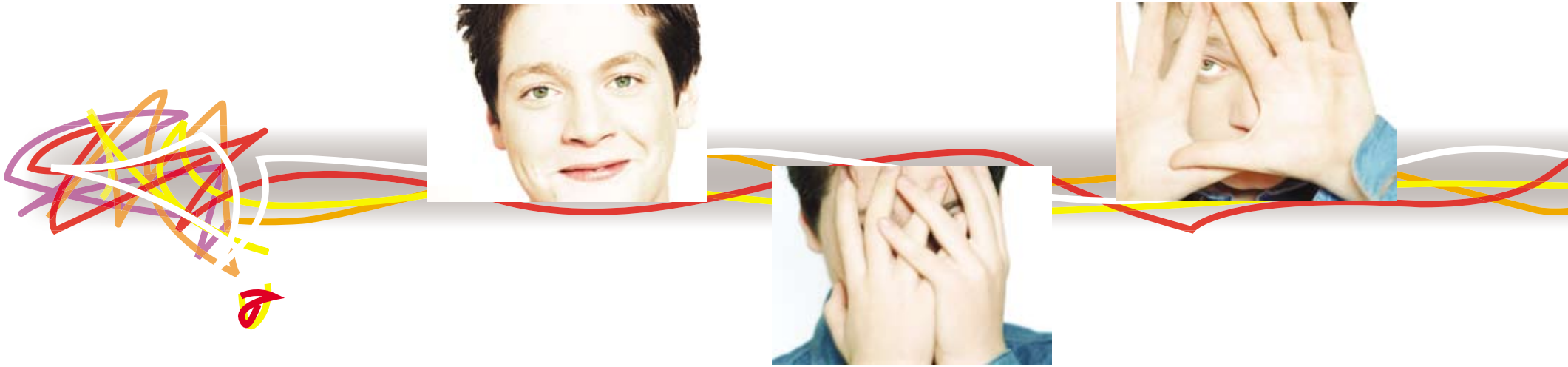
The Schizophrenia Research Institute is the only Australian Institute solely dedicated to finding the answer to schizophrenia.

Schizophrenia is the third leading cause of disability in young people.

Onset usually occurs in adolescence. 30% attempt suicide, 5% succeed.

One in every hundred people will develop schizophrenia.

Schizophrenia often leads to unemployment, drug abuse, family trauma, homelessness, and imprisonment.



Schizophrenia Research Institute • Annual Report • 2007 – 2008
The Institute is supported by NSW Health and is a National Health and Medical Research Council Accredited Independent Research Institute.

Schizophrenia can arise in any family.

Contents

Building on solid ground

Peter Maher
Chairman

With the official launch of the Australian Schizophrenia Research Bank and the Macquarie Group Foundation Chair of Schizophrenia Research, the past year has seen some expansive changes to the Institute's program.

The 2007–2008 year has built on the solid ground prepared, and has scored some palpable hits, with the first full year of operation for the Australian Schizophrenia Research Bank resulting in over 1,000 Australians consenting to join this world first program. Similarly, the Schizophrenia Research Laboratory*, headed by Professor Cyndi Shannon Weickert, has made remarkable progress in the short time since the former NSW Premier Morris Iemma officially launched the laboratory in October. I would like to acknowledge Julie White and the Macquarie Group Foundation for their wonderful support for this initiative.

These and other advances have been accompanied by substantial increases in research funding received and distributed by the Institute, including $2.45 million from NSW Health to establish a new Chair of Schizophrenia Epidemiology and Population Health and a Schizophrenia Evidence Library in partnership with the University of NSW. We are indebted for the ongoing support the Institute has received from NSW Health, in particular from Prof. Richard Matthews and David McGrath.

From its standing start twelve years ago, the Institute is now running with world-class scientists, and attracting ongoing support from charitable foundations, corporate and individual supporters. However, the World Health Organisation estimates that 40 per cent of the 200 million disabled people in the world suffer from mental disorders, and that schizophrenia is 'Youth's Greatest Disabler'. It therefore seems clear that research into this illness still does not receive the funding levels justified by the numbers of young people and their families it affects.

The key to redressing this support deficit is in attracting more public attention to the prevalence and severity of the illness, and to the potentially world-changing effects of accelerated research into its treatment and prevention. With this in mind, I thank Singleton Ogilvy & Mather for launching the Australian Schizophrenia Research Bank so effectively last year, and for their continued support in devising the refreshed 'branding' on which the Institute's new website and this Report have been based. Of equivalent support value was the Investment and Financial Services Association's adoption of the Institute as a Community Partner, and the subsequent large donation made by members at their annual Gala Dinner in August.

Aiding this drive for wider awareness and increased funding, supporters and their guests attended our annual 'Cocktails & Consciousness' event in September to be both informed and entertained by MC Lex Marinos, and presentations by key scientists.

I also wish to welcome our new Fundraising and Partnerships Director Helen Connealy who joined the Institute in February. Helen has hit the ground running, developing a plan to enhance, diversify and build on the Institute's funding base.

On behalf of the Institute, I thank valued Directors Andrew Mohl, Irene Moss and Michael Reid who stepped down from the Board during the year. I also would like to acknowledge Jack and Judy Gibson's long-standing contribution to the Institute, which is featured in this Report.

The year has seen significant expansions of our unique 'Institute without walls' network, and increasing scope and momentum in all activities. The virtual model of the Schizophrenia Research Institute brings together the best minds in schizophrenia research to work together in a cohesive and cost effective approach. New knowledge about schizophrenia, new possibilities for its treatment and prevention, and stronger hopes for the future are now emerging from the efforts of our research team.

*The Macquarie Group Foundation Chair of Schizophrenia Research based at the Schizophrenia Research Laboratory is a joint initiative of the Schizophrenia Research Institute, University of NSW, Prince of Wales Medical Research Institute, and the Macquarie Group Foundation. It is supported by NSW Health.

A finer focus

Professor Vaughan Carr

Chief Executive Officer

Since the Institute began operations in 1996, the field of schizophrenia research has been steadily evolving as new information has accumulated on all major fronts, including molecular genetics, molecular and cellular neuroscience, cognitive neuroscience, therapeutics and epidemiology.

Major technological advances have been critical in enabling this impressive growth of information to occur. More difficult than simply piling up new knowledge, however, is the task of putting it all together in a coherent pattern, a cogent conceptual framework that can point the way ahead and guide new research in the direction of achieving the goals of the Schizophrenia Research Institute, namely to find the ways to prevent or cure schizophrenia.

Much of the new knowledge acquired in the past decade or so suggests that a useful conceptual framework is one that regards schizophrenia as a particular disorder or sequence of disorders in the development of the nervous system. That is, we are thinking about schizophrenia as the result of abnormal brain development affecting the placement of and connections between neuronal cells. Within this framework we are trying to achieve convergence among molecular, cellular, cognitive, clinical and epidemiological scientists on pivotal research questions with the aim of building a translational research momentum that has the ultimate goals of finding better treatments and means for prevention.

An example of this translational research is Professor Cyndi Shannon Weickert's discovery that a particular oestrogen receptor involved in brain development is dysfunctional in people with schizophrenia. The finding was published in early 2008 and has led to a clinical trial of a new adjunctive treatment, a drug that is already in existence (but not systematically tried in schizophrenia) and modulates the functioning of that particular oestrogen receptor.

The Institute's research panels are also fostering collaborative initiatives to converge around key aspects of neurodevelopment relevant to schizophrenia. The Developmental Neurobiology Panel has commenced a multi-site program of systematically investigating several aspects of the schizophrenia susceptibility gene neuregulin-1. The Cognition and Connectivity Panel's clinical and cognitive scientists are investigating ways to detect more accurately those ultra-high risk young people who subsequently go on to develop schizophrenia; this panel, with the aid of epidemiological expertise and in collaboration with educational authorities, is also exploring ways of identifying risk factors for schizophrenia and other mental disorders, as well as protective or resilience factors, among primary school children and tracking outcomes over time by means of record linkage.

Much of the foregoing and a range of other research projects are underpinned by the Institute's infrastructure facilities, which include the Australian Schizophrenia Research Bank, the Schizophrenia Research Register, the NSW Tissue Resource Centre and 'Gift of Hope' brain donor program. Each has had a record-breaking year in terms of recruitment and supplying both participants and post-mortem brain tissue for the research projects of the Institute and other organisations. Brief overviews of these research activities are provided elsewhere in this Annual Report.

With the past year's development of the Australian Schizophrenia Research Bank and the Macquarie Group Foundation Chair of Schizophrenia Research, permanent positions supported by the Institute have risen from 45 to 60. There are also 39 students supported by the Institute working towards PhD, Masters or Honours degrees. These students are the future of schizophrenia research and the Institute regards their support as a very important investment.

Total research volunteers recruited by the Australian Schizophrenia Research Bank, Schizophrenia Research Register, and 'Gift of Hope' brain donor program have risen from 1750 to 3250.

During the year an independent review of our scientific program since 2001 was conducted, and its report submitted to the Board strongly endorsed the direction being taken by the Institute. I welcome this as further evidence that our 'institute without walls' is thriving and delivering good quality research output.

Recruitment to the Institute's new Chair in Schizophrenia Epidemiology and Population Health and the associated proposed Evidence Library, a further partnership with the University of New South Wales, has been proceeding over several months. We are aiming to make appointments and initiate these programs in the upcoming year.

I warmly congratulate all our scientists and research students for their achievements this year, and I extend my thanks to all of the Institute's supporters without whom our scientific work could not be conducted.

Our gratitude to Jack and Judy Gibson

Jack Gibson was a hero to many. To schizophrenia research, he and his wife Judy were much more.

Institute representatives were among the 800 mourners at Jack Gibson's funeral held in Cronulla on 14 May. His passing marked the end of a 20 year commitment to the Institute – from the days when it was little more than an idea in the minds of a few scientists and parents, to this year when its national and international status is well established.

Jack left behind a legacy of kindness and generosity and was, together with his wife Judy, fundamental to the inception and development of the Neuroscience Institute of Schizophrenia and Allied Disorders (NISAD), which has become today's Schizophrenia Research Institute.

Like many of the early supporters, Jack and Judy had a personal stake in helping to generate more schizophrenia research in Australia. Their eldest son Luke developed the illness and passed away in 1988. Through the tragic death of their son and his struggle with this disease, this couple made it their responsibility to create awareness of the need to get help.

Jack and Judy worked tirelessly, organising fundraising gala dinners and events, attracting influential people to the cause, and donating proceeds from Jack's four books. Together, they have raised a total of $1.5 million in support for schizophrenia research in Australia, and it is impossible to imagine the development of the Institute without their support.

In 2008, Jack and Judy Gibson's contribution to schizophrenia research in Australia was acknowledged when they received Research Australia's Macquarie Group Foundation Great Australian Philanthropy Award. This prestigious annual award recognises philanthropy over a period of time by an individual or family to health and medical research. Previous recipients have included Frank Lowy, Lady Mary Fairfax and Dame Elisabeth Murdoch.

The Schizophrenia Research Institute also established the Jack and Judy Gibson Postdoctoral Fellowship for Schizophrenia Research in their honour. Judy Gibson continues as an invaluable advocate of the Institute's mission, as our second Life Governor.

Thanks to the research volunteers who make research possible

The Institute has established a range of programs that allow people with schizophrenia and others to enrol as volunteer research participants and brain donors. The Schizophrenia Research Register and the 'Gift of Hope' Brain Donor Program were commenced in 1998, and have steadily expanded in membership year by year. The Institute also supports the NSW Tissue Resource Centre, the major Australian source of post-mortem brain tissue.

In the 2007-2008 year the Register attracted 333 new enrolments, and provided subjects for 32 studies. The 'Gift of Hope' enrolled 57 new donors, and the NSW Tissue Resource Centre collected 57 new brain cases while providing tissue for 6 schizophrenia-focused studies.

In 2007 these infrastructure resources were joined by the Australian Schizophrenia Research Bank, the biggest Australian schizophrenia research project ever undertaken.

The Australian Schizophrenia Research Bank

With major funding from the National Health and Medical Research Council, the Pratt Foundation, Ramsay Health Care, and Perpetual Trustees, the Australian Schizophrenia Research Bank is coordinated from the Institute's centre in Newcastle. This national collaboration, led by the Schizophrenia Research Institute, involves many of the leading Australian schizophrenia research groups. Participating centres now include:

Brisbane:	University of Queensland, Queensland Centre for Mental Health Research
Sydney:	Prince of Wales Medical Research Institute
Newcastle:	University of Newcastle, Centre for Brain and Mental Health Research, Hunter Area Pathology Service
Melbourne:	University of Melbourne, Melbourne Neuropsychiatry Centre.
Perth:	University of Western Australia, Centre for Clinical Research in Neuropsychiatry
Orange:	Centre for Rural and Remote Mental Health

The task of this initiative is to recruit 2,000 schizophrenia patients and 2,000 controls in five years, and to obtain brain scans, blood samples (to obtain DNA profiles) and clinical information which will be compiled and cross-referenced into a unique database, of enormous value to Australian and international researchers.

With the donated help of Singleton Ogilvy & Mather, Ogilvy PR Health, Plush Films, Black Dog Photography, McKesson Asia Pacific, and Russell Crowe's voiceover for the TV appeal, the national recruitment campaign was launched in May 2007. So far, 2,400 volunteers have expressed interest, over 1,000 have enrolled, and 350 have commenced/completed the assessment process in their local centres. The first studies to analyse and report results using this facility will be conducted in the coming year.

The genetic underpinnings of schizophrenia

Solving the complexities involved in genetic susceptibility to schizophrenia is critical for understanding the interplay of causal factors involved. The Institute's research teams at several centres have been investigating how gene expression in a number of brain areas may be altered in schizophrenia.

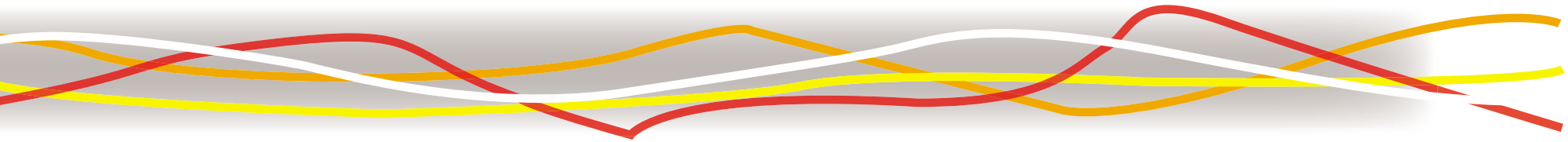
Tracking the basis of abnormal gene expression

The Institute's research team at the University of Newcastle has investigated how gene expression is altered in schizophrenia. Using post-mortem brain tissue from the superior temporal gyrus (STG) and microarray analysis, the team found altered expression in several genes involved in brain development and neurotransmission. Interestingly, some of the changes in gene expression seen in this area of the brain were similar to those previously identified in peripheral blood lymphocytes. The Newcastle team is currently exploring whether these changes in gene expression are localised to the STG or are more widespread across other brain regions implicated in schizophrenia such as the prefrontal cortex.

Recent advances in understanding gene regulation have included the role of small micro-RNA molecules in the silencing, or turning off, of gene expression. In further research, the Newcastle group revealed that a specific micro-RNA molecule (miRNA 181b) was up-regulated in the STG, and that schizophrenia-related genes in the same brain area were reduced in expression. Since the STG includes the primary auditory cortex, and may be involved in the common schizophrenia symptom of 'hearing voices', this finding is highly promising, as it provides a potential mechanism that could simultaneously alter many of the genes implicated in schizophrenia.

The effect of anti-psychotic medication on gene expression

Antipsychotic drugs are the most effective treatment for the symptoms of schizophrenia, yet their mechanism of action remains largely unknown. A study conducted by Schizophrenia Research Institute researchers at the Prince of Wales Medical Research Institute involved the examination of antipsychotic drug effects on gene expression profiles following 7 day treatment of laboratory animals with conventional (haloperidol) or atypical (clozapine or olanzapine) antipsychotic drugs. Microarray analysis was used to determine the gene profile following drug treatment and further analysis of 19 specific genes revealed that three genes were significantly upregulated and ten genes significantly downregulated by antipsychotic drug treatment. Four of the verified dysregulated genes encode proteins that are involved in voltage-gated ion channels, which are crucial for neurotransmission. This regulation is occurring predominantly in dopamine neurons, which have long been thought to be dysfunctional in the brains of patients with schizophrenia. These results may implicate a novel role for ion channels in antipsychotic drug effects and suggest future targets for therapy.



How animals are helping research into mental illness

Because the genomes of rats and mice are 85 percent identical to human, many important clinical features of schizophrenia can be simulated in animal models, thereby allowing researchers to conduct valuable investigations without involving human subjects.

The mouse who taught us about Neuregulin

The process of brain development from foetus to adult in mice is very similar to that of humans. One of the most important genes involved in brain development is Neuregulin-1 (NRG1) and this gene is also one of the most promising schizophrenia susceptibility genes. The Institute team based in the Garvan Institute examined the influence of NRG1 on behaviour and susceptibility to environmental and drug effects by using mice developed to have changed NRG1 expression (Nrg1 mice), and comparing their behaviour with normal mice. The Nrg1 mice mice showed increased activity, altered anxiety and heightened sensitivity to environmental factors – all consistent with the pathophysiology of schizophrenia. The study also provided the first evidence that Nrg1 may be involved in regulating the serotonin system. Further investigations of affected neurotransmitter systems continue.

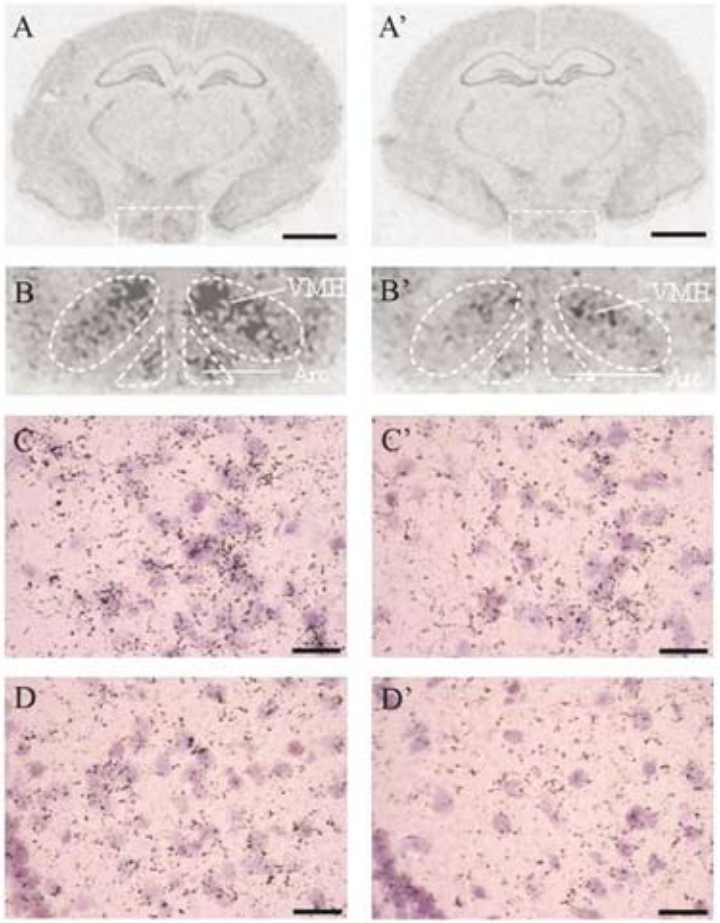
The mechanisms of a drug-induced model of schizophrenia

Treatment with phencyclidine (PCP) has been used extensively to model aspects of schizophrenia in rodents, and to explore the possibility of an NMDA glutamatergic treatment as alternative to the current dopamine-based medications. The Institute team at the University of Wollongong tested the long-term effects of perinatal PCP administration in rats, and demonstrated that an early brain insult from PCP results in behavioural deficits and brain chemical changes that last into adulthood that are relevant to schizophrenia symptoms and pathology.

In collaboration with Institute researchers at the Australian Nuclear Science and Technology Organisation, the Wollongong team also investigated brain changes in rats following repeated PCP treatment – with a view to defining its effects on NMDA receptor function. The results suggested that altered NMDA receptor function is a long-lasting effect of PCP.

Side effects of antipsychotic medications

Although antipsychotic medications remain the mainstay of managing schizophrenia, their side effects are often an obstacle to patients maintaining ongoing treatment. Further, the changes they cause to neurotransmitter systems in the brain are difficult for researchers to distinguish from those caused by the illness. Institute researchers have used rodent models of antipsychotic treatment to investigate effects on a number of neurotransmitter systems.



Muscarinic changes in schizophrenia

The Institute's team at the University of Wollongong examined changes in muscarinic M1 receptor expression in rat brains after treatment with typical and atypical antipsychotics. A similar trend for increased expression of these receptors was seen in several brain areas after treatment with different medications, suggesting that the reduced M1 receptor expression seen in schizophrenia patients was due to the illness rather than its treatment, providing further evidence of this system being a potential candidate for the development of new treatments.

Clozapine effects on serotonin system

The Wollongong team also examined the effects of clozapine and haloperidol on the serotonin system in rats, finding that clozapine had considerably greater effects than haloperidol, with decreased serotonin receptor expression in a number of brain areas. This finding suggests that alterations in serotonin neurotransmission mediate some clinical effects of the atypical antipsychotic clozapine.

Medications and obesity

Weight gain and hyperglycaemic side effects of the newer 'atypical' antipsychotics are a serious long-term health threat to patients. Using rats, the Wollongong team examined the effect of several antipsychotics on the histamine H1 receptor expression in the hypothalamus, a brain area critically involved with energy regulation. Olanzapine, but not ariprizole or haloperidol, was found to reduce H1 expression, and this reduction was related to weight gain. In a further study, olanzapine but not haloperidol was found to alter the expression of peptide YY (PYY), one of the key proteins involved in appetite regulation. This suggests that changes to PYY expression may account for some differences of treatment effect between typical and atypical antipsychotics, and that neuropeptide Y receptors may be a potential target for new treatments aimed at reducing weight gain side effects.

The link between cannabis and schizophrenia

Use of street drugs including LSD, methamphetamine and cannabis have been linked with significantly increased probability of developing psychosis. In particular, recent findings in neuroscience have lent credence to a link between cannabis and schizophrenia. An endogenous cannabinoid system has been identified, and in rat brains cannabis receptors have been shown to collocate with dopamine D1 receptors. These findings indicate a mechanism whereby cannabis use increases schizophrenia risk, and Institute researchers continue to investigate this mechanism.

Cannabis effects on the mouse brain

A collaborative team of Institute researchers at the University of Sydney and the Garvan Institute have continued their study of cannabis effects on mice developed to have changed expression of the neuregulin1 gene. When given a one-off dose of Δ9-tetrahydrocannabinol (THC), the psychotropic agent in cannabis, these mice were shown to be more sensitive to its behavioural effects compared to normal mice. Corresponding to these behavioural changes, increased neuronal activity was found in Nrg1 mice following THC administration. Interestingly this heightened neuronal activity was only seen after exposure to mildly stressful behavioural testing. As susceptibility to schizophrenia is associated with long-term cannabis usage, further research is investigating the effects of chronic cannabis exposure on the behaviour and brain chemistry of these mice.

Cannabis and psychosis risk

A group of Institute researchers located at the Universities of Newcastle and Wollongong completed a major review of 145 studies linking cannabis use to schizophrenia. The review came to three important conclusions: (1) The risk of psychosis is increased by around 40% in people who have used cannabis; (2) There is a dose-response effect, leading to an increased risk of 5–200% in the most frequent users; and (3) If using cannabis increases risk, as research suggests, 13% of psychotic outcomes in young people would not have occurred if cannabis had not been consumed.

Cannabis, psychosis and brain damage

Also at Wollongong, long-term cannabis users and non-users participated in an MRI study investigating the effects of cannabis use on brain structure and function. This study was conducted in collaboration with researchers at the University of Melbourne. Structural MRI scans demonstrated reduced hippocampus and amygdala volumes in cannabis users - brain areas rich in cannabinoid receptors and involved in many aspects of learning and emotion regulation. These reductions were proportional with cumulative cannabis exposure over 10 years. Users also showed low-level psychotic symptoms and deficits on verbal learning measures. This research is being extended into schizophrenia populations who do and do not use cannabis.

The cognitive patterns of disability

The Institute's Cognition and Connectivity Panel focuses on research investigating abnormal brain development as the basis of disordered cognition and neural connectivity in schizophrenia. Combining methodologies from cognitive neuroscience, and cognitive and clinical research, these researchers address hypotheses relating genetic and environmental factors to the development of abnormal neural network organisation and connectivity in schizophrenia.

The cognitive processes of hallucinations

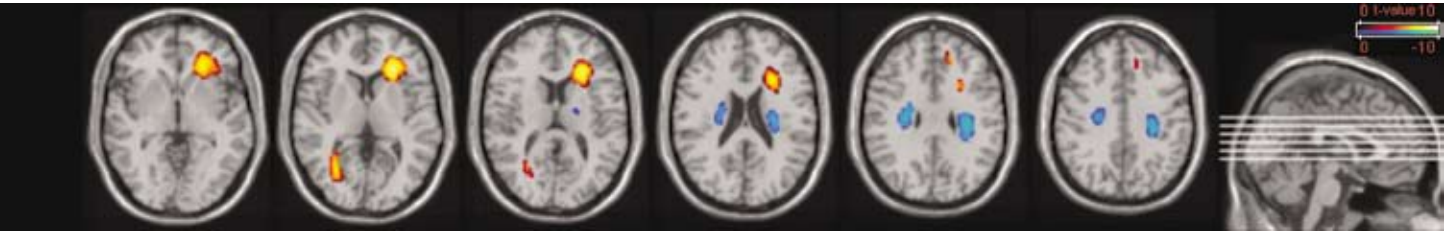
Intentional inhibition is an important cognitive process, which allows us to limit or stop unwanted thoughts or memories. At the University of Western Australia, Institute researchers have investigated the cognitive processes involved in auditory hallucinations, and found that subjects predisposed to 'hearing voices' have impairments in intentional inhibition. This suggests a mechanism whereby interventions aimed at improving thought control strategies are known to reduce the frequency and impact of hallucinations in schizophrenia. Further, heightened anxiety was found to exacerbate the inhibition deficit, leading to more prominent symptoms. Thus treatment for affective symptoms such as anxiety and depression is important in the overall treatment of schizophrenia.

White matter erosion

Abnormal brain connectivity has long been thought to underlie schizophrenia, and Institute-supported researchers at the Brain Dynamics Centre, University of Sydney, Westmead Hospital have shed more light on one of the causes. Using MRI, the team found that white matter, the key anatomical feature involved in neural connectivity, was reduced in volume in the frontal and temporal lobes of first episode schizophrenia patients. When rescanned 2-3 years later, further white matter loss was observed compared to healthy controls. This suggests that a progressive loss of white matter could underlie some of the dysfunctional neural connectivity and symptoms of schizophrenia.

Mismatch Negativity

Auditory system abnormalities have long been suspected to present in people with schizophrenia and Schizophrenia Research Institute researchers have previously shown a reduction in the amplitude of an early auditory event-related brain potential in schizophrenia, mismatch negativity (MMN), which has been proposed as a biological marker of vulnerability for the illness. The Institute's University of Newcastle team has found a different pattern of MMN reduction in those with schizophrenia for a short time, compared to those who had a longer length of illness. These results provide complementary information on the onset and progression of neuropathological changes that underlie the reduction in MMN in schizophrenia.



The Macquarie Group Foundation Chair of Schizophrenia Research

The Schizophrenia Research Laboratory*, headed by Prof. Cyndi Shannon Weickert, was officially opened in October by the former Premier of NSW, Morris Iemma. During the past year, recruitment of staff and scientists has been completed, the laboratory fully equipped and functional, and the innovative research program is now well underway.

Oestrogen discovery leads to Institute's first schizophrenia drug trial

Following the discovery that a brain receptor that normally stimulates growth in adolescence is hampered in people with schizophrenia, the Weickert team is testing whether a drug that may overcome this deficiency can be of benefit to people with schizophrenia. A large number of biological samples from people with schizophrenia and their close relatives were used by the research team, who discovered that people with schizophrenia are likely to have a different gene (ESR 1) that codes for the oestrogen receptor – thereby affecting the brain's maturation process. Recruitment of 80 male and female schizophrenia patients to trial a new drug treatment (raloxifene) has begun. This study will be supported by an NHMRC Project Grant.

Neuregulin in schizophrenia and bipolar disorder

The Neuregulin gene NRG1 and its associated ErbB4 receptor regulate key neurodevelopmental processes in the brain during puberty, and is currently considered one of the most promising schizophrenia susceptibility genetic pathways. Prof. Weickert's team examined NRG1 and ErbB4 protein levels in the prefrontal cortex of post-mortem brains from people affected by schizophrenia and bipolar disorder, and compared them to levels found in normal brain tissue. Increased protein levels for certain forms of NRG1 and ErbB4 were found in the schizophrenia tissue, relative to bipolar and controls, suggesting that the mechanisms underlying NRG1 changes in schizophrenia are distinct from those of bipolar disorder. This provides further insight into how NRG1 and ErbB4 signalling may be involved in the development of schizophrenia.

The dysbindin-1 gene and the hippocampus

The team also examined another susceptibility gene for schizophrenia, dysbindin-1, and its expression in the hippocampus, a brain area involved in many aspects of memory. Using post-mortem schizophrenia brain tissue, the study found reduced dysbindin expression in several hippocampal areas, and these changes were correlated with synaptic markers also implicated in schizophrenia. This is important as it begins to link alterations in genes with known pathological changes found in the brains of people with schizophrenia.

*The Macquarie Group Foundation Chair of Schizophrenia Research based at the Schizophrenia Research Laboratory is a joint initiative of the Schizophrenia Research Institute, University of NSW, Prince of Wales Medical Research Institute, and the Macquarie Group Foundation. It is supported by NSW Health.

Joining forces to make breakthroughs

After 12 years of development, the Schizophrenia Research Institute has assembled an impressive variety of knowledge, skills and techniques within its nationwide network of research centres. Whilst many of these groups actively collaborate, in 2006, the Institute initiated a process of facilitating large-scale collaborative Panel research programs involving scientists in different centres – with the aim of combining talents to achieve larger-impact outcomes. Three such programs commenced in 2007–2008.

Unraveling the Neuregulin gene

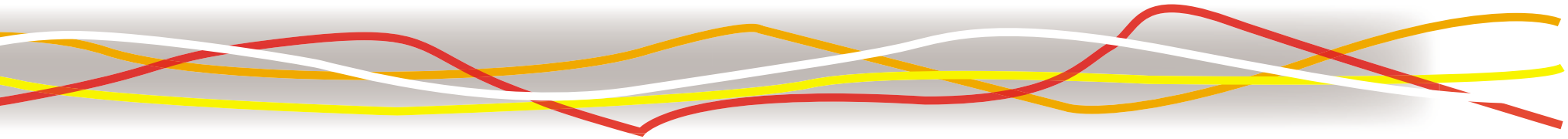
The Institute's Developmental Neurobiology Panel is investigating the Neuregulin-1 (NRG1) gene, considered to be one of the most promising schizophrenia susceptibility genes. The Panel is developing two resources for this research program: post-mortem brain tissue from a large cohort of schizophrenia patients and matched controls, and brain tissue from a variety of developmental time points from mice bred to have altered NRG1 expression. This tissue will be examined by the individual centres for a variety of features including gene, protein and neurotransmitter receptor expression. The results from these various studies will then be collected and collated, this multifaceted investigation aiming to shed new light on the complex NRG1 gene system.

Ultra-high risk of transition to psychosis

One of two long-term initiatives developed by collaborating members of the Cognition and Connectivity Panel, this multi-centre study is examining young people who have been referred to mental health services in Newcastle, Orange and Sydney, and who are identified as at ultra-high risk of developing psychosis. Statistics show that around a third of young people deemed as high-risk will develop psychosis within 12 months. Institute researchers in the three centres will conduct cognitive assessment tests, obtain DNA samples and MRI brain scans of all subjects at the time they are referred to early intervention services. They will then be followed up during the five-year project, and complete a similar assessment. The study aims to provide a clearer picture of the transition to psychosis, as well as to identify any protective factors in those who do not develop psychosis. A pilot project commenced in 2007-2008, and was subsequently awarded over $1.5 million in support from the NHMRC.

Risk factors in childhood development

Now in its early stages, the second collaborative program of the Cognition and Connectivity Panel aims to follow the development of a large cohort of children, including those with early markers for aberrant brain development. Baseline assessment of each child in attention, intellectual function, academic performance, motor control and social/emotional functioning will take place and the cohort followed throughout adolescence and early adulthood when a range of health and related outcomes can be measured. A pilot project commenced in 2007-2008, supported by Janssen-Cilag.



Preparing the way for national interventions

In 2007, the Institute in partnership with the University of New South Wales, was awarded funding from NSW Health to establish a Chair in Schizophrenia Epidemiology and Population Health, and an Evidence Library focused on schizophrenia. These initiatives will seek to provide a more immediate benefit by making key contributions to policy development and clinical practice standards.

Chair in Schizophrenia Epidemiology and Population Health

There is a paucity of Australian schizophrenia research targeting large populations, such as epidemiological surveys, record linkage studies, longitudinal large cohort studies, and meta-studies 'mining' existing databases. This paucity diminishes the capacity to identify causal factors such as genetic predisposition, cannabis use, immigration and urbanicity, as well as reducing the ability to track variations in incidence and prevalence - all of which could have important national health implications.

The aim of the new Chair in Schizophrenia Epidemiology and Population Health will be to conduct research in schizophrenia epidemiology and population health using new and existing local, national and international databases and/or relevant biomedical technologies. The position will complement Prof. Cyndi Shannon Weickert's focus on developmental neurobiology and provide the necessary population research infrastructure and applied technical expertise for the interventions described above. In 2007–2008, an international search was commenced to recruit an experienced researcher for this Chair with the aim of commencing the position in the upcoming year.

Schizophrenia Evidence Library

In parallel with the Chair of Schizophrenia Epidemiology and Population Health, the Institute is developing a Schizophrenia Evidence Library. The Evidence Library will gather, collate, store and continually update relevant schizophrenia and psychosis-related research findings, and make them available via a searchable database. This will include compiling existing reviews and conducting original reviews and meta-analyses, preparing and disseminating summaries of major findings, and forming collaborative links within the population health and epidemiology research community.

This library will serve as a resource to scientists, clinicians, government, consumer and carer groups, and the general public, and will help to inform policy and clinical guideline development. It may also be used by scientists to identify pertinent research questions and knowledge gaps. In 2007–2008, a recruitment drive was begun to locate a Research Officer to manage the development of the Library, and discussions were held with a number of design companies regarding the structure of the database and website, which is planned for launch in the upcoming year.

Shining a light on Schizophrenia

"What this disease does to people shouldn't be accepted within society. The way it systematically destroys someone's life to the point where there is such a high suicide rate amongst people that suffer from it – it's one of the major human rights issues in a developed country like Australia."

Angela Greensill, schizophrenia patient

Believing in a better future, a world where mental illness is understood, with improved treatments, and possible cures - this is what links all of our supporters with everyone at the Schizophrenia Research Institute.

We are lucky to have such passionate and loyal supporters who appreciate the urgency and importance of our mission. Gifts come from individuals, foundations and trusts, corporates, government and the community.

This financial year has seen a 7.6% percentage increase in donations. This is largely due to our new partnership with IFSA (Investment and Financial Services Association) and a gradual increase in direct mail.

Regular Givers

We are grateful for all donations. However regular giving (a monthly donation by credit card) is the most efficient way for us to plan how to use your kind donations in the best manner. Regular gifts allow us to:

- Predict our future income
- Commit to more research programs
- Be more efficient (it costs less to collect and process than multiple once-off gifts)

We promise to use your money wisely – we can email the newsletter, not post it, process your gifts in the most cost-effective manner and importantly strategically plan more medical research into schizophrenia.

Marketing

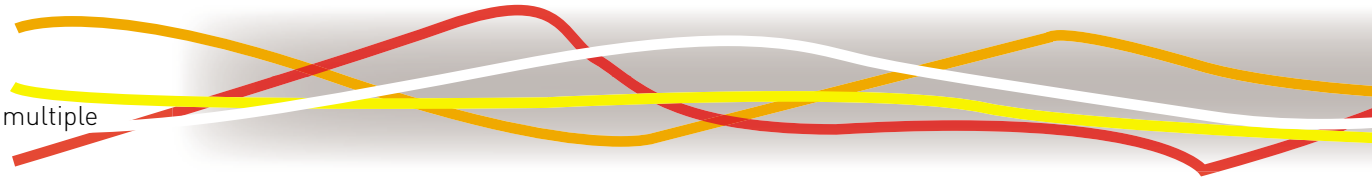
Our thanks to Singleton Ogilvy & Mather for the creative branding, TCO Pty Ltd for the new DVD and Photolibrary.com for our new images.

Our Thanks

Thank you to all our supporters – your help ensures:

- Collaborative medical research – working together not in competition to make a difference
- Bringing the patients and researchers together – for a disease that takes so much away, the Australian Schizophrenia Research Bank gives people with schizophrenia the opportunity to be involved and make a difference

We really appreciate your loyalty and will continue to express our thanks at our annual Cocktails & Consciousness event. Thank you to those who have attended and we hope to see many more of you in the future.

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Carr V, Draganic D. The Macquarie Group Foundation Chair of Schizophrenia Research. The Macquarie Group Foundation, 2007-2012 ($1,375,000).

Carr V, Loughland C, Schall U, Scott R, Jablensky A, Mowry B, Michie P, Catts S, Henskens F, Pantelis C. Siemens diffusion tensor imaging acquisition software for Magnetom Avanto. NHMRC Equipment Grant, 2007 ($7,640).

Draganic D, Carr V. Schizophrenia Research Institute and ANSTO Postdoctoral Fellowship in Schizophrenia Research. Australian Nuclear Science and Technology Organisation, 2007-2010 ($121,400).

Draganic D, Carr V. Well-being in schizophrenia: the role of emotion in auditory hallucinations. A collaborative SRI/CCRN study. Ron and Peggy Bell Foundation, 2007-2008 ($10,000).

Duffy L, Draganic D, Carr V. The Australian Schizophrenia Research Bank: Freezer. State Trustees, 2008 ($9,000).

Karl T, Arnold J, Huang XF, McGregor I. The role of cannabis in an Nrg1 animal model of genetic vulnerability to schizophrenia. NHMRC Project Grant, 2008-2010 ($437,125).

Karl T. The role of major components of cannabis (9-tetrahydrocannabinol and cannabidiol) in an Nrg1 animal model of genetic vulnerability to schizophrenia. Ramaciotti Establishment Grant, 2008 ($28,285).

Loughland C. Visuo-cognition and emotion processing in schizophrenia. Schizophrenia International Research Society Conference Travel Grant, 2008 ($1,000).

The following grants were awarded to Institute researchers and administered by their host institutions. Institute infrastructure support played a key role in the award of this funding:

Cairns M, Tooney P. A road map of schizophrenia associated gene and miRNA expression in the dorsolateral prefrontal cortex. Hunter Medical Research Institute Project Grant, 2008 ($25,000).

Carr V, Schall U, Lewin T, Conrad A. A layered ten-year audit of clients presenting to a community-based serice for young people at high risk of psychosis. Australian Rotary Health Research Fund Evaluation Grant, 2008 ($50,800).

Dedova I. ISBRA/RSA Joint 2008 Congress. National Institute on Alcohol Abuse and Alcoholism Travel Grant, 2008 ($2,800).

du Bois T. Perinatal NMDA receptor blockade alters D2, NMDA and M1/M4 receptors in later life: implications for pathological processes of schizophrnia. Schizophrenia International Research Society Conference/Travel award, 2008 ($1,000).

Green M. University of New South Wales Vice-Chancellors Post-doctoral Fellowship, 2008-2010 ($215,705).

Green M. Remediation of facial affect processing deficits in schizophrenia. Schizophrenia International Research Society Travel Award, 2008 ($1,000).

Loo C, Mitchell P, Weickert T, Taylor J, Sachdev P. Machine for Transcranial Magnetic Stimulation (TMS). UNSW Major Research Equipment and Infrastructure Initiative, 2007 ($94,110).

Michie P, Budd B, Karayanidis F, Todd J, Smith D, McKenzie, Hunter M. Brain Electrical Source Analysis Software (BESA). NHMRC Equipment Grant, 2008 ($11,000).

Miller D, Karl T. Does genetic predisposition to schizophrenia (i.e. neuregulin 1 mutation) alter the susceptibility to drugs of abuse in an animal model for this mental disorder? NSW Institute for Psychiatry Fellowship, 2008 ($63,350).

Newell K, Huang XF. Neuregulin 1 and ErbB4 mRNA and protein expression in schizophrenia. University of Wollongong Research Council Small Grants Scheme, 2007-2008 ($12,400).

Newell K. An investigation of neuregulin 1 expression following perinatal NMDA hypofunction. University of Wollongong Faculty of Health and Behavioural Sciences Small Grant, 2008 ($5,000).

Newell K. Are CB1 receptors more sensitive at adolescence than adulthood in Sprague-Dawley rats. University of Wollongong Faculty of Health and Behavioural Sciences Early Career Research Grant, 2008 ($3,000).

Schall U. Siemens diffusion tensor imaging acquisition software for Magnetom Avanto, University of Newcastle Faculty of Health Research Equipment Grant, 2007 ($25,000).

Shannon Weickert C. Confocal microscope. Clive and Vera Ramaciotti Foundation Major Equipment Grant, 2007 ($30,000).

Shannon Weickert C. Enhancing neurogenesis in adult primate brain. UNSW Gold Star Award, 2008 ($40,000).

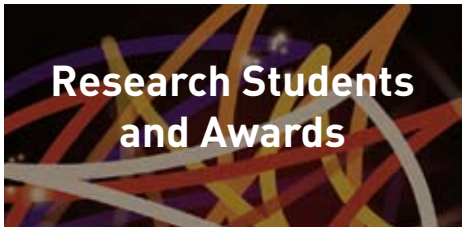
Solowij N, Yucel M, Lubman D, Ciarrochi J, Heaven P. Determining the cognitive sequelae of adolescent cannabis use: a longitudinal cohort study. NHMRC Project Grant, 2008-2010 ($252,125).

Tooney P, Cairns M, Scott R, Kelly B, Carr V. Neurobehavioural Genetics Network. NSW Health, 2008-2011 ($2,450,000).

Tooney P, Cairns M. Investigation of genetic and epigentic mechanisms underlying dysregulation of RGS4 in schizophrenia. University of Newcastle Strategic Pilot Grant, 2007-2008 ($17,000).

Tooney P, Michie P, Schall U, Scott R, Stain H, Atkinson R. Brain science and young peoples mental health: a gene expression study in young people at ultra high risk of developing schizophrenia. Hunter Medical Research Institute Project Grant, 2008 ($25,000).

Weickert T, Shannon Weickert C. Clinical trial of a selective estrogen receptor modulator in schizophrenia. UNSW Faculty Research Grant, 2008-2009 ($30,000).



Degrees Awarded

The Institute supported the following students who were awarded higher degrees:

DOCTOR OF PHILOSOPHY

Dr Penny Newson
University of Newcastle, September 2007

Dr David Wheeler
University of Sydney, October 2007

MASTERS

Ms Gali Lawrence
University of Newcastle, March 2008

HONOURS

Ms Amy Dawson
University of Wollongong, December 2007

Ms Erin Gardiner
University of Newcastle, December 2007

Summer Student Scholars

Ms Rasha Gendy
Prince of Wales Medical Research Institute

Ms Elizabeth Kent
University of Newcastle

Mr Alexander Provost
University of Newcastle

Mr Sai Ruthirakumar
University of Wollongong

Early Career Researcher Award

Dr Tim Karl
Schizophrenia Research Institute

Vaughan Carr
Executive Director / Chief Executive Officer.
Professor of Psychiatry University of Newcastle; Director, Centre for Brain and Mental Health Research, University of Newcastle; Past President, Australasian Society for Psychiatric Research.
Board Member since 2004.

Stanley Victor Catts
Non-Executive Director / Founding Chair of Schizophrenia Research Institute (formerly NISAD) 1995-1999.
Professor of Community Psychiatry, University of Queensland, and Royal Brisbane and Women's Hospital. Fellow Royal Australian and New Zealand College of Psychiatrists. Chair, Scientific Steering Committee, Australia Psychosis Research Network.
Board Member since 1995. Chairman 1995 -1999.

Matthew Cullen
Non-Executive Director.
Co-President of McKesson Asia-Pacific Pty Ltd and Visiting Medical Officer St Vincent's Hospital Sydney. Fellow Royal Australian and New Zealand College of Psychiatrists, Member Australian Institute of Company Directors, and Associate Fellow Australian College of Health Service Executives.
Board Member since 28 April 2004.

Sam Lipski AM
Non-Executive Director.
Chief Executive of The Pratt Foundation. Formerly President of the State Library of Victoria, columnist for the Melbourne Age, the Sydney Morning Herald, The Australian and The Bulletin. Member of the Order of Australia for his services to the media. In 2003 he was awarded the Centenary Medal of Australia for services to journalism.
Board member since July 2007.

Peter James Maher
Chairman / Non-Executive Director.
Group Head of Macquarie Group Ltd's Banking and Financial Services Group. Current Chairman of Macquarie Equities Limited, Chairman of Macquarie Financial Services Holdings Ltd, board member of Macquarie Investment Management Ltd, board member of Religare Macquarie Wealth Management Ltd, board member of Brook Asset Management Ltd, board member of OzForex Pty Ltd and Deputy Chairman of the Investment & Financial Services Association.
Board member since 2003.
Appointed Chairman 2006.

Rita Mallia
Non-Executive Director.
Senior Legal Officer / Co-ordinator for Construction Forestry Mining Energy Union, formerly Workers Compensation Officer. Director of NSW Dust Disease Board, Member of Construction Industry Reference Group. Director, Asbestos Diseases Research Foundation.
Board Member since 2003.

Patricia Michie
Non-Executive Director.
Pro-Vice Chancellor (Research), University of Newcastle, Professor of Psychology, School of Psychology, Faculty of Science and Information Technology University of Newcastle. Adjunct Professor in the School of Psychiatry & Clinical Neuroscience, University of Western Australia.
Board member since 2000.

Andrew Mohl
Non-Executive Director.
Managing Director and Chief Executive Officer, AMP Limited since October 2002. Previous roles in AMP included Managing Director of AMP Financial Services and Managing Director of AMP Asset Management.
Board member since 2002.
Resigned: 23 October 2007.

Irene Moss AO
Non-Executive Director.
Previously Commissioner, Independent Commission Against Corruption (1999-2004), Ombudsman NSW (1995 - 1999), Magistrate (1994-1995), Federal Race Discrimination Commissioner, Human Rights and Equal Opportunity Commission (1986-1994). Officer in the General Division of the Order of Australia (AO) 1995.
Board member since 27 April 2005.
Resigned: 24 October 2007.

Trish Oakley
Company Secretary / Non-Executive Director.
Associate Director, Elton Consulting, specialising in strategic communications. Formerly Director, Meridian Media. Chief of Staff, Andrew Refshauge's Office, NSW Government (1995-1999), Press Secretary and Political Strategist for Dr Refshauge as Deputy Leader of the Opposition (1990-1995). Former Journalist, Australian Broadcasting Corporation.
Board member since 2001.

Christos Pantelis
Non-Executive Director.
Foundation Professor of Neuropsychiatry and Scientific Director of the Melbourne Neuropsychiatry Centre at The University of Melbourne and Melbourne Health. Honorary Principal Research Fellow at the Howard Florey Institute and the Centre for Neuroscience Victoria. Board Member of the Mental Illness Fellowship of Victoria (since 2004) and member of the Scientific Advisory Council of Neurosciences Victoria (since 2006).
Board Member since 2004.

Michael Reid
Non-Executive Director.
Previously Director General of the Ministry for Science and Medical Research in New South Wales, Director of the Policy and Practice Program at the George Institute for International Health, University of Sydney, Director General of NSW Health. Adjunct Professorships in the Faculty of Medicine at the University of Sydney and the Faculty of Public Administration at the University of Western Sydney.
Board member since 2006.
Resigned: 7 January 2008.

Alexandra Rivers
Non-Executive Director.
Carer, Psychologist, ex-academic, Member Guardianship Tribunal, NSW; (Guardian and Litern, Children's Court NSW; Guardian and Litern, Administrative Decisions Tribunal NSW;) Vice President Schizophrenia Fellowship of NSW, and Aboriginal Education Council of NSW; Member, Governing Committee Australian Consumers' Health Forum. Mental Health Carer and Consumer National Register.
Board Member since 2003.

Christopher Rex
Non-Executive Director.
Chief Executive Officer and Managing Director (2008 onwards) and Chief Operating Officer (1995-2008), Ramsay Health Care. Former General Manager of Macquarie Hospital Services.
Board member since 2006.

Cynthia Shannon Weikert
Non-Executive Director.
Macquarie Group Foundation Chair of Schizophrenia Research, Schizophrenia Research Institute/University of NSW/Prince of Wales Medical Research Institute. Unit Chief, MiNDS (Molecules in the Neurobiology and Development of Schizophrenia). Clinical Brain Disorders Branch, National Institutes of Health, 2004-2007. Senior Staff Fellow, NIH, NIMH, Clinical Brain Disorders Branch, April 1999-April 2004.
Board Member since February 2007.

The abridged consolidated financial position accounts and financial performance for the year ended 30 June 2008 have been prepared from audited financial statements, passed by the Board of Directors, who are responsible for the presentation of those financial statements and the information they contain. For a better understanding of the scope of the audit by KPMG, this report should be read in conjunction with KPMG's report on the unabridged financial statements. This report may be obtained from:

Schizophrenia Research Institute, 384 Victoria Street, Darlinghurst NSW 2010
Ph: (02) 9295 8407

Financial Performance for the year ended 30 June 2008:

Income	**2008**	**2007**
Fundraising	833,638	772,785
External grant income	3,420,415	2,598,988
Sundry income	108,945	82,635
Total	4,362,998	3,454,408
Less Expenses		
Research	3,328,103	2,689,372
Fundraising, marketing, communications	287,404	506,536
Administration	217,870	251,777
Total	3,833,377	3,447,685
Net Surplus (loss)	529,621	6,723
Opening retained earnings	782,119	763,876
Transfer to retained earnings	529,621	11,520
Closing retained earnings	1,311,740	782,119
Retained earnings	1,311,740	782,119

Thank you to all our supporters.

For privacy reasons we have chosen not to list all our individual supporters but would like to take this opportunity to thank and acknowledge these kind people who have given us gifts - this generosity and commitment of the community is vital to our ongoing success.

We are grateful for the ongoing support of our Major Partners:

Government

- NSW Health
- National Health and Medical Research Council

Foundations and Trusts

- The Pratt Foundation
- NARSAD Research
- The Hunt Family Foundation

Corporate

- Macquarie Group Foundation
- Investment and Financial Services Association (IFSA)
- Ramsay Health Care
- Janssen-Cilag Pty Ltd

Many thanks go to the following organisations for their support:

Foundations, Trusts and Grants

- Australian Nuclear Science and Technology Organisation
- Baxter Charitable Foundation
- Clive and Vera Ramaciotti Foundation
- Paint A Rainbow Foundation
- Patrick Brennan Trust
- Perpetual Trustees
- Ron & Peggy Bell Foundation
- State Trustees Australia Foundation

Corporate

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- ASX-Reuters Charity Foundation
- Australian Wealth Management
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- CFMEU NSW
- Colonial First State
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- Ernst & Young
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- MBF Clearview
- Paynter Dixon

- Pfizer Pty Ltd
- Portfolio Partners Ltd
- Smith & Osborne (NSW) Pty Ltd
- State Street Australia Ltd
- Suncorp Wealth Management
- Touchstone Group
- UBS Global Asset Management
- Vanguard Investments Australia
- Westpac Banking
- Westpac Life

Pro Bono

- Bright Print
- Chubb
- Coca-Cola Amatil
- KPMG
- Photolibrary.com
- Singleton Ogilvy & Mather
- TCO Pty Ltd
- Turning Point
- Yalumba

Workplace Giving

- Australian Charities Fund
- ABN AMRO
- Barclays Global Investors Australia Pty
- Charities Aid Foundation
- Deutsche Bank
- Insurance Australia Group (IAG)

Community Groups

- Avondale Golf Club Ltd
- Banks House Support Group
- Hornsby Ku-ring-gai Association of Mental Health
- Lions Club of Kiama Inc
- Rotary Club of North Sydney

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Website: www.schizophreniaresearch.org.au