

HEADLINES

SCHIZOPHRENIA RESEARCH INSTITUTE AUGUST 2008

Genetic discovery leads to new treatments for schizophrenia

Leading schizophrenia researcher, Professor Cyndi Shannon Weickert, has discovered that a brain receptor that normally stimulates growth in adolescence is hampered in people with schizophrenia.

Recently published in *Human Molecular Genetics*, the findings open up new opportunities for treatments for schizophrenia, commencing with a three year clinical drug trial next month.

Professor Shannon Weickert, Macquarie Group Foundation Chair of Schizophrenia Research, led the study, along with international collaborators at the National Institutes of Health (USA). Professor Shannon Weickert sees this as one of the most important papers in her career. She explained:

"We now know that this brain receptor doesn't work in the normal way for people with schizophrenia. With this drug trial we can begin to stimulate it and try and get the neurodevelopmental program back on track. For some patients we could see improvements in language and memory."

Researchers are recruiting 80 male and female patients with schizophrenia who will receive this new therapy in addition to their ongoing medication. For six weeks, patients will take a drug called raloxifene, a hormonal modulator that stimulates the estrogen receptor in the brain but does not affect estrogen levels in other parts of the body. The brain changes testosterone into estrogen before it hits the estrogen receptor. The aim is to learn how this hormonal modulator can influence thought processing in schizophrenia and determine whether it could be used as a novel therapeutic treatment for cognitive problems in patients.

This drug is already used for cancer and osteoporosis and this is the first time it will be used in males with schizophrenia and in patients with schizophrenia under 40 years of age.



Prof. Cyndi Shannon Weickert (centre) with team members at the Schizophrenia Research Laboratory.

About the Research

Schizophrenia usually occurs during adolescence. When puberty hits, the brain is asked to change by activating genes that may have been dormant during childhood. People with schizophrenia are more likely to have a different gene (ESR 1) that codes for the estrogen receptor and less likely to be able to awaken the dormant genes during maturation. Brain proteins like the estrogen receptor regulate the degree to which specific genes are expressed and can even switch genes on and off.

268 post mortem brains (176 males, 92 females), and the genetic profiles of members of 122 schizophrenia-affected families were used in the study. The novel findings suggest that ESR1 may be a 'candidate gene' for schizophrenia and the mechanism of this association may involve alternative gene processing and function.

Any patients with schizophrenia aged between 18 and 40 years and on a stable medication program who may be interested in participating in the hormonal modulator program should contact Kristy Dunlop at 02 9399 1142, email: k.dunlop@unsw.edu.au for more information.

*Shannon Weickert CS, Miranda-Angulo AL, Wong J, Perlman WR, Ward SE, Radhakrishna V, Straub RE, Weinberger DR, Kleinman JE. Variants in the estrogen receptor alpha gene and its mRNA contribute to risk for schizophrenia. *Human Molecular Genetics*, 2008; 17; 2293-2309.

The Macquarie Group Foundation Chair of Schizophrenia Research 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.



Our Gratitude to Jack and Judy Gibson

Institute representatives were among the 800 mourners at Jack Gibson's funeral held in Cronulla on 14 May. Jack left behind a legacy of kindness, generosity and empathy and was fundamental to the growth of the Schizophrenia Research Institute. Jack and Judy have always been passionate about schizophrenia - their eldest son Luke had the disease and passed away in 1987.

Jack and Judy raised over \$1.5 million in support for schizophrenia research over the last 20 years. From organising formal fundraising dinners and donating proceeds from Jack's four books to attracting influential people to the cause, their generosity and diligence was relentless. This passionate commitment has provided vital support to the Institute and educated many about the need for research into schizophrenia. Judy Gibson continues as an invaluable advocate of the Institute's mission.



Prof. Vaughan Carr
Chief Executive Officer

On the Cutting Edge

The recent Schizophrenia International Research Society conference, held in Venice, was attended by several Institute scientists. They led symposium presentations on cognitive processing and the prodrome of schizophrenia, and presented on a diverse array of other topics. Among the prominent recurring themes throughout this conference were the challenges of new drug development, the role of cannabis in the cause and progression of schizophrenia, neurodevelopmental models of the disorder, the pathophysiology of schizophrenia, and early detection and treatment of the illness. Each of these themes reflects areas of research in which the Schizophrenia Research Institute already has active ongoing programs of investigation.

As reported on the front page, Prof. Shannon Weickert's neurodevelopmental research has identified a genetic abnormality in the estrogen receptor in the brain in schizophrenia. A controlled clinical trial of a new drug treatment is now in the planning stages; it aims to determine whether a novel treatment can improve some of the cognitive deficits and disability associated with schizophrenia.

The third theme, *cannabis*, is highlighted in the work of Nadia Solowij and colleagues who have demonstrated abnormalities in the brains of heavy cannabis users. The similarities with schizophrenia are striking. Other work on the same theme by Martin Cohen and colleagues has compiled the evidence for an association between cannabis use and risk for schizophrenia. Evidence for cannabis as a component cause of schizophrenia is growing stronger.

Seeing these strong results gave me great pride in our scientists while at the international conference in Venice, and rightly places our Institute's work at the cutting edge of schizophrenia research, successfully competing on the international stage.

Cannabis, Psychosis and Brain Damage

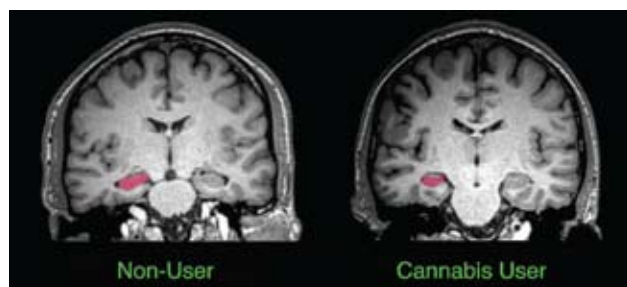
Recent research sheds new light on the cannabis question

A collaborative MRI brain imaging study¹ initiated by Dr Nadia Solowij's group at the University of Wollongong set out to determine whether heavy cannabis use by people with no mental disorders was associated with anatomical changes in the hippocampus and the amygdala – two brain areas known to be altered in schizophrenia.

The cannabis users were found to have an averaged 12 per cent volume reduction of the hippocampus, and a 7 per cent reduction of the amygdala compared to controls.

Fifteen long-term cannabis users aged around 40 years, and sixteen age-matched non-users participated in the MRI study, and all subjects also completed tests measuring low-level psychotic symptoms and verbal learning abilities. Cannabis users tested marginally positive for borderline psychotic symptoms, and significantly worse than controls on verbal learning. This is the first study of heavy cannabis users to demonstrate significant dose-related hippocampal volume reductions. Dr Solowij commented:

"These results demonstrate a link between long-term cannabis users and psychotic experiences, such as persecutory beliefs and social withdrawal. Long-term users have also progressed the loss of memory by around 15 years. With an average age of 39, the trial group had the memory capabilities of a 55 year-old. This loss of memory could be likened to the damage suffered by patients with mild traumatic brain injury."



MRI brain scans showing a 12% reduction of the hippocampus in a long-term cannabis user.

With further support from the Schizophrenia Research Institute, Dr Solowij's group is extending this research into schizophrenia populations who do and do not use cannabis.

CANNABIS AND PSYCHOSIS RISK

Cannabis use leads to an increase in risk of psychosis and many psychotic episodes could be avoided, according to a recent review of studies. Dr Martin Cohen has led a group of Schizophrenia Research Institute researchers located at the Universities of Newcastle and Wollongong who have completed a major review² 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 per cent in people who have used cannabis;
2. There is a dose-response effect, leading to an increased risk of 5–200 per cent in the most frequent users;
3. If using cannabis increases risk, as research suggests, 14 per cent of psychotic outcomes in young people would not have occurred if cannabis had not been consumed.

Other research has found that cannabis use prior to the age of 15 confers the greatest risk, due to the drug's effect upon the neurodevelopmental processes occurring in the adolescent brain.

Many other studies have contributed to the literature on the subject, warranting the comprehensive review of all data to assist clinicians in evaluating cannabis use in patients.

1. Yücel M, Solowij N, Respondek C, Whittle S, Fornito A, Pantelis C, Lubman DI. Regional brain abnormalities associated with heavy long-term cannabis use. *Archives of General Psychiatry* 2008; 65: 694-701.

2. Cohen M, Solowij N, Carr V. Cannabis, cannabinoids and schizophrenia: integration of the evidence. *Australian and New Zealand Journal of Psychiatry* 2008; 42: 357-368.

The National Focus on Fighting Schizophrenia

The 2007 launch of the **Australian Schizophrenia Research Bank (ASRB)** aimed to attract 2,000 people with schizophrenia and 2,000 controls to join. The initial TV ad (with Russell Crowe's voice) attracted a large number of people: 2,400 expressed interest, over 1,000 have consented to date, and 414 of these are now in the assessment program.

Great news occurred in April this year when NSW Health awarded \$2.4 million to support genetics research into schizophrenia and other disorders in the Hunter region. A proportion of this money will be used to conduct genetic studies on the samples collected for the ASRB.

We are well on the way in our 5-year project to create an internationally unique schizophrenia research resource, enabling much more meaningful studies to be conducted, and accelerating the search for prevention and cure.

This is the first time a truly national Australian effort in schizophrenia research has been sustained, and the Institute thanks all supporters for helping to make it happen.



The Schizophrenia Research Institute's ASRB centres in Australia

FUNDRAISING NEWS FROM HELEN CONNEALY

RECORD-BREAKING DONATIONS

Thanks to all our kind supporters – you'll be delighted to know that donations in response to my May letter have broken all records, and these much needed funds will be used to help the **Australian Schizophrenia Research Bank**.

PRO-ACTIVE INSTITUTE STAKE HOLDERS

Key Institute stakeholders have also been fundraising: Chairman **Peter Maher**, and Life Governor **Don McDonald** held birthday parties at which guests donated gifts of money to the Institute. As the **Macquarie Group Foundation** matched all monies that Peter raised, both events raised a total of over \$26,000. Thanks and Happy Birthday!



Congratulations also to Institute Board member **Christopher Rex** (left) on his appointment to CEO of **Ramsay Health Care**, a valued Corporate Partner of the Institute.

WORKERS AIDING RESEARCHERS

The partnership between staff, business and charities is growing in the 21st century. The Schizophrenia Research Institute has benefited from workplace giving to the tune of nearly \$190,000 over the last ten years.

The generosity of individuals is often matched by employers and all gifts are pre tax, making it simple and straightforward. For some, being part of a **Workplace Giving Program** can mean more than just giving regular donations:



IAG Team Manager, Kim Montgomery (left) had been giving regularly through her payroll to her charity of choice, the Schizophrenia Research Institute. She decided she would like to connect more personally, and so she volunteered to help with the Institute's fundraising ball **Spark of Genius**, and with the **ASX Reuters Charity Foundation** sailing regatta, which supports the Institute.

Both events raised significant amounts for the Institute and their success would not have been as easy without the necessary help of volunteers. When the opportunity came along to be part of a television advertisement aimed at recruiting people to take part in the country's largest brain research project, the Australian Schizophrenia Research Bank, seven staff from IAG volunteered. Kim was there and found it to be a really positive experience. "I had a wonderful day, the people involved were great to be around. I'm just so passionate about the research that is being done," said Kim.

The Schizophrenia Research Institute also thanks the individual and matched donations of the **Australian Charities Foundation**, **Charities Aid Foundation** and the staff of **ABN AMRO**, **Deutsche Bank** and **IAG** for supporting us with workplace giving.



Ramsay Health Care Ran for Research!



250 staff from **Ramsay Health Care** ran in the **Sun Herald City-2-Surf** on Sunday 10th August to raise funds for the Institute. Please think about doing the same at these similar events:

PERTH City-2-Surf

on 31st August.

Suncorp Bridge to BRISBANE

on 7th September.

Samsung MELBOURNE Marathon

on 12th October.

ADELAIDE Sunday Mail City to Bay

on 21 September.

Just get a team together, and go to **www.everydayhero.com.au**, select us as your chosen charity and register.

Community Aid

Paint a Rainbow continues to support schizophrenia research this year, bringing their total of donations in just three years to \$75,000. Thanks to Pat Sergi and all the Paint a Rainbow staff.

Thanks also to all those in the community who help us, in particular to **Avondale Golf Club Ltd**, **Banks House Support Group**, **Hornsby Ku-Ring-Gai Action of Mental Health Inc** and the **Rotary Club of North Sydney**.

HELP RESEARCH AND WIN A CAR!



ASX Reuters Charity Foundation held a fantastic golf day and gala dinner in February 2008 – thanks to David Brocklehurst (left) and his hard-working team. Their fundraising efforts have brought huge benefits to the Institute. The Foundation's next sailing regatta will take place on Friday 17 October 2008 out of Middle Harbour Yacht Club.

We have 350 **Art Union ticket books** to sell from September 2008 – there are great prizes including a car – see the website for details: www.asxreuterscharity.com.au/mainsite/site/html/art_union.htm

If you would like to buy or sell some books for the Institute they cost \$100 per book (6 tickets in a book). Please call on (02) 9295 8407.



**Our annual supporter event
Cocktails and Consciousness
will be held on
Thursday 28th October 2008
so please keep that date free in your
diary. Invitations will be sent later
in the year.**

In Memoriam Gifts

Our condolences and thanks go to seven families who have suffered bereavement, and who have asked mourners to donate to the Institute in lieu of flowers at the funerals of Gregory Lema, Ben Hawden, Cameron Burley, Anthony Raymond Merchant, Chance Mullins, Fergus Robert McAlpine, and Mark Douglas Springgay. A gift was also received in memory of Jason Barnes, who died in 2003.

IFSA Make it Two Years in a Row

The Schizophrenia Research Institute will attend the **Investment and Financial Services Industry (IFSA)** annual conference as a charity partner for the second year running. Funds will be raised at the conference which will be held on the Gold Coast on 6-8th August 2008.



No-fees Share Sale Donations

ShareGift Australia provides Australian shareholders with the opportunity to sell their shares and donate the proceeds to charity, without having to pay brokerage fees.

Selling and donating through ShareGift Australia ensures that the proceeds of the sale benefit the Schizophrenia Research Institute. For more information go to www.sharegift.org.au

The Perfect Card for 2008

Make your Christmas Cards really meaningful this year by logging on to www.christmascards4charity.com.au/sri to choose from a wide range of great cards for the festive season.

40c per card will be donated back to the Schizophrenia Research Institute.

*Many thanks to our government and major corporate supporters who have renewed their commitment to us and donated recently (Feb-Jun 2008). And welcome to **Yalumba** who have joined us as our wine sponsor.*

NSW HEALTH

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ERNST & YOUNG
Quality In Everything We Do

The Schizophrenia Research Institute is the only national medical research institute solely dedicated to discovering the ways to prevent and cure schizophrenia. The Institute is NHMRC accredited and is funded by government grants (NSW Health & NHMRC), corporate and private donations. A registered charity throughout Australia, further donations can be given at www.schizophreniaresearch.org.au or by phoning (02) 9295 8407.

Please help by completing and mailing this form to Schizophrenia Research Institute, 384 Victoria Street, Darlinghurst, NSW 2010, or fax to (02) 9295 8415, or simply call (02) 9295 8407.

Name: _____ Address: _____ Postcode: _____

☐ Cheque enclosed (made out to Schizophrenia Research Institute): \$ _____

☐ Please debit my credit card: \$ _____ ☐ Bankcard ☐ MasterCard ☐ Visa ☐ Amex

Card No: _____ Cardholder's Name: _____

Expiry Date: _____ Signature: _____

☐ Please include me on the mailing list to receive free HeadLines

Email: contact@schizophreniaresearch.org.au

Web: www.schizophreniaresearch.org.au



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