Annual Report 2010

Barwon Psychiatric Research Unit

In partnership with The University of Melbourne (Department of Clinical and Biomedical Sciences), Barwon Mental Health Drug & Alcohol Services and Healthscope.

THE UNIVERSITY OF MELBOURNE

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Forewords

The Barwon Psychiatric Research Unit (BPRU) continues to grow in productivity, and increasingly is publishing research that is at the cutting edge globally. Noteworthy recent adherents include the first data that the antioxidant N-Acetyl cysteine treats the core symptoms of schizophrenia and bipolar disorder. Extending this, the unit is completing two large-scale trials in bipolar disorder and depression. The unit has also provided novel data that diet quality and smoking are independent risk factors for depression. Recognition for the achievements of the unit include Michael Berk receiving a commendation in the Ministers Award for Mental Health, Felice Jacka being awarded a NHMRC Post-doctoral fellowship and a NARSAD Young Investigator Award, Seetal Dodd obtaining the Samuel Gershon Award and Lana Williams winning the Health and Lifestyle category in the G-force Researcher of the Year Award, and the Australasian Society Psychiatric Research (ASPR) Early Career Researcher Award.

Despite limited resources, BPRU has continued to punch above its weight in maintaining a publication rate similar to that of much larger research centres and at the same time has expanded its funding base and student load. It is a very productive group, producing consistently high quality outcomes from a relatively small resource base. The unit provides unique clinical, teaching and research opportunities for students and graduates across a number of medical and related disciplines.

The Faculty of Medicine, Dentistry and Health Sciences is Australia's premier biomedical research faculty. Biomedicine at the University of Melbourne has been ranked no. 1 in Australia and no. 14 in the world (Times Higher Education Supplement 2010). The excellent research conducted by hospital based research units, such as BPRU, is a contributing factor to this global recognition.

I am delighted with the outstanding leadership given by Professor Berk in this most important Unit within the University Department of Clinical and Biomedical Sciences at Barwon Health.

Prof James A. Angus AO
Dean
Faculty of Medicine, Dentistry and Health Sciences
The University of Melbourne

THE UNIVERSITY OF MELBOURNE

Research provides an important dimension to Barwon Health. An organisation that invests in research believes in informed change and Barwon Health needs to translate this new information into practice. The Barwon Psychiatric Research Unit typifies this commitment and they will make a significant contribution to Barwon Health being a leading health service. The team led by Professor Berk continues to excel and delivers international class research outcomes. Well done.

Dr David Ashbridge
Chief Executive Officer
Barwon Health

Barwon Health

Professor Berk and his team continued to produce high quality research in the area of clinical psychiatry, submitting a number of papers to peer review journals and receiving a number of research grants during the year. A program to rotate advanced trainees from Barwon Health to The Geelong Clinic under the supervision of Professor Berk is well established, enabling trainees to gain valuable experience in treatment of clients with high prevalence disorders. This reaffirms that high quality research and training can be achieved through public/private partnerships in mental health.

Ms Gaylyn Cairns
State Manager-Victoria
Mental Health and Rehabilitation Hospitals
Healthscope Ltd

Healthscope

Introduction from Prof. Berk

Professor Michael Berk

The productivity of the Barwon Psychiatric Research Unit 2010 continued to increase, both in quantity and more importantly in quality. High impact papers were published in prestigious journals including the American Journal of Psychiatry, the British Journal of Psychiatry, the Journal of Clinical Psychiatry and Neuroscience and Biobehavioural reviews.

A number of members of the team were successful in obtaining grants and awards. Dr Lana Williams was successful in attaining a highly competitive NHMRC grant for the study of SSRI antidepressants and their effects on bone. She also was successful in gaining an Academy of Science travel grant to visit collaborators in Norway during 2011. Dr. Felice Jacka was rewarded by the granting of a prestigious NHMRC post-doctoral fellowship and a NARSAD Young Investigator Award. We were also successful in partnering with the MHRI in obtaining a $23 million CRU grant. Frank Giorlando was successful in attaining a FRANZCP grant, and both Frank Giorlando and Steve Moylan won a Pfizer neuroscience grant. Dr. Felice Jacka also won the Health and Lifestyle category in the G-force Researcher of the Year Award, Smart Geelong Research.

The unit produced a number of novel research findings that are clinically and practically significant. Two novel studies were published, showing that the cholesterol lowering drugs, statins, that have anti-oxidative and anti-inflammatory properties, reduce the risk for the development of depression. This work builds on our biomarker data showing that inflammatory markers increase the risk for the development of depression. We showed that smoking worsens the outcome of bipolar disorder. We have some of the world's first data that diet quality is a risk for the development of depression and that exercise can reduce the risk for the development of depression. This body of work contributes to our aim of producing a body of evidence regarding risks for depression in a public health context, leading to the possibility of an evidence based public health message for the primary prevention of depression. Previously aving shown high rates of Vitamin D insufficiency in people with depression, we have also now completed a large clinical trial of vitamin D for mood symptoms in the elderly.

The major change for the team is the transfer of Barwon Health research facilities from a University of Melbourne umbrella to Deakin University. The unit thrived and grew under the stewardship of the University of Melbourne, but the transition of the team to Deakin University, concordant with the opening of the Deakin Medical school, brings a host of new opportunities and partnerships. We believe that this move will further accelerate the productivity of the team.

We would like to sincerely thank the University of Melbourne, Deakin University, Healthscope and Barwon Health for their conjoint and ongoing support of the research unit.

Drug safety

The large range of modern drugs available for the treatment of mental illness have helped improve the lives of thousands, perhaps even millions, of people who have suffered from mental illness. These drugs have helped people manage their illnesses, prevented or reduced the recurrence of illness and controlled symptoms of illness. Although people with mental health difficulties have benefited greatly from modern drug treatments, these treatments are also know to have risks. Researchers at the Barwon Psychiatric Research Unit work to understand and reduce the risks associated with drug treatment of mental illness in several ways.

1. We have gathered data on adverse effect of drug treatment to improve our knowledge and understanding of associated risks with drug treatment. We have collected considerable data on the adverse effects of the drug *clozapine*, which can adversely impact blood cells and cardiac health and can cause weight gain and diabetes. Specifically, we have novel data showing that clozapine can adversely impact cardiac muscle function.

2. Our Geelong based epidemiological resource provides epidemiological data on drug treatment. With these data we have already demonstrated a link between treatment

with SSRI antidepressants and reduced bone density. An NHMRC project led by Dr Lana Williams was obtained in 2010 with the aim of expanding this project to determine the impact on fracture rates and to examine the differential effects of different SSRIs on bone in collaboration with the HUNT study based in Norway.

3. We are conducting *in-vitro* experiments to investigate adverse effects of psychotropic drugs on bone. Serotonin is used by osteoblasts and osteoclasts for cell signalling. Many psychotropic drugs change the amount of serotonin present in the environment around these cells and this may impact bone health. The safety of antidepressants is being tested in the laboratory using osteoblast and osteoclast cell cultures.

4. We have been involved in the publication of many guidelines, which assist clinicians to make well-informed and balanced treatment decisions. These include publications about the safe use of drugs for the evidence-based treatment of various mental illnesses as well as publications about safe treatments in special populations, such as pregnant and breast-feeding women.

Highlighting our global role in this area, Dr Seetal Dodd has recently been appointed Editor-in-Chief of the scientific journal *Current Drug Safety*.

Our research enables better assessments of the risks and benefits of drug treatment, which allows clinicians to make safer treatment decisions.

The Drug Investigation Team.
From left: Professor Berk, Dr Seetal Dodd, Dr Yiming Wang, Dr Lana Williams, Dr Fiona Collier, A/Prof Julie Pasco and Dr Jason Hodge.

Genetic prediction of response to antidepressant medication

Dr Ajeet Singh (MD candidate)

For many patients with mental illness antidepressant medication is a crucial component of their care. For the more severe cases of depression, biologically based treatments such as antidepressant medications are a cornerstone of treatment. Unfortunately the process of finding the most effective and tolerable medication for an individual patient is a process of trial and error, often taking months. During this time patients remain subject to the distressing and impairing impacts and risks associated with major depression.

In this doctoral study, the role of certain genes in helping predict response to antidepressant medication is being studied. The commonly prescribed antidepressants venlafaxine (Efexor) and escitalopram (Lexapro) are being studied in a real-world clinical sample. Their response to the medication is being examined and linked to their unique gene profiles for medication response. Genes involved in how well the medication can enter the brain and genes involved in mood regulation are being studied. The hope is this study may help light the way towards one day doctors being able to determine what medication at what dose a patient needs to most likely get better without any problematic adverse effects. Such genetically 'personalised medicine' is referred to as pharmacogenomics, and looks set to be the first wide-spread clinical use of the Human Genome Project in medicine.

Through matching patients sooner to effective tolerable medication, this research has scope to reduce the disability burden of major depression.

This is a cutting edge multicentre international research trial. At this stage over 100 participants have been recruited, with the largest site of recruitment to date being Geelong. It is anticipated that project will be completed in March 2011, with results being announced at the ASPR conference in December 2011. A 'Young Investigator' grant from The Royal Australian and New Zealand College of Psychiatrist has been awarded to Dr. Ajeet Singh for this study.

Oxidative biology

From left: Dr Seetal Dodd, Karen Hewitt (researcher), Prof Michael Berk, Dr Olivia Dean and Kristi-Ann Villagonzalo (PhD candidate).

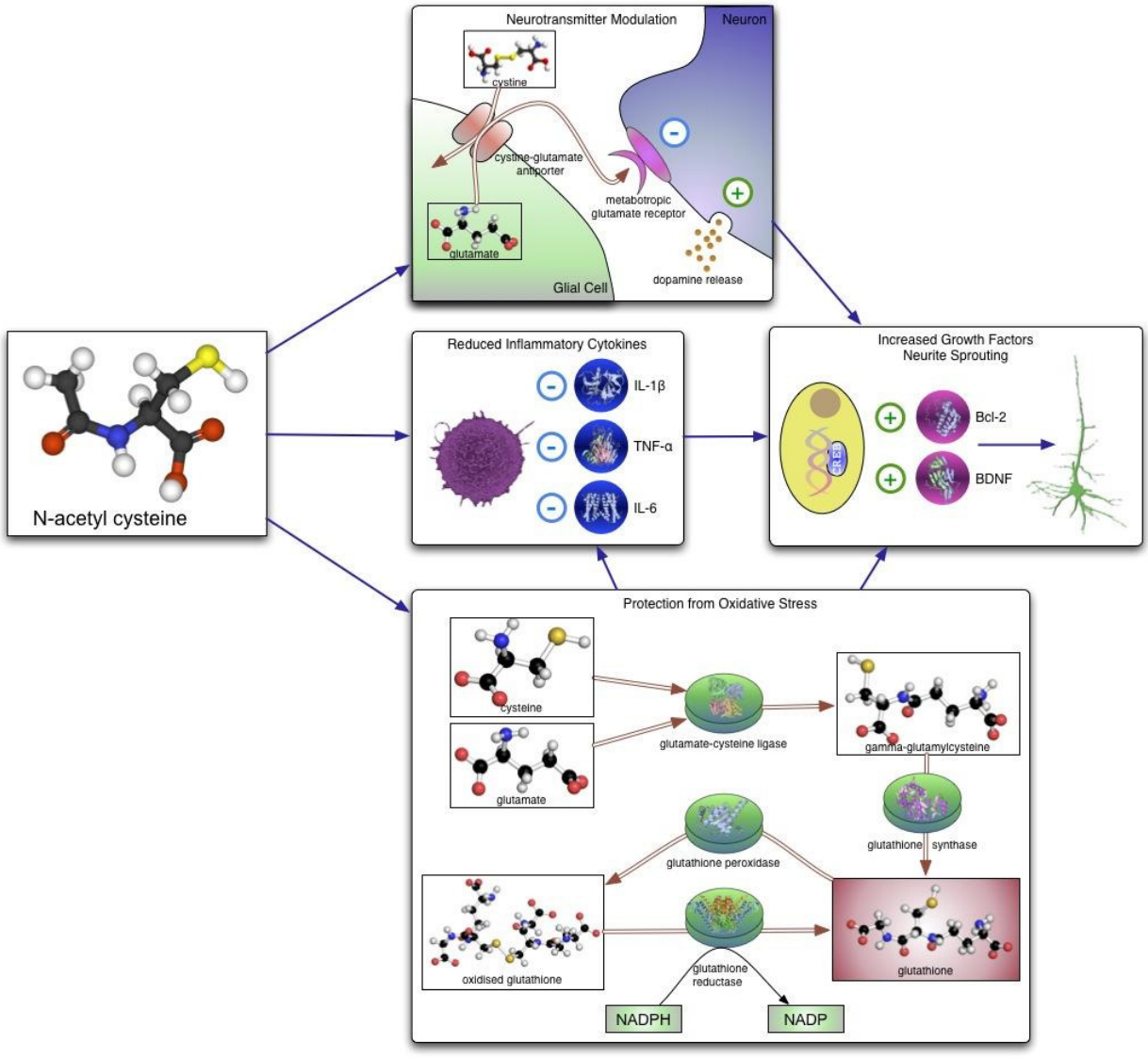
Changes in oxidative biology are increasingly thought to play a role in the pathophysiology of psychiatric illness. Oxidative balance requires a synergy between the levels of antioxidants in a person's brain and the levels of oxidative species, better known as free radicals. These are produced due to energy generation as part of normal brain function. In many psychiatric disorders, this balance is altered with a decrease in the levels of antioxidants and an increase in free radicals, and this imbalance is believed to lead to changes in the way the brain functions, ultimately contributing to the symptoms of these disorders.

Our unit is currently tyring to determine how oxidative biology is involved in psychiatric illness and provide new treatments based on these changes. We have a multitude of approaches to investigate this issue, ranging from basic science through to clinical trials. We have shown that there are changes in the brain's primary antioxidant, glutathione and that it has effects on memory and sensorimotor gating in animal models. We have also shown that treatment with the antioxidant precursor, N-acetyl cysteine (NAC) can reduce symptoms in people with bipolar disorder and schizophrenia. Based on these results we are currently running more clinical trials investigating NAC. We have completed a larger maintenance trial in people with bipolar disorder, the results of which are currently being analysed. Additionally, we are also now trialing NAC in the treatment of unipolar (clinical) depression and in children with autism.

Within these trials we are actively trying to ascertain how changes in oxidative biology impacts on the symptoms experienced by people with psychiatric illness. We are currently investigating peripheral markers (blood samples) to measure antioxidant levels and pathways involved in producing and altering antioxidants, and are using brain imaging (magnetic resonance spectroscopy) to directly visualise changes in key brain metabolites. We are also involved in projects investigating post-mortem brain tissue to directly measure changes in the brains of individuals who were diagnosed with a mental illness.

Moreover, we are also investigating the source of these changes. Research is beginning to suggest that changes inside mitochondria, the cells' energy powerhouse, are playing a large role in the changes in oxidative biology and we are actively investigating these changes. Similarly, changes in immune function have also been suggested to be involved with these oxidative changes and we are also currently pursuing these factors. Lastly, we are looking at changes in key genes in the oxidative defence pathways, and have shown that one gene, glutamate cysteine ligase, may be altered in people with depression and bipolar disorder.

Overall, our unit is working towards better understanding the role oxidative biology is having in psychiatry illness and identifying new therapies to improve outcomes for individuals with these disorders.



Dean et al (In Press)

Outcomes of the common mental disorders

Dr Lana Williams

Depressive and anxiety disorders impose huge costs, both on the individual and the community, yet we have an incomplete understanding of their impact on physical health. Given the high prevalence and associated public health-care costs of common physical illnesses, such as cardiovascular disease, type 2 diabetes, obesity, osteoporosis, and fragility fracture worldwide, it is important to investigate and better understand the association of these illnesses with mental health issues. Understanding the association between chronic physical disease and psychiatry is vital to successful health promotion, health care delivery, and disease management.

Over the past 6 years, we have been developing a program of research investigating outcomes associated with depressive and anxiety disorders, within an epidemiological context. This research has been conducted in conjunction with the Geelong Osteoporosis Study (GOS), a large epidemiological study involving a population-based sample of over 2000 women and men randomly selected from electoral rolls for the region (Barwon Statistical Division). The GOS was originally developed to investigate predictors and consequences of osteoporosis, but recently expanded to examine psychiatric illness and other common diseases. The 15 year follow up of these women is scheduled for next year and this research program is currently being replicated in more than 1000 men from the Barwon region, adding further strength to this large-scale project.

Results of this research to-date have revealed that approximately one in three (35%) women have experienced a mood and/or anxiety disorder as determined by a structured clinical interview (SCID-IV/NP). At the time of the study, 14% were identified as having a current illness, with mood disorders being the most common condition. Furthermore, we found depression to be associated with reduced bone mineral density and to increase the risk of fracture by 60%. We were also the first to show that the SSRI group of antidepressants may increase the risk for osteoporosis.

This program of work will generate important information that can be used to provide an insight into the interaction between physical and mental health. Also, a wide range of social, psychological and biological factors such as the presence of inflammation and/or oxidative stress, are being investigated, which may explain these associations. This project is an invaluable resource for collaborative studies, both nationally and internationally. A collaboration between the world-renowned Nord-Trondelag Health (HUNT) Study, Norwegian University of Science and Technology (NTNU), and The University of Melbourne has been developed, which allows for further investigations in even larger population studies based in Norway.

Prevention of common mental disorders

Depression and anxiety are highly prevalent conditions, and the burden they impose on individuals and the community is enormous.

Dr Felice Jacka

Traditionally, mental health problems have been seen as 'separate' from the other common, chronic physical illnesses such as heart disease, type 2 diabetes and cancer. However, many of the lifestyle factors that influence our risk for these physical diseases, such as diet, exercise and smoking, also influence the biological systems that are known to be involved in the development of depression and anxiety, such as the immune system and oxidative stress. Importantly, these lifestyle factors are open to modification, affording the possibility of a preventative approach to these mental illnesses.

In our research unit we have been developing a highly innovative program of research that examines how our lifestyles interact with our risk for mental health problems. This is being done with the ultimate goal of developing an evidence-based public health message for the primary prevention of the common mental disorders. Working with the Geelong Osteoporosis Study (GOS), we are gathering valuable data from a representative sample of adults from the Geelong region, and using these data to investigate the role that lifestyle may play in increasing or decreasing our risk for depression and anxiety.

For example, we have recently published data in the British Journal of Psychiatry, one of the top international scientific journals, showing that smoking is an independent risk factor for major depression in women. In this study, we identified women who smoked, but who had not had any depressive episodes, at the GOS baseline assessment in the mid 1990's. We then identified who among these women went onto develop depression over ten years of follow up, and found that those who smoked were much more likely to develop major depression than those who didn't. We took into account many other factors that may be related to both smoking and depression, but these did not explain the increased risk for depression seen in women smokers. In a separate study, conducted within a clinical sample of people with bipolar disorder, we also identified that individuals with mania were less likely to respond to treatment and remained more symptomatic if they were smokers. There are many biological explanations for the relationship between smoking and depression, and these findings are an important reminder that smoking is damaging to many aspects of our health, both physical and mental.

Our newest research focuses on diet. We have identified that women who eat a diet high in 'whole foods' such as vegetables, fruit, whole grains, lean meats, fish and low fat dairy are less likely to have either depression or anxiety. On the other hand, women who eat a diet high in 'junk' and processed foods are more likely to have depression, than those eating a diet lower in those sorts of foods. These findings have been published in the American Journal of Psychiatry, also one of the leading international scientific journals in the field of psychiatry. We have also collaborated with researchers at the Murdoch Children's Research Institute, Deakin University, and Barts and the London School of Medicine and Dentistry (UK), on several studies designed to examine the impact of diet quality on adolescent depression. Once again, the results of these studies suggest that a poor quality diet may be a risk factor for depression. Given that three quarters of psychiatric illnesses begin in adolescence and young adulthood, these findings may have important public health implications for reducing the risk of depression across the life course. In 2011 we will also work closely with researchers in Norway to examine the impact of early life nutrition on the development of mental health problems in children.

We are also investigating the relationship between work and leisure time physical activity and the common mental disorders in men and women. We will be continuing and extending our international and domestic collaborations with other organisations involved in population health research. It appears, for example, that lower levels of physical activity are associated with an increased risk for developing depression. Our ongoing investigations will provide important data to support a preventative approach to mental illness that is highly innovative and of real importance in reducing the burden of these illnesses in the community. These studies will provide the evidence for a coherent public message about how to minimise the risk for depression.

Online Psychological Interventions

Online psychological interventions are gaining increasing prominence both in the research and health care sphere. These interventions overcome the barriers to accessing specialist programs and services, particularly in areas where such programs are non-existent.

The diversity of programs offered is growing. and includes a range of interventions targeted at specific disorders including unipolar depression, anxiety disorders, bipolar disorder, substance abuse, eating disorders, and sexual dysfunction.

The Barwon Psychiatric Research Unit is currently evaluating one of the first online self help programs for Bipolar Disorder called MoodSwings www.moodswings.net.au. This intervention is based on the MAPS program, an effective group based program for bipolar disorder, developed by Lesley Berk, under the stewardship of Professor David Castle.

The MoodSwings program is completely online. It is entirely self-help and offers adjunctive psychosocial tools and information to help manage bipolar disorder. It includes a number of core modules that cover information about bipolar disorder and strategies to assist in staying well. There is also a moderated discussion board, and follow up booster sessions. We have developed two different versions of MoodSwings and are comparing whether there is any difference to the information version, in comparison with a more intensive Cognitive Behavioural Therapy (CBT) approach.

Front: Sue Lauder (PhD candidate) and Emma Gliddon (Hons. Student)

As an extension of the program this year, the MoodSwings program has been updated to be even more automated and has included feedback from previous participants to improve the program further. This updated MoodSwings (MoodSwings 1.5) has been tested via a usability study and is currently being piloted with a clinical sample, with further studies planned in 2011.

We have recruited 156 participants for the initial MoodSwings study, and 22 participants in the updated MoodSwings 1.5 pilot. Results for both MoodSwings trials were finalised at the end of 2010.

Bipolar Disorder research

Bipolar disorder research is perhaps the predominant focus within the Barwon Psychiatric Research Unit. Multiple research projects have focus on bipolar disorder, and this is the area for which the unit is internationally best known.

One of the largest studies currently active is the first study to attempt to answer the question of which potential mood stabilising agents have the best neuroprotective properties after a first-episode of mania? In the study, individuals who have had a first-episode of mania will be randomised to receive either lithium or quetiapine and they will be followed up for a period of a year using brain imaging and neuropsychology to determine which agent best protects the brain.

Our oxidative biology program has a major focus on bipolar disorder. Having shown that N-acetyl cysteine effectively treats the symptoms of depression in bipolar disorder, we are now attempting to answer the question of whether N-acetyl cysteine has the ability to prevent relapse in individuals with bipolar disorder. As part of this research project we are also examining biomarkers including measures of inflammatory and oxidative stress as well as neuroimaging in conjunction with our research partners led by Professor Gin Malhi at the University of Sydney.

Within the Geelong Osteoporosis Study we are examining physical outcomes such as bone mineral density, diet and pain and a range of other factors in those individuals who are found to have bipolar disorder. In 2010, an independent study examining these clinical questions in a larger sample of individuals with bipolar disorder was commenced.

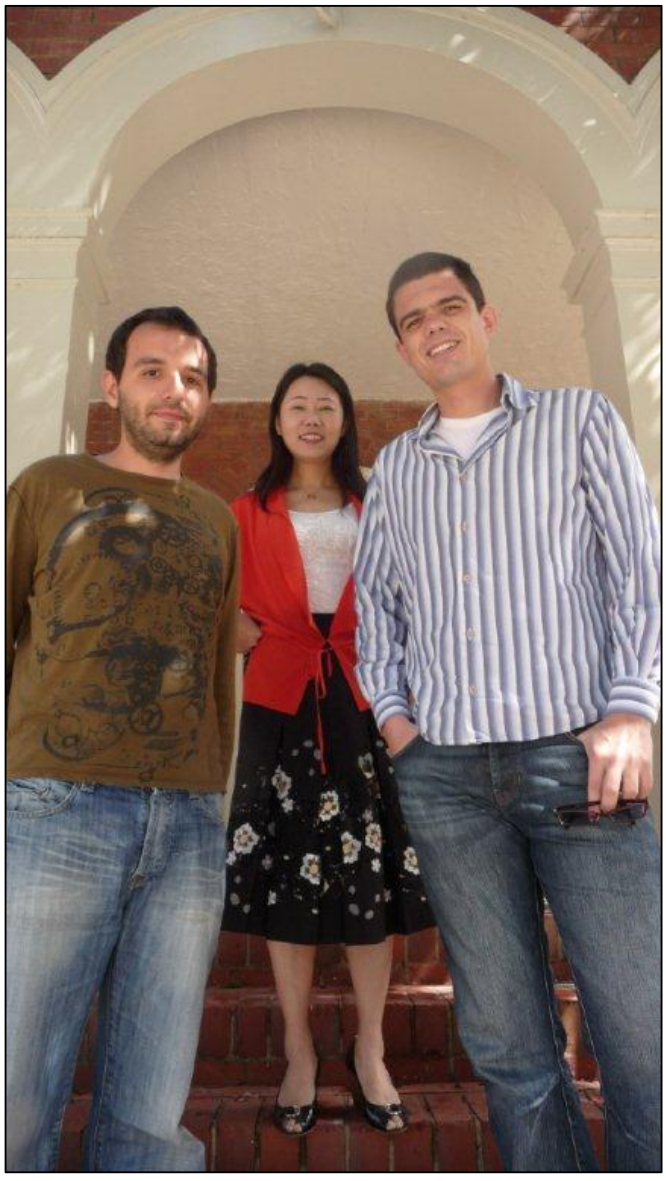
We are continuing to analyse the very rich database that exists within the Bipolar Comprehensive Outcomes Study. To date our focus has been on clinical questions including the role of smoking and the impact of mixed states in bipolar disorder. We plan

to analyse the data pertaining to illness beliefs and illness behaviour in the forthcoming year.

The Bipolar Depression Rating Scale was developed and first validated by the unit and is a tool that was specifically designed for measuring symptom severity in bipolar depression. It has subsequently been translated into several other languages and validation studies have been replicated.

We have also been fortunate to have a range of collaborations to further investigate issues pertaining to bipolar disorder. These collaborations have allowed our unit access to all the clinical studies of olanzapine in bipolar disorder. We have interrogated the database to see whether a small number of episodes predict a better response to treatment and indeed this appears to be the case. We have done a similar study in the STEP BD databse, and confirmed that stage of illness predicts outcome.

A further focus is on carer-burden in bipolar disorder. A Delphi study to develop guidelines for carers of people with bipolar disorder has been completed, and there are plans to develop an intervention based on the results of the study. This intervention is Internet-based, and is found at www.bipolarcaregivers.org. The evaluation of Moodswings is scheduled to be completed in 2011, after which a broader role out of this an Internet based intervention for people with bipolar disorder can commence.



A new study investigating altered perceptions of time in patients with bipolar disorder commenced in 2010 and is expected to produce novel and interesting data over the next few years.

In 2010 we were enriched by the arrival of three visiting post-doctoral fellows, from Spain, China and Brazil, who joined our bipolar research team.

From left: Dr Marc Udina (Spain), Professor Yiming Wang (China), Dr Pedro Vieira da Silva Magalhães (Brazil)

Dissociation and Changes in the Perception of Time

In our everyday lives, we take for granted the cohesive sense of self, our environment and time, all of which are essential for any activity. When people experience dissociation, these normal perspectives become disturbed, resulting in changed perception of the relationships between objects, the placement of their bodies in space and the flow of events.

These symptoms lead to significant impairment and anxiety. The prevalence of dissociative symptoms in the general community and in psychiatric populations has been underestimated until recently. We now know that up to 80% of psychiatric hospital patients have significant dissociation in addition to their primary diagnosis. The causes of these debilitating symptoms are only partially understood, leading to significant difficulty in management and rehabilitation. A particular area where more research is necessary is understanding of how dissociation in time occurs and how it may be measured.

This doctoral study aims to combine a number of research methods to better understand how the perception of time is altered in psychiatric disease. It has involved an ongoing collaboration between the Department of Clinical and Biomedical Sciences, University of Melbourne and the Department of Physiology, Development and Neuroscience at the University of Cambridge. In particular, the research focuses upon changes in the perception of the "flow" of time and ordering of events. In addition to questionnaires, participants are asked to report the ordering of two flashed lights that are presented close to when they make a large eye movement. This often results in an illusion whereby they see the second flash before the first.

Dr Frank Giorland,(PhD candidate)

We have been investigating physiological models that may explain this effect as well as observing how ketamine alters people's perception of the illusion. The studies have also used MRI imaging to better understand brain regions involved in temporal perception.

The upcoming research will involve recruiting 25 patients with Bipolar Disorder and assessing how their responses to the tests are related to illness. This series of studies aim to provide insights into dissociation from a broad perspective, starting with the person's experience and working towards precise descriptions of how brain function may be altered and contributing to these difficult to treat states.

Drugs and alcohol

Carolyn Coulson (PhD candidate)

Alcohol abuse and dependence in Australia is estimated to cost in excess of 10 billion annually in lost productivity, treatments costs and alcohol related crime, violence and death. Even relatively low levels of alcohol can impact upon social, psychological and physical health, although the threshold for safe levels of alcohol use is incompletely understood. While the harms of excess alcohol consumption receive frequent media attention, a discrepancy still exists between the guidelines for healthy or safe drinking and the consumption patterns of the population. In addition, the link between level of alcohol use and other psychiatric pathology is incompletely understood.

This PhD project aims to investigate within a large community-based sample of men (aged 20-93) the age related prevalence of alcohol consumption and psychiatric co morbidity including the impact on general health, quality of life and subjective wellbeing. Specifically we aim to investigate which patterns of alcohol consumption are associated with an increased likelihood of obesity, frequent falls, common medical conditions and psychiatric disorders such as depression, anxiety disorders including posttraumatic stress disorder and other substance use disorders.

We have currently collected data from over nine hundred male participants with plans to complete assessments in the last half of 2010. The data collected provides us with information about participants' bone health, medical history, clinical measurements (blood pressure, height, weight and waist circumference), psychiatric history, alcohol use, diet, quality of life, subjective wellbeing and physical activity. This data allows us to investigate a wide range of research questions relating to the health of men from the local community. Our research will hopefully enable Australian men to make well-informed decisions about the possible harms associated with alcohol consumption.

Psychiatric Hormone treatment for Women with Mental Illness

Two world-leading trials are being undertaken in Geelong for women experiencing mental illness. These projects are examining whether adding oestrogen to standard antipsychotic medication can improve response to treatment and general well being in women with schizophrenia, schizoaffective, or schizophreniform disorder. The projects, being led by Professor Jayashri Kulkarni, of the Alfred Hospital, in conjunction with Professor Michael Berk from Geelong, and others, are being conducted across Victoria. Dr Barbara Hanna is co-ordinating the Geelong arm of the project. Schizophrenia affects one in one-hundred people and it has a profound impact on people's lives.

Dr Barbara Hanna

It is thought that oestrogen can be protective for women against the early onset of severe symptoms of schizophrenia, such as delusions, hearing voices and reduced cognition. Life-cycle studies have shown that women are more vulnerable for either a first episode psychosis or relapse of existing illness at major hormonal changes such as postpartum, during menstruation and during the menopause. Oestrogen has been found to improve emotional symptoms, memory, information processing and concentration, and with post-menopausal women, improve bone density. Oestrogen is introduced into the pharmaceutical regime through transdermal estradiol patches for the younger women or through oral medication for post-menopausal women, with both regimes being very safe provided regular health checks are carried out. Women of childbearing age wear the patches for 8 weeks whilst post-menopausal women take tablets for12 weeks. Women are not required to cease current medication and they are monitored regularly throughout the trial. The lengths of the trials are short enough so as not to cause the side effects commonly associated with oestrogen use.

The impact of accident circumstance variables on mental and physical health outcomes following serious motor vehicle accidents

With approximately 1 in 5 people being injured in a motor vehicle accident (MVA) over the course of their lifetime, the experience of an MVA is one of the most common traumatic events likely to occur to individuals in Western countries. The extent of physical injuries sustained in these accidents varies from the relatively benign to the catastrophic and the psychological recovery of individuals varies similarly. Somewhat surprisingly, however, the extent of psychological distress experienced by individuals is not always commensurate with the extent of physical injuries sustained. This project will explore the combined characteristics of individuals and MVA circumstances that are likely to produce ongoing psychological distress among MVA survivors.

Jason Thompson (PhD candidate)

It is hypothesised that the accident circumstance variable of perceived fault would delay physical and mental health recovery through the mechanism of learned helplessness and locus of control. MVA survivors who experience an accident where they were not at fault will perceive greater external locus of control in driving situations than clients who were at fault. Similarly, they will be more likely to attribute likelihood of involvement in accidents to external, chronic and global factors.

Stock photo

Grants (2010)

University Department of Clinical and Biomedical Sciences Barwon Health, Community and Mental Health, in partnership with the University of Melbourne, Healthscope and Barwon Health

Ongoing funding for 2010

1) Preventative and early intervention strategies in emerging mental disorders in young people. Pat McGorry, Ian Hickie, Henry Jackson, Alison Yung, Nick Allen, Jane Edwards, Andrew Chanen, Daniel Lubman, Gregor Burger, John Gleeson, Michael Berk, Warrick Brewer. NHMRC – Centre of Clinical Research Excellence (CCRE) – Orygen Youth Health. *$ 2 million.* Duration 2005-2010.

2) Neuroprotective Properties of Quetiapine versus Lithium in a First Episode Mania Cohort: 12-month Neuroanatomical, Neurochemical and Neuro-cognitive Effects and Preliminary Data of Prophylactic Properties (study code D1443C00002).

3) Michael Berk, Karen Hallam, Nellie Lucas, Craig Macneil, Melissa Hasty, Linda Kader, Michaela O'Regan, Thomas Callaly, Philippe Conus, Saji Damodoran, Peter Brotchie, Christos Pantelis, Murat Yucel, Patrick D McGorry. $1.68 million awarded June 2006. Project duration 4 years.

4) Multi-site Double-blind Randomized Controlled Study of Estradiol plus Neuroleptic versus Placebo plus Neuroleptic in the Treatment of Psychotic Symptoms in Women with Schizophrenia.

5) Professor Jayashri Kulkarni; Professor Michael Berk, A/Professor Paul Fitzgerald; Mr Anthony Decastella; Professor Saji Damodaran Maximum $83,842 per year if all milestones met. Stanley MRI #05T-742.

6) NHMRC ID 454356. Developing evidence for the primary prevention of depressive disorders: The role of diet and physical activity. Chief Investigators: A: Prof Michael Berk, B: Dr Julie Pasco, C: Dr Colin Bell, D: A/Prof Evie Leslie, E: Ms Felice Jacka (2007: $23,850 2008 $108,150 2009 $108,150 2010 $117,900 2011 $87,000) Funding approved$445,050.

7) Stanley MRI Oct 2006: Testing the glutathione dysfunction hypothesis of Bipolar Disorder: A Double Blind Randomised Placebo Controlled Trial of N-Acetyl Cysteine. Investigators: Berk, Dodd, Ng, Dean, Copolov, Bush. $769,350.00 over 3 years. SMRI#06TGF-996.

8) BeyondBlue: "Moodswings" Michael Berk, Sue Lauder, Seetal Dodd, Andrea Chester, Leon Pitterman, David Castle. $134,573.

9) NHMRC Project Grant 2007. 509103. A prospective study of inflammatory cytokines as common factors in the aetiology of both depression and osteoporosis. $280,463. A/Pr Julie Pasco, Prof Michael Berk, Dr Margaret Henry, Dr Seetal Dodd. 3 years from 2008-2010.

10) Antioxidants In Unipolar Depression: A Double Blind Randomised Placebo Controlled Trial of N-Acetyl Cysteine. Michael Berk, Felicity Ng, Seetal Dodd, Ashley Bush, Gin Malhi, Olivia Dean. Australian Rotary Health Research Fund (ARHRF). Awarded $59,865.60 for 2010.

11) Depression and Physical illness: The link with pain, cardiovascular factors and osteoporosis (extension study). Michael Berk, Lana Williams, Julie Pasco, Seetal Dodd, Felice Jacka. Eli-Lilly- $ 50 000. Duration 2009-2010.

12) Guidelines for monitoring of patients receiving treatment for Major Depressive Disorder. Michael Berk and Seetal Dodd. Servier. $25,000. 2009-2010.

13) The Efficacy of N-acetylcysteine as an adjunctive treatment in unipolar depression. $400,000NHMRC Project Grant – AWARED October 2009 ID 628395. CIA Prof Michael Berk, CIB Prof Gin Malhi, CIC Dr Seetal Dodd, CID Dr Olivia Dean, CIE A/Pr Jim Lagopoulos, CIF Dr Felicity Ng. TOTAL 2010 $207,500 2011 $192,500.

14) Antioxidants In Unipolar Depression: A Double Blind Randomised Placebo Controlled Trial of N-Acetyl Cysteine. Michael Berk, Felicity Ng, Seetal Dodd, Ashley Bush, Gin Malhi, Olivia Dean. Australian Rotary Health Research Fund (ARHRF). Awarded $59,865.60 for 2010.

15) Efficacy of N-Acetyl Cysteine In Autism: A Double Blind Randomised Placebo Controlled Trial . Michael Berk, Seetal Dodd, Bruce Tonge, Kylie Gray, Avril Brereton. Australian Rotary Health Research Fund (ARHRF) pilot project grant. Awarded $38,500 for 2010.

16) Evaluation of "Moodswings" – Eli-Lilly investigator initiated grant - successful $36,150 commencing April 2009 as per 5 milestones of $7,150 then $7,250.

Successful 2010 Grants

1) NHMRC Training Fellowship Application: 628912 – Jacka. Australian Based Public Health Fellowship. Scientific Title: Lifestyle as a modifiable risk factor for the common mental disorders. AU $285,000 over four years.

2) NHMRC Project Grant Application: 1009367. Scientific Title: Selective serotonin re-uptake inhibitors (SSRIs) and osteoporosis: Mechanisms and clinical consequences. $409,140 over a period of 3 years commencing in 2011. CIA Lana Williams, CIB Jason Hodge.

3) Australian Academy of Science Travel grant 2010- ($6,500) awarded to Dr Lana Williams- "Psychotropic medication use and bone health: Linking a prescription and fracture registry to the HUNT Study, Norway".

4) Neuroscience Research (NSR) grant - Pfizer $34,000 plus $3,400 GST awarded to Steven Moylan - Bipolar disorder in a community sample.

5) Neuroscience Research (NSR) grant - Pfizer $28,000 plus $2,800 GST bipolar study awarded to Frank Giorlando - Altered perceptions of Time in Patients with Bipolar Disorder.

6) RANZCP Young Investigator Grant 2010 - $3722.14 awarded to Frank Giorlando - Altered perceptions of Time in Patients with Bipolar Disorder.

7) ASBD/AZ Scholarship - $61 322.14 over a maximum of 3 years with an initial $5000 plus three monthly instalments awarded to Frank Giorlando.

8) CRC For Mental Illness 201000104 – RP1. Australian Government Department of Innovation, Industry, Science and Research. $23 million over seven years. Michael Berk – Biomarkers and treatment interventions for psychoses and mood disorders.

9) NARSAD Young Investigator Award 2010 – USD $16,350 awarded to Felice Jacka - Contribution of early life diet and nutrition to the development of behavioural problems in children: a large cohort study.

Publications (2010)

1) Macneil CA, Hasty MK, Conus P, Berk M. Termination of therapy: what can clinicians do to maximise gains? Acta Neuropsychiatrica 2010;22: 43-45.

2) Berk L, Hallam KT, Colom F, Vieta E, Hasty M, Macneil C, Berk M. Enhancing medication adherence in patients with bipolar disorder. Human Psychopharmacology 2010;25,1: 1-16.

3) Castle D, White C, Chamberlain J, Berk M, Berk L, Lauder S, Murray G, Schweitzer I, Piterman L, Gilbert M. Group-based psychosocial intervention for bipolar disorder: randomised controlled trial. The British Journal of Psychiatry 2010;196(5);383-388.

4) Lubman DI, Berk M. Pharmacotherapy for co-occurring alcohol and drug disorders in schizophrenia and bipolar disorder: where is the evidence? Acta Neuropsychiatrica. 2010;22(2):95-97.

5) Magalhaes PVS, Berk M, Cereser KM, Kunz M, Gomes FA, Fernandes BS, Jakobson L, Kapczinski F, Gama CS. Validity of the Portuguese version of the Bipolar Depression Rating Scale. Acta Neuropsychiatrica. 2010;22(2):100-101.

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9) Callaly T, von Treuer K, Dodd S, Berk M. Mental health services for young people – the challenge of integrating services. Acta Neuropsychiatrica. 2010; 22(3):158-160.

10) Conus P. Cotton S, Schimmelmann BG, Berk M, Daglas R, McGorry PD, Lambert M. Pretreatment and outcome correlates of past sexual and physical trauma in 118 bipolar 1 disorder patients with a first episode of psychotic mania. Bipolar Disorders. 2010;12(3);244-252.

11) Francey S.M, Nelson B, Thompson A, Parker A.G, Kerr M, Macneil C, Fraser R, Hughes F, Crisp K, Harrigan S, Wood S.J, Berk M, McGorry P.D. Who needs antipsychotic medication in the earliest stages of psychosis? A reconsideration of benefits, risks, neurobiology and ethics in the era of early intervention. Schizophrenia Research. 2010;119(1-3);1-10.

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15) Williams LJ, Jacka FN, Pasco JA, Henry MJ, Dodd S, Nicholson GC, Kotowicz MA, Berk M. The prevalence of mood and anxiety disorders in Australian women. Australian Psychiatry. 2010;18(3):250-255.

16) Grunze H, Vieta E, Goodwin GM, Bowden C, Licht RW, Möller HJ, Kasper S WFSBP Task Force On Treatment Guidelines For Bipolar Disorders. The World Federation of Societies of Biological Psychiatry (WFSBP) Guidelines for the Biological Treatment of Bipolar Disorders: Update 2010 on the treatment of acute bipolar depression. World J Biol Psychiatry. 2010;11(2):81-109.

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31) Fullerton JM, Tiwari Y, Agahi G, Heath A, Berk M, Mitchell PB. Assessing oxidative pathway genes as risk factors for bipolar disorder. Bipolar Disorders. 2010;12:550-6.

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2) Maes M, Galecki P, Chang YS, Berk M. A review on the oxidative and nitrosative stress (IO&NS) pathways in major depression and their possible contribution to the (neuro) degenerative processes in that illness. Progress in Neuro-Psychopharmacology & Biological Psychiatry (in press May 2010).

3) Maes M, Ruckoanich P, Chang YS, Mahanonda N, Berk M. Multiple aberrations in shared inflammatory and oxidative and nitrosative stress (IO&NS) pathways explain the co-association of depression and cardiovascular disorder (CVD), and the increased risk for CVD and due mortality in depressed patients. Progress in neuro-psychopharmacology & biological psychiatry. (in press June 2010).

4) Magalhães PV, Dean OM, Bush AI, Dopolov DL, Malhi GS, Kohlmann K, Jeavons S, Schkaitz I, Anderson-Hunt M, Berk M. N-acetyl cysteine add-on treatment for bipolar II disorder: a subgroup analysis of a randomized placebo-controlled trial. Journal of Affective Disorders. (in press 2010).

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Book Chapters (2010)

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3) Ng F, Cahill C, Malhi G, Berk M. Bipolar II disorder: Assessment and treatment. Book chapter in Bipolar Disorder, a clinician's guide to treatment management. Edited by Yatham LN and Kusumakar V. ISBN 978-0-415-96136-3. Published 2009 Taylor & Francis Group, LLC.

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Conference presentations (2010)

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