

A joint centre of

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The University of Melbourne**

and

**NorthWestern Mental Health
Melbourne Health**

www.neuropsychiatry.org.au

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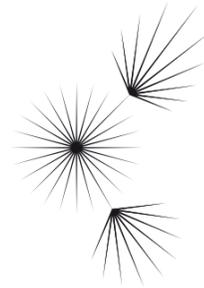
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Melbourne Neuropsychiatry Centre 2006



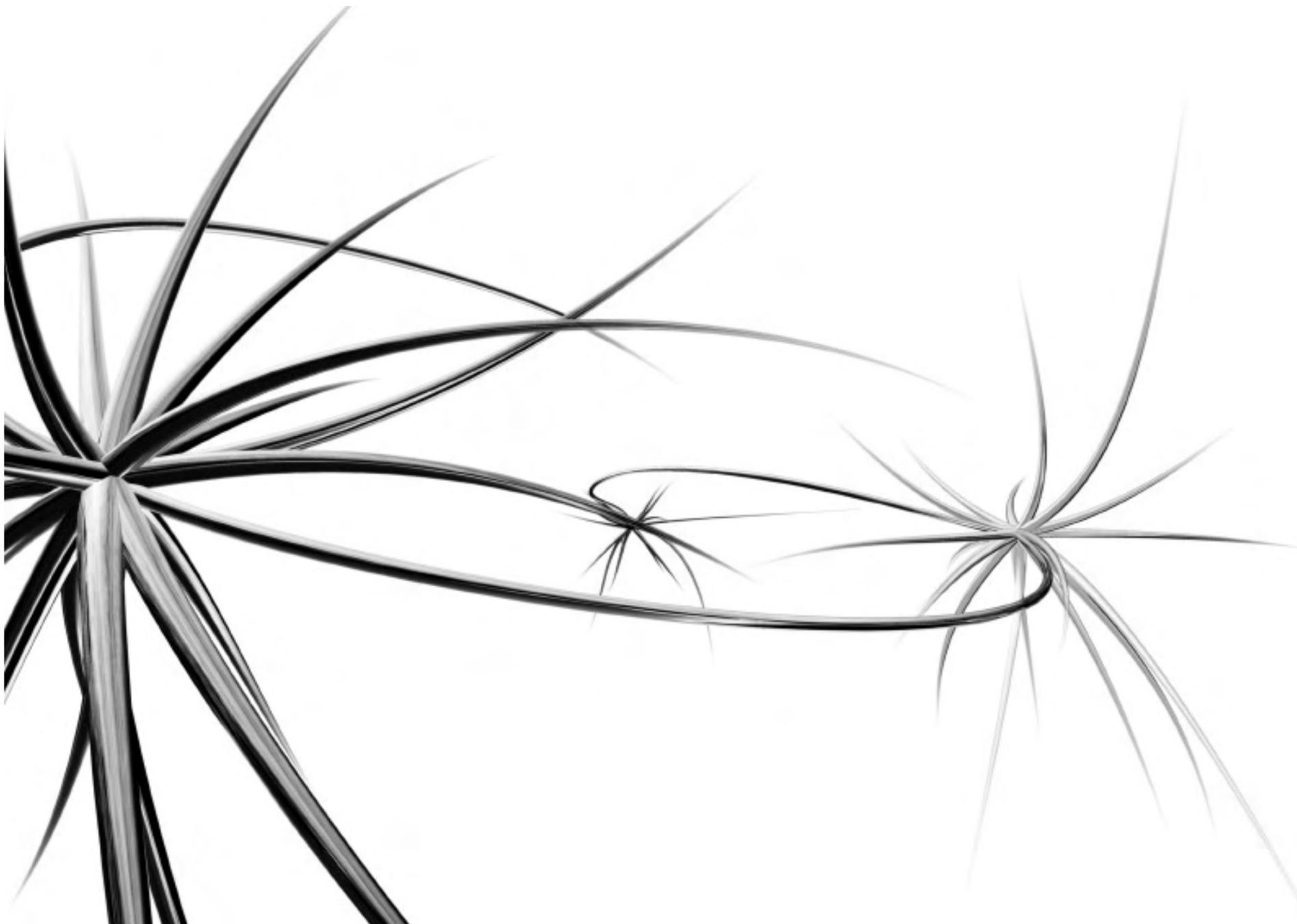
Melbourne
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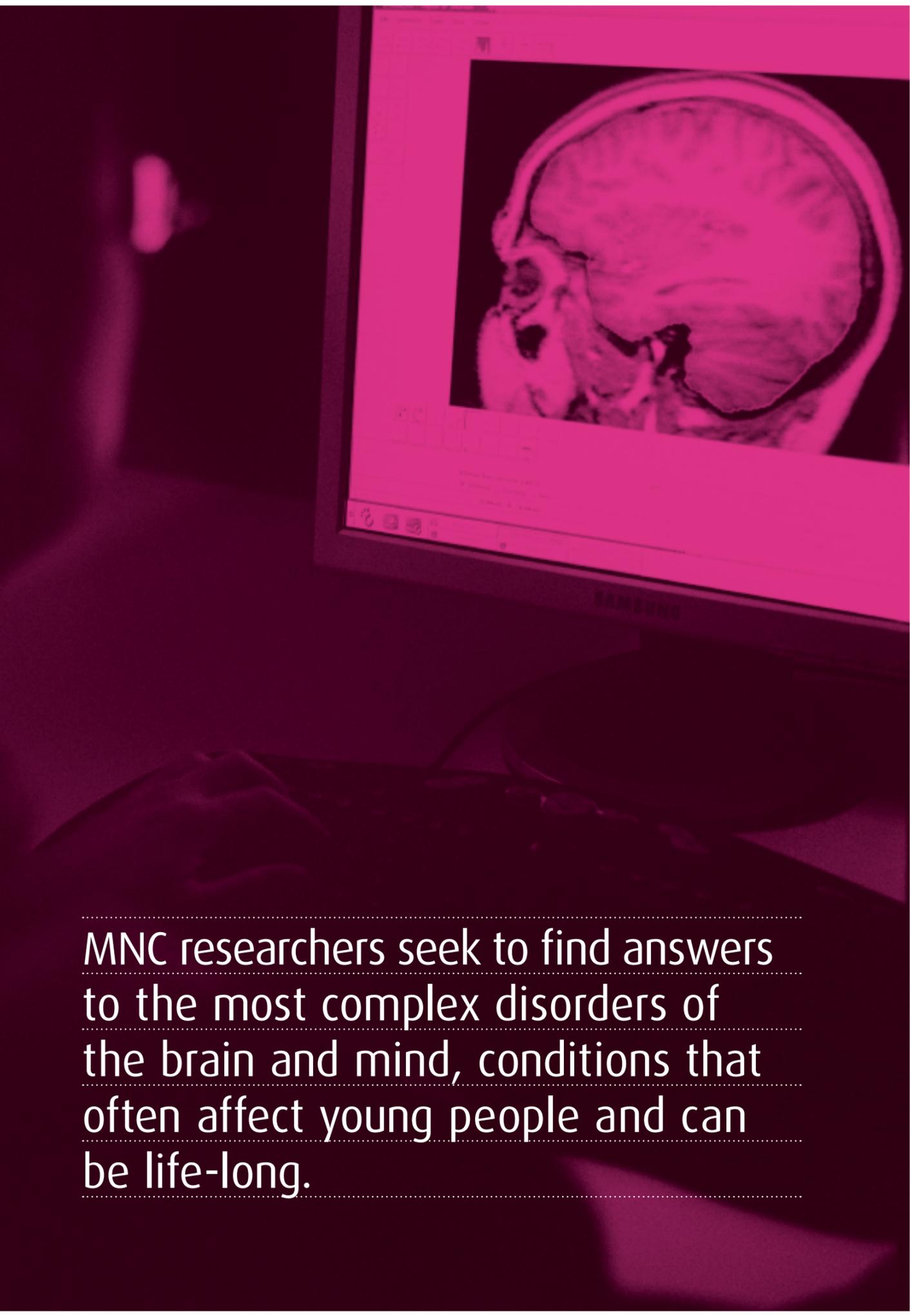
2006
Report



MELBOURNE HEALTH

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MNC researchers seek to find answers to the most complex disorders of the brain and mind, conditions that often affect young people and can be life-long.

1.0

FOREWORD

1.1

Professor Bruce Singh MBBS (Sydney) PhD (Newcastle) FRACP FRANZCP. Divisional Director and Clinical Director, NorthWestern Mental Health. Cato Professor and Head of Department of Psychiatry, The University of Melbourne.

The major clinical and research components of the MNC have been strongly, but informally, aligned since 2001. These links provided the foundation for the 2004 establishment of the MNC as a collaboration between Melbourne Health and The University of Melbourne. The MNC brings together a body of research and clinical expertise which is unique in Australia and will help to advance our knowledge and treatment of neuropsychiatric conditions. The close liaison between research and practice helps attract and retain leading researchers, helps enrich the professional life of academic and clinical staff and leads to better patient outcomes.

Thanks are due to the MNC research and clinical directors, Professor Pantelis and Dr Velakoulis, the Centre's staff, ORYGEN, and other MNC clinical and academic collaborators. In addition to the support of Melbourne Health and The University of Melbourne, thanks are also due to the Department of Human Services Mental Health Branch, the Howard Florey Institute, Neurosciences Victoria and the State Government.

1.2

Professor James A Angus BSc (Sydney) PhD (Sydney) FAA. Dean, Faculty of Medicine, Dentistry and Health Sciences. The University of Melbourne.

The establishment of a Chair in Neuropsychiatry and of the Melbourne Neuropsychiatry Centre reflects the increasing importance of neuropsychiatry as a research and clinical discipline. This development provides unique clinical, teaching and research opportunities for students and graduates across a number of medical and related disciplines.

This report shows that MNC has achieved impressive growth in research performance. It is a very productive group, 'punching above its weight' by producing consistently high levels of output from a relatively small resource base. It maintains a focus on quality, with a high proportion of its papers appearing in high-impact, peer reviewed scientific and medical journals.

Melbourne has recently been ranked in the top 15 global neurotechnology clusters by independent market analysts¹. Melbourne is grouped with Munich, Montreal, Singapore, and Tokyo as an emerging cluster of neurotechnology excellence and a "place to watch". The MNC is rapidly emerging as a key player in the application of neurosciences into psychiatric research and clinical practice.



1.3

Professor Christos Pantelis (MNC Scientific Director),
Dr Dennis Velakoulis (MNC Clinical Director)

This first report of the Melbourne Neuropsychiatry Centre provides an overview about our evolution, our recent work and the inspiring young scientists that are now developing cutting-edge frontiers in neuropsychiatry. Our Centre is characterised by drive, enthusiasm, and the search for excellence, making it a vibrant and generative place to work. We seek to find answers to the most complex disorders of the brain and mind, conditions that often affect young people and can be life-long.

This report represents the culmination of more than a decade of research and clinical work we began in the early 1990's. Prof Pantelis had just returned from London, where he had worked with Prof Thomas Barnes and Dr Hazel Nelson to establish initial work investigating the neuropsychology of schizophrenia. He had also just completed a fellowship at the National Institute of Mental Health (NIMH) in Washington DC, where he commenced imaging work with Dr Daniel Weinberger and Dr Richard Coppola. After returning to Melbourne, and with initial support from Mental Health Research Institute (MHRI), he established the Cognitive Neuropsychiatry Unit at the MHRI and established neuropsychological and neuroimaging work in Melbourne. Concurrently, Dr Velakoulis was training in clinical neuropsychiatry in the Neuropsychiatry Unit at The Royal Melbourne Hospital under the mentorship of Dr John Lloyd. Dr Velakoulis then commenced as a Research Fellow in the Cognitive Neuropsychiatry Unit. In 2000 Prof Pantelis was appointed as Associate Professor and established an academic clinical and research facility at Sunshine Hospital, being the first academic unit in the Western suburbs of Melbourne. In 2001 Dr Velakoulis was appointed Director of the Neuropsychiatry Unit at The Royal Melbourne Hospital.

Our work during this period at the MHRI and then Sunshine and Royal Melbourne Hospitals provided the foundation for brain imaging and neuropsychological investigations of disorders such as schizophrenia and obsessive-compulsive disorder. Many of our current senior collaborators and researchers had started with us at that time, either as students or as registrars in training. They have now developed into independent researchers and clinicians who are inspiring a new generation in neuropsychiatry research and clinical practice. It has been exciting to contribute and facilitate this growth.

We thank Professor Bruce Singh, Professor James Angus and Mr Chris Gibbs for their vision to establish the discipline of neuropsychiatry in Victoria. We are grateful to The University of Melbourne, Melbourne Health, Department of Human Services, the State Government, Neurosciences Victoria, Neurosciences Australia and the Howard Florey Institute for their ongoing support. In particular, we thank Professor Fred Mendelsohn, Professor David Penington, Mr William Hart, Professor Emeritus Sir Gustav Nossal, Dr Paul Scown and Dr Peter Brennan, Dr Ruth Vine, Minister The Honourable Bronwyn Pike and Minister The Honourable John Brumby for supporting the establishment of the Centre.

We thank our collaborators, both national and international, that have led to new initiatives to explore important questions in neuropsychiatry. Most particularly, we thank Professor Patrick McGorry and staff at ORYGEN Youth Health and the ORYGEN Research Centre for their ongoing support and collaboration.

The Melbourne Neuropsychiatry Centre (MNC) is a joint centre of Melbourne Health (NorthWestern Mental Health) and The University of Melbourne (Department of Psychiatry). It comprises the Neuropsychiatry Unit at The Royal Melbourne Hospital (RMH), the Cognitive Neuropsychiatry Unit and Adult Mental Health Rehabilitation Unit (AMHRU) at Sunshine Hospital, and the Neuropsychiatry Imaging Laboratory located at the National Neuroscience Facility within The University of Melbourne, Parkville.

This first report of the MNC provides an overview of the major activities, scientific achievements and key publications that led to the creation of the Centre. The goals of the MNC are:

1. To improve our understanding of disorders of the brain and mind
2. To improve the quality of care for patients with complex mental health problems and disorders
3. To establish a Victorian neuropsychiatry centre of clinical, research and academic excellence, which ensures that specialised knowledge and skill become part of everyday clinical practice
4. To provide neuropsychiatric training and education to mental health professionals and other health disciplines

What is Neuropsychiatry?

Psychiatry is the branch of medicine that deals with the diagnosis, treatment, and prevention of mental and emotional disorders. Psychiatrists use multiple diagnostic and treatment modalities that incorporate biological, psychological and social approaches. Neuroscience involves basic science investigating the structure and function of the brain and nervous system.

Neuropsychiatry is the interface between basic and clinical neuroscience and psychiatry. It includes:

- Neurobiological approaches to the study and treatment of psychiatric disorders (Biological Psychiatry)
- The understanding of disorders in which cerebral or systemic pathology contributes to the mental state (Organic Psychiatry).

The staff at MNC focus on furthering our understanding of neurobiological, psychiatric and psychological factors involved in mental illnesses, through the application of new knowledge acquired from research in a clinical (patient-based) context. Research innovations are made possible by the specialised approach of MNC researchers across a number of disciplines. This includes fields as diverse as neuroscience, psychiatry, neuropsychology, genetics, statistics, medical imaging, mathematics, physics, engineering, and information technology.

Together with the most recent advances in medical imaging and information technology, we are now better placed to understand the structure and functioning of the brain in health and illness than ever before.

The clinical arms of the MNC deal with a wide range of clinical disorders including:

- Severe forms of schizophrenia and psychosis (usually considered as treatment-resistant cases, and often with associated comorbid substance abuse)
- Other severe psychiatric illnesses with associated cognitive, behavioural or functional disturbances
- Atypical and early-onset dementias that manifest with psychiatric and behavioural changes
- Severe psychiatric illnesses associated with brain insults, or with abnormalities on brain imaging
- Neurological and medical illnesses with consequent psychiatric symptoms
- Diagnostically difficult or challenging conditions.

Why is research in this field so important?

Mental health is becoming increasingly important because disorders of the brain and mind (neurological and psychiatric conditions) and their sequelae pose the largest health, economic and social capital burden to Australia of any disease group. According to the Department of Human Services², by 2016 disorders of the brain and mind will represent the highest health burden in Victoria.

In 2003 Prof Pantelis was part of a Prime Ministerial Science Engineering & Innovation Council (PMSEIC) working group to advise the Prime Minister on 'Disorders of the Brain and Mind'. The full report (available at www.dest.gov.au) highlighted the burden of disease issues relevant to schizophrenia and revealed the extent of the ongoing social and functional disabilities that affect these patients and their quality of life. In any one month, some 58,000 Australian adults with schizophrenia or another psychotic illness will be in contact with mental health services.

What is Unique about the MNC?

Ability to Contrast Emerging and Chronic Stages of Illness

The clinical facilities at The Royal Melbourne and Sunshine Hospitals diagnose and treat a broad range of psychiatric conditions particularly patients with chronic, challenging and/or long term conditions including schizophrenia, depression, obsessive-compulsive disorder, bipolar disorder and dementia.

The success of the MNC is strongly tied to its links with a broad range of clinical populations across psychiatry and neurology. In order to investigate the relationship between mental illness and the brain it is important to understand mental symptoms and cognition in a variety of clinical conditions. Through the MNC and its collaborators we are able to undertake research in patients with:

- Chronic schizophrenia (Sunshine Hospital; Adult Mental Health Rehabilitation Unit, AMHRU)
- The earliest stages of psychosis and other disorders, such as personality disorders, substance abuse, depression and bipolar disorder; this includes studying young people at high risk of developing such conditions (with ORYGEN Youth Health & ORYGEN Research Centre (ORC) headed by Prof Patrick McGorry)
- Neurodegenerative disorders, such as younger onset dementia and Huntington's disease (RMH Neuropsychiatry Unit)
- Epilepsy (with RMH Neurosciences Comprehensive Epilepsy Program headed by A/Prof Terence O'Brien)
- Neuropsychiatric sequelae of other neurological conditions (with Neurosciences at RMH, headed by Prof Stephen Davis and Prof Andrew Kaye).

Our approach to psychosis has been to characterise the features apparent in those with advanced illness and then to investigate how these abnormalities have evolved. This is achieved by studying and following up patients at earlier illness stages, and also by studying people who are pre-illness but at a high risk for developing the condition. Using this approach we have provided novel insights into the nature, extent and progression of brain changes in schizophrenia from before illness onset and how these changes relate to outcome.

Importantly, such a longitudinal approach also informs the development of intervention strategies, aimed at delaying or even halting the onset of illness.

Our work in neurological diseases such as epilepsy and neurodegenerative disorders, which are associated with high rates of psychiatric illness, provides us with another window into understanding the neurology of psychosis.

While much of our research relies on describing groups of patients, there is much to be learnt from the description of individual patients. This approach has proved useful in our work, especially for less common conditions or syndromes.

We are now investigating normal and abnormal brain changes during adolescence (in collaboration with project leader A/Prof Nick Allen, ORC) to understand the emergence of psychiatric illnesses.

Academic and Clinical Integration

The structure of the MNC, with clinical facilities at The Royal Melbourne Hospital and Sunshine Hospital, allows for the translation of research findings into clinical practice.

- Patients benefit because the MNC researchers are working at the cutting edge of research
- Medical research is improved by direct contact with patients
- Service delivery is improved by the rapid dissemination and translation of leading edge ideas into wider practice across the hospital system.

An Internationally Unique Library of MRI Brain Scans

The third distinctive feature of the MNC is access to a unique brain imaging databank as a research resource. Prof Pantelis and Dr Velakoulis are pioneers in applying brain imaging to psychiatric research in Australia. In 1993 they established one of Australia's first structural Magnetic Resonance Imaging (MRI) based studies in psychosis and schizophrenia. Since then this MRI brain bank has grown to over 2,500 scans and associated neuropsychological and clinical data across a number of neuropsychiatric conditions. This resource includes an internationally unique cohort of over 250 young people at high risk for schizophrenia and other psychoses, and 334 participants who have had subsequent follow-up scans over a 10 year period. We are now using the latest developments in neuroinformatics to establish this imaging databank (MNC Brain Imaging Library) as a readily accessible research resource and platform. This will facilitate new approaches to imaging analysis and will further foster national and international collaborations.

Summary of Achievements

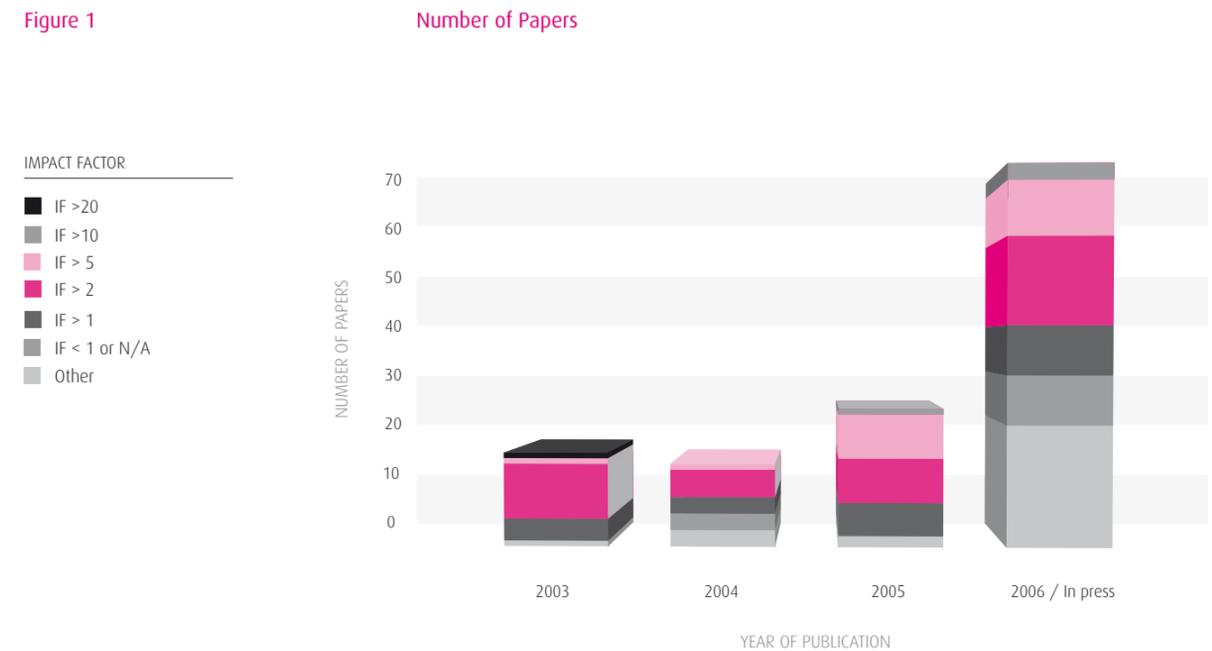
The MNC has succeeded in attracting national and international collaborators and high calibre students from a number of disciplines; has increased its external funding base; and has increased the number of publications in high impact journals (details available at www.neuropsychiatry.org.au).

Successful grants

- Value of projects driven by MNC: \$2,211,933 (18 projects)
- Value of projects where MNC provided collaborative support: \$2,021,041 (14 projects)
 - *This includes grants provided by Philanthropic organizations (Rebecca L. Cooper Foundation and the Norma Licht Trust) and Industry support (incl. Eli Lilly, Bristol-Myers Squibb, Astra Zeneca, Pfizer and the National Institute of Drug Abuse)*
 - *In 2005 the Centre was part of a successful \$7.4 million NH&MRC Program Grant, in collaboration with ORYGEN Research Centre, Department of Psychology at The University of Melbourne and the Brain and Mind Research Institute (Sydney). This is the first Victorian-based Program Grant in Psychiatry and focuses on the different stages of psychosis from before the onset of illness.*

The MNC has published over 100 papers since its inception.

Figure 1



Publications: 125 papers, including two books currently in press

- The growth in journal papers, books and chapter publications since the launch of the Centre in 2004 is illustrated in Figure 1.

Student projects

- Number of student projects: 47 students (2003-2005)
- Number of completed higher degrees: 17 degrees awarded.

In the short time since the MNC was established senior staff have undertaken supervision of over forty students. Many of these projects have already appeared as publications in prominent journals.

Presentations at national and international conferences, including invited talks at symposia and plenary sessions

- Number of conference abstracts >120
- MNC's research leaders are regularly invited to present at national and international meetings.



Research & Clinical Leaders

Top Row (Left to Right):

Dr Linda Kader, Dr Stephen Wood,
Dr Mark Walterfang, Dr Murat Yücel,
Dr Marc Seal & Ms Bridget Soulsby.

Bottom Row (Left to Right):

Prof Christos Pantelis, Ms Barbara
Stachlewski, Dr Dennis Velakoulis
& Mr Jim Murray.

Absent: Dr Amelia Scholes &
A/Prof Robyn Hayes.

Professor Christos Pantelis MB BS MD MRCPsych (UK) FRANZCP.
Professor of Neuropsychiatry, The University of Melbourne
Scientific Director, Melbourne Neuropsychiatry Centre

Prof Christos Pantelis is Foundation Professor of Neuropsychiatry and Scientific Director of the Melbourne Neuropsychiatry Centre at The University of Melbourne and Melbourne Health. He holds honorary Principal Research Fellow positions at the Howard Florey Institute and the Centre for Neuroscience. He is also Director of the Adult Mental Health Rehabilitation Unit (AMHRU) located at Sunshine Hospital, which is a purpose-built 26-bed inpatient unit for patients with severe forms of schizophrenia and other psychoses. Prof Pantelis heads a team of researchers that have been undertaking neuroimaging and neuropsychological work in schizophrenia and psychosis over the last 12 years in Australia. His work has focused on brain structural and functional changes during the transition to psychosis. He is co-Chief Investigator on a \$7.4 million NH&MRC Program Grant, commencing in 2005, that focuses on the neurobiology of emerging severe mental illness during late brain development. He has won a number of national and international awards for his work in schizophrenia, and most recently was awarded the Selwyn-Smith Medical Research Prize from The University of Melbourne. He is currently a Board Member of the Mental Illness Fellowship of Victoria (since 2004), and Board Member of Neuroscience Institute of Schizophrenia and Allied Disorders (NISAD) (since 2004) and member of the Scientific Advisory Council of Neurosciences Victoria (since 2006). He is also a member of various national and international advisory boards and committees on cognition in psychosis, neuroimaging in psychiatry, and drug treatments in schizophrenia. He is on the Editorial Boards of Schizophrenia Research, Australian & New Zealand Journal of Psychiatry, Journal of Cognitive Neuropsychiatry, International Review of Psychiatry, Acta Neuropsychiatrica, and Early Intervention in Psychiatry.

Dr Dennis Velakoulis MBBS MPM DipCrim FRANZCP.
Clinical Director, Melbourne Neuropsychiatry Centre

Dr Dennis Velakoulis is a Consultant Neuropsychiatrist. He was appointed Clinical Director of the MNC in September 2004 and has been Director of the Neuropsychiatry Unit at The Royal Melbourne Hospital since August 2001. Since 1994 he has been involved in the development of a program of neuroimaging and cognitive research in neuropsychiatric disorders, particularly schizophrenia. Dr Velakoulis has published on the role of neuroimaging in clinical psychiatry, and on conditions including organic psychoses and dementia. He has been a chief investigator on 6 NH&MRC grants since 1997 and has over 60 peer reviewed publications, the majority directly related to research arising from these grants. Dr Velakoulis' work is recognised at an international level and provided strong international impetus for the investigation of brain structural changes in the early stages of psychosis. He has been an invited speaker at international conferences, symposia and workshops. Dr Velakoulis' clinical areas of expertise include neuropsychiatric aspects of schizophrenia, epilepsy, Huntington's disease, atypical dementias, movement disorders, other neurological disorders and the development of a neuropsychiatric cognitive screening tool.

Dr Stephen Wood MA (CANTAB) PhD

Dr Wood completed his undergraduate degree at Corpus Christi College, Cambridge, in 1994, followed by a PhD at the Institute of Child Health, London, in 1998. Since migrating to Australia at the end of 1997, he has worked with a number of research groups in Melbourne, and full time with the MNC since early 1999. His primary research interest concerns brain development during adolescence, and how alterations to this developmental process produce altered behaviours (including mental illness). Most of his research work to date has been in early psychosis, and particularly in the ultra-high risk cohort (in collaboration with the PACE clinic, ORYGEN Research Centre). Dr Wood was awarded an NH&MRC Clinical Career Development Award and a Fellowship from the National Alliance for Schizophrenia and Allied Disorders (NARSAD). These fellowships commenced in 2005. He is on the NorthWestern Mental Health Research & Ethics Committee, and the Editorial Board of the journal of Early Intervention in Psychiatry.

Dr Murat Yücel BA (Hons) Clinical PhD (Neuropsychology)

Dr Yücel holds a joint appointment as a Senior Research Fellow/Senior Lecturer at the MNC & the Substance Use Research and Recovery Focussed (SURRF) Program at ORYGEN Research Centre and The University of Melbourne. His work involves neurobiological and cognitive-affective neuroscience research into psychiatric disorders, as well as drug and alcohol abuse. Dr Yücel also has professional training in clinical neuropsychology and has been working in the field of neuropsychiatry for a number of years. His work has been well-received internationally, as is evident by his publications in leading international journals and presentations at national and international conferences. Dr Yücel has won awards at major international conferences including a Young Scientist Award at the 10th Biennial Winter Workshop on Schizophrenia in Davos, Switzerland as well as a Young Investigator Award at the 11th Biennial Meeting, International Congress on Schizophrenia Research, Colorado, USA. He is also the member of several national and international organisations, registration boards and research committees. He is on the NorthWestern Mental Health Research & Ethics Committee and on the Editorial Board of Acta Neuropsychiatrica.

3.5

Dr Marc Seal BBSc (Hons) PhD

Dr Marc Seal is currently employed as a Post Doctoral Research Fellow with the MNC. His appointment followed a series of accomplishments including the NARSAD Young Investigator Award (2003-2004), an International Travelling Fellowship Award from the Wellcome Trust (2001-2003), and a National Institute of Health (US) Postgraduate Travel Award (2000). During his international fellowship, Dr Seal studied at the Neuroimaging and Brain Imaging Analysis Unit at the Institute of Psychiatry, London. This opportunity permitted Dr Seal to develop specialised knowledge in neuroimaging techniques that are invaluable to the MNC and its research investigations. Dr Seal is currently involved in a number of research investigations within the MNC as well as national and international collaborations. These include studies examining cortical changes and cognitive deficits that occur in schizophrenia and bipolar disorder, the effects of illicit drug use on cognition, and a study examining brain activation in deaf individuals using sign language. Dr Seal has also completed professional training in clinical neuropsychology.

3.6

Associate Professor Robyn Hayes BOccThy GradDipp Com PhD

A/Prof Robyn Hayes currently holds a joint position with NorthWestern Mental Health (NWMH) and La Trobe University, School of Occupational Therapy. She has been working in both the research and clinical fields of occupational therapy for approximately 29 years and has extensive knowledge regarding people with serious mental illness. A/Prof Hayes has conducted clinical research studies with individuals experiencing mental illness, particularly schizophrenia. She also provides consultation on investigations conducted within her role at NWMH. She has published in high-quality international peer-reviewed journals, and has had two papers rated as "of outstanding interest" by Current Opinion in Psychiatry. She is also a reviewer for US National Institute of Mental Health (NIMH) and the Behavioural Science Track Awards for Rapid Transition (B-START), and is a regular reviewer for several journals including the Australian Occupational Therapy Journal, the Scandinavian Journal of Occupational Therapy, the Australasian Journal on Aging, and Schizophrenia Research.

3.7

Associate Professor Geoff Stuart BA BSc (Hons) PhD

A/Prof Geoff Stuart has an extensive research career with expertise in both the psychopathology of schizophrenia and also a major interest in structural neuroimaging in psychiatric disorders. He has published numerous papers in peer reviewed journals, including papers in the foremost psychiatry and neurology journals. Based on expertise he brought from extensive early work in biostatistics and visual sciences, A/Prof Stuart developed a new method for the accurate and rapid measurement of intracranial volume on T1 MRI images, an important control for global atrophy when measuring the volume of brain structures. In 2000 he was awarded the highly competitive U.S. NARSAD Young Investigator Award (National Alliance for Research on Schizophrenia and Depression) to develop novel imaging methods for structural imaging in schizophrenia. This two-year funding enabled A/Prof Stuart to examine the different registration techniques used in automated neuroimaging analysis and to develop a technique that looks specifically at the 3-D morphometry of brain and skull structures. He has been invited to present at various conferences including Human Brain Mapping and the International Congress on Schizophrenia Research. A/Prof Stuart worked actively with the Centre until the end of 2005.

3.8

Dr Mark Walterfang MBBS (Hons) FRANZCP

Dr Walterfang graduated in medicine from The University of Queensland with honours in 1993, and completed his Fellowship of the Royal Australian and New Zealand College of Psychiatrists in 2000. He has been a Consultant Neuropsychiatrist at The Royal Melbourne Hospital Neuropsychiatry Unit since 2001. His past appointments have included Consultant Psychiatrist at the Adult Mental Health Rehabilitation Unit at Sunshine Hospital (2001-02), Academic Fellow at The University of Melbourne Department of Psychiatry (2001-02) and Senior Research Fellow at the Mental Health Research Institute as part of a Stanley Foundation Centre Grant (2003-05). Dr Walterfang is currently undertaking a PhD investigating the corpus callosum and other white matter tracts in patients at different stages of psychosis, using multiple MRI imaging modalities. His interest in white matter disorders has led to a number of clinical studies in neurological and neurodegenerative disorders such as Niemann-Pick Type C and adrenomyeloneuropathy. Dr Walterfang has also played a leading role in the development and validation of a number of clinical tools (NUCOG, Cogrisk, BATCH) for the assessment of cognition and behaviour.

3.9

Dr Linda Kader MBBS MD FRANZCP

Dr Kader is a consultant psychiatrist recently employed at the Adult Mental Health Rehabilitation Unit (AMHRU), Sunshine Hospital. She completed her basic medical training at the All India Institute of Medical Sciences, New Delhi, in 1996. She specialised in psychiatry at the same institute in 2001. Her MD thesis was a family study of 126 patients with schizophrenia using family history methods. Dr Kader came to Melbourne in early 2002 and worked initially at Orygen Youth Health, Melbourne where she has been involved in a research project in first-episode bipolar disorder. In 2005, she obtained her Fellowship with the Royal Australian and New Zealand College of Psychiatrists. Dr Kader's interests include early psychosis, neurobiology of schizophrenia, treatment-resistant disorders, bipolar disorder, psychiatric genetics and psychotherapy. She was awarded Best Intern during her medical training and a Travelling Fellowship from the Royal College of Psychiatrists, UK.

3.10

Dr Amelia Scholes BA Hons DPsy (Clin Neuro) MAPS CCN

Dr Amelia Scholes is a neuropsychologist with extensive experience across neuropsychiatry, aged psychiatry, and child and adolescent psychiatry. She is currently the Senior Neuropsychologist at the Neuropsychiatry Unit, The Royal Melbourne Hospital and Alfred Hospital Child and Adolescent Mental Health Service. She manages and coordinates the neuropsychology program at the Neuropsychiatry Unit, The Royal Melbourne Hospital. This role includes the provision of professional development programmes, telepsychiatry consultations, student training, and liaison with universities and psychology/psychiatric services. Dr Scholes completed her doctoral thesis examining the effectiveness of a self-monitoring/family counselling intervention for children with ADHD and their families. Her subsequent research has included studies into the health and coping strategies of parents of adolescents with cystic fibrosis, the patterns of psychotropic drug use in SRS residents, the cognitive outcomes of bitemporal versus bifrontal ECT, and working memory function in children with writing disorders. Dr Scholes is currently supervising a study of neuropsychological functioning in patients on chemotherapy and has played a lead role in authoring two booklets on younger onset dementia in collaboration with the Alzheimer's Association.

4.0

PROFILES OF SENIOR ADMINISTRATION STAFF

4.1

Mr Jim Murray Business Manager BBus MEI Grad Dip App Finance

Mr Murray provides management services to the MNC. He is CEO of Atholl Business Consulting, which advises on the business aspects of technical and scientific organisations. He has advised Melbourne, Monash, RMIT, Deakin and Swinburne Universities, as well as the CSIRO, CRCs, independent research institutes and spin-off companies. He has led projects ranging from organisation restructures, business planning, feasibility studies, market research and commercialisation. Mr Murray is a former Director, Business Strategy in the Melbourne practice of the global accounting firm Ernst & Young. He is a Director of the MonashLink Community Health Centre and a Director of the BioMelbourne Network.

4.2

Ms Barbara Stachlewski Office Manager & Personal Assistant

Ms Stachlewski has been with MNC since 1997 following a career in providing administrative support for clinical and academic services at the Mental Health Research Institute (MHRI) and the Royal Park & Alfred Hospitals. Ms Stachlewski's expertise in academic and administrative support has been instrumental to the development of the MNC, including the period of the Centre's formal establishment, and leading into its expansion to the Sunshine Hospital and Parkville campuses. Her current interests and objectives are to further develop the workflow processes used in the running of MNC, including finances, human resources, in addition to staff, student and visitor coordination and support.

4.3

Ms Bridget Soulsby Information Technology and Laboratory Manager BSc

Ms Soulsby started with the Centre in 1998 as an undergraduate student from Swinburne University of Technology whilst completing her degree in Medical Biophysics and Instrumentation. Ms Soulsby has developed expertise in neuroimaging analysis techniques and has organised and developed the Centre's data and information resources. In 2004 Ms Soulsby designed and installed the Neuropsychiatry Imaging Laboratory in the Parkville campus, providing storage for over 2,500 MRI scans already acquired, as well as the resources required for neuroimaging analyses. Ms Soulsby is currently undertaking her Masters in Information Management and Business Systems and her areas of interest within the MNC are in developing the Centre's MRI Bank/Library, informatics and neuroimaging methodologies.



Together with our collaborators*,
our centre was the first to show that
brain changes occur as schizophrenia
is developing.

* ORYGEN Research Centre (Melbourne),
Institute of Psychiatry (London) and Cambridge University (UK)

5.0

RESEARCH & CLINICAL STREAMS

The MNC specializes in five streams that are described below. Each of these streams is led by the MNC's research leaders and is directed by work that has developed from their respective research and clinical interests. The senior staff work collaboratively across each stream so, while the streams help to provide an overview of the research areas in which we are all involved, there is substantial overlap across these areas and they are generally integrated.

5.1

Schizophrenia & Affective Disorders

Research Approach

Prof Christos Pantelis has focussed on all stages of psychosis from pre-psychosis (individuals at incipient risk of developing a psychotic illness) through to patients with chronic schizophrenia. His most influential work has been studies at the earliest stages of the illness.

In a series of papers, including a landmark paper published in the Lancet in 2003, he and his team, in close collaboration with ORYGEN Research Centre, Cambridge University and the Institute of Psychiatry (UK), demonstrated for the first time that progressive brain changes occur in schizophrenia and early psychosis during the transition phase, from a premorbid 'ultra-high risk' state to active psychotic illness. He also demonstrated that abnormalities were apparent prior to onset of psychosis; findings that may be relevant to predicting who is at incipient risk of developing a psychosis. Prof Pantelis was awarded the Selwyn-Smith Medical Research Prize from The University of Melbourne for this work.

Further work on the neuropsychological functioning at the earliest stages of psychosis has also identified potential markers of illness or its prognosis, including findings that spatial working memory (Wood et al) and the ability to identify smells (Brewer et al) are apparent prior to illness onset. This research has confirmed that progressive changes commence before the onset of illness and continue over the first two to four years of schizophrenia. This work has challenged the dominant notion that these brain abnormalities in psychosis and schizophrenia have necessarily occurred during early brain development (pre- or peri-natal).

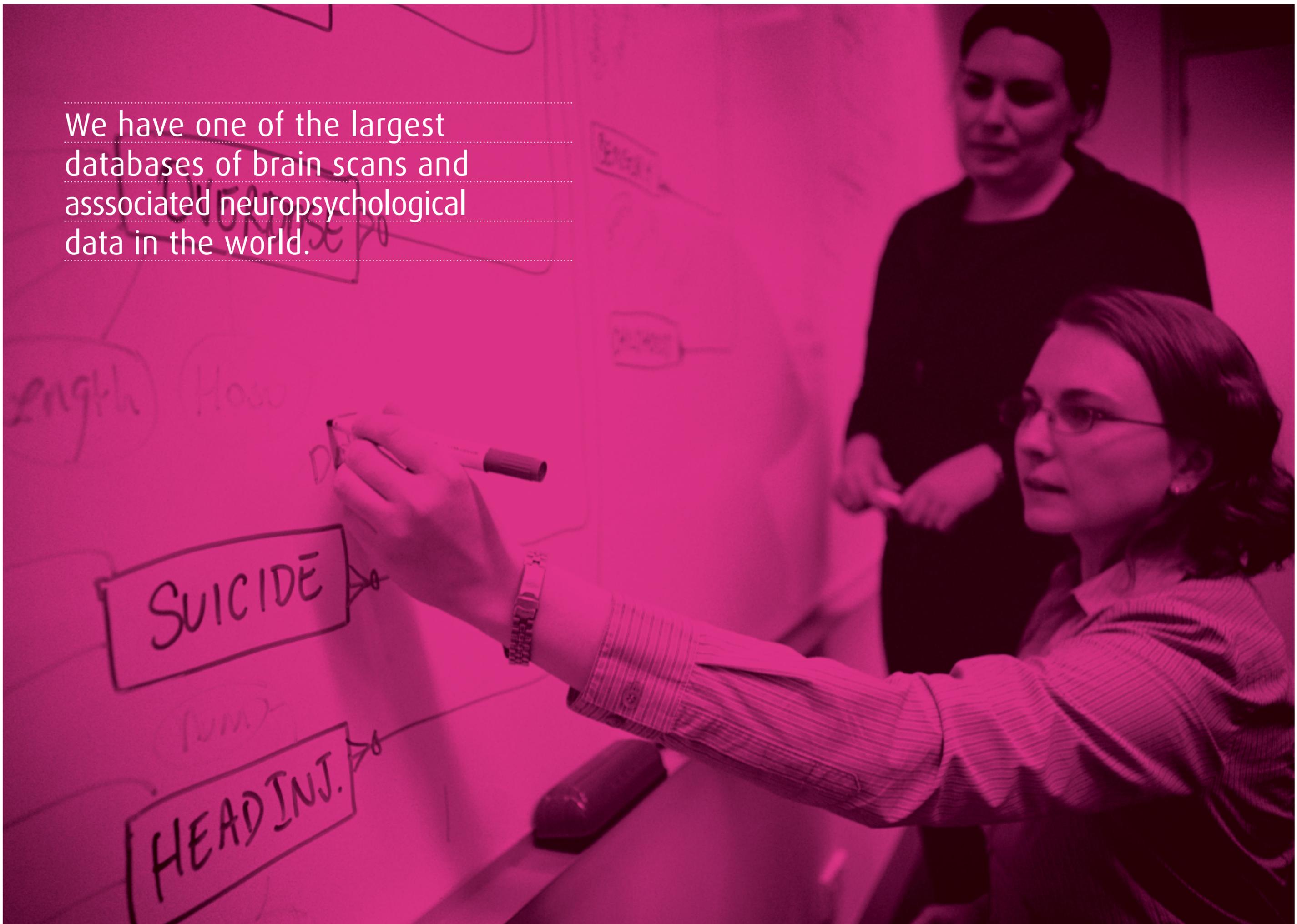
These studies have led to further longitudinal work to examine the nature, extent and timing of progressive brain changes in psychotic disorders, including schizophrenia and mood disorders. These changes are being considered in the context of normal and anomalous brain maturation (see Adolescent Development of Brain & Behaviour section below).

Research Goals

The work of this stream aims to better understand the brain mechanisms involved in schizophrenia, bipolar and other mood disorders. By mapping the nature and extent of brain structural and functional changes throughout their course we hope to:

- Understand the brain mechanisms underlying these conditions
- Link the clinical features to the brain changes
- Understand how interventions can modify these changes and improve patient outcomes.

We have one of the largest
databases of brain scans and
associated neuropsychological
data in the world.



Research Highlights

We have been developing and using newer imaging analysis techniques to study these conditions cross-sectionally and longitudinally. The work in this stream has been in close collaboration with Prof Patrick McGorry, A/Prof Alison Yung, Dr Lisa Phillips and their colleagues at ORYGEN Research Centre. Increasingly, we are also taking a brain maturational perspective to understanding these dynamic brain changes in psychosis (this is further elaborated in the Adolescent Development of Brain & Behaviour stream below).

Progressive brain changes in psychosis

Dr Daqiang Sun, co-supervised by A/Prof Geoff Stuart, undertook longitudinal MRI studies as part of his successful PhD thesis. They demonstrated that such changes are dependent on both the stage of maturation of the brain and the age at which the illness develops, and that the observed changes are relevant to understanding functional deficits. More recently, Dr Sun has been working at UCLA in Prof Tyrone Cannon's lab. This productive collaboration with Prof Cannon, Prof Paul Thompson and their colleagues at UCLA (USA) is further exploring brain changes in these early illness stages using sophisticated methods developed in their lab.

Dr Stephen Wood has been undertaking a range of research projects in schizophrenia at its earliest stages, including investigations of memory and brain imaging studies. His expertise in using Magnetic Resonance Spectroscopy (MRS) has provided insights into the chemistry of the living brain. An important study from this work has identified that N-acetyl-aspartate (NAA: a marker of neurons) levels in the dorsal part of the brain's frontal lobe at the onset of schizophrenia predicts outcome at two years. This work was accepted for publication in the Archives of General Psychiatry.

In an NH&MRC funded study, Dr Dennis Velakoulis and Dr Stephen Wood, Casey O'Brien and colleagues from ORYGEN Research Centre have completed an investigation examining brain imaging and neuropsychological changes 10 years after a first psychosis episode. Preliminary findings will be presented at the International Congress of Schizophrenia Research (ICOSR) in 2007.

Stress, HPA function and pituitary volume

In collaboration with Dr Carmine Pariante and colleagues from London's Institute of Psychiatry as well as colleagues from Athens, we have investigated the role of stress in explaining brain changes during illness onset. In seminal publications this work has demonstrated that enlarged pituitary volumes are apparent in the high-risk individuals who subsequently develop psychosis and in first-episode psychosis patients. The enlarged pituitary is considered to reflect abnormal HPA function related to stress hormones, which may explain the brain structural changes observed. Measures of the stress hormone cortisol are now being examined in relation to brain structural measures. Dr Belinda Garner undertook the work on pituitary size in the pre-psychotic groups as part of her PhD thesis, and also looked at rat models of stress and their impact on function (in collaboration with Dr Maarten van den Buuse from MHRI).

Genetic vulnerability

The Australian Study of Twins with Psychosis (ASTP) is a large, multi-centre study being conducted in collaboration with Prof Bryan Mowry and colleagues from The University of Queensland. This study is concerned with identifying neuroimaging and cognitive markers of genetic vulnerability to psychotic disorders such as schizophrenia and bipolar disorder. Findings will be used to guide molecular genetic research in an attempt to identify new susceptibility genes for mental illness. Dr Gregor Berger (ORYGEN) has also established a biobank for genetic material, which will allow us to assess how genetics are related to the abnormal brain indices identified in schizophrenia and psychosis.

Bipolar disorder

Together with Prof Michael Berk and other colleagues from Barwon Health, researchers from MNC are about to commence a study investigating the neuroanatomical and neuropsychological changes in bipolar disorder. This project aims to investigate whether there are any correlations between cognitive performance and alterations to brain structures, in the hope of developing a greater understanding of bipolar disorder and the way in which it affects an individual's life. Further work in bipolar disorder is underway with Dr Gin Mahli (Black Dog Institute, NSW) and Dr Sophia Frangou (IOP, London).

Subcortical structures

Dr Dennis Velakoulis, Dr Stephen Wood and colleagues have also undertaken one of the largest studies of hippocampus and amygdala size at various stages of psychosis and schizophrenia, from before illness onset. This study was published by Archives of General Psychiatry and shows that smaller hippocampi are found in established schizophrenia while enlarged amygdalae are found in non-schizophrenic psychoses.

Dr Mark Walterfang and Dr Marc Seal are also undertaking a series of studies examining white matter changes in schizophrenia and early psychosis in a number of collaborations including Monash Neurosciences, Brain Research Institute, The University of Queensland, and colleagues from Toyama University (Japan).

As part of his PhD thesis, Dr Mark Walterfang has examined the major white matter tracts connecting the two sides of the brain, the corpus callosum. He has shown that abnormalities are evident prior to the onset of a psychotic episode. Further changes develop with progression of the illness, involving those areas of the callosum that connect with other brain regions implicated in schizophrenia.

The anterior cingulate cortex

Dr Murat Yücel is investigating the anterior cingulate cortex (ACC) in schizophrenia and obsessive-compulsive disorder as part of an NH&MRC funded study, as well as other disorders, including depression, bipolar disorder, substance use and personality disorders (discussed further below). A number of PhD students are working closely with him on this work:

- Dr Ben Harrison recently completed his PhD, examining the ACC in schizophrenia from illness onset and is now undertaking a NH&MRC CJ Martin post-doctoral fellowship to pursue this work further. He is working with Prof Jesus Pujol in Barcelona and will be returning to complete his fellowship with MNC
- Alex Fornito, PhD student is examining the ACC in detail comparing schizophrenia and bipolar disorder. In this series of studies he is assessing the ACC and its connections with the frontal brain regions, and is also examining the cognitive and emotional parts of the brain and how they are affected in these disorders.

Intervention and treatment

In collaboration with Dr Gregor Berger at ORYGEN Research Centre, we have been examining the neurobiological effects of interventions used in psychosis, including fish oils, lithium and various antipsychotic drugs.

In collaborative work on an NH&MRC funded study headed by A/Prof Brian Dean and Dr Suresh Sundram from MHRU, we are examining the role of muscarinic receptors on cognition in schizophrenia. These receptors may be relevant to the features of the disorder and to treatment.

Sunshine Hospital Node - Adult Mental Health Rehabilitation Unit (AMHRU)

A/Prof Robyn Hayes and Ms Deidre Bradshaw offer a unique contribution to the team by focusing on the psychosocial and behavioural aspects of mental illness and the impact that it places upon the individual, family and friends, and the community. They are seeking to understand the varied types of problems, including neuropsychological difficulties, that individuals with mental illness are experiencing by assessing their needs within clinical settings or the home environment. From this they aim to develop environmentally adaptive intervention strategies to help with these problems 'in situ'.

In a further collaboration with A/Prof Carol Harvey, Gillian Plant (The University of Melbourne) and Ms Ellie Fossey (La Trobe University) we are examining whether neuropsychological ability predicts psychosocial functioning in patients with schizophrenia living in the community.

Dr Linda Kader is conducting research on non-biological modes of treatment for the predominantly treatment-resistant patient group in the Unit. Creative arts therapy, music therapy, and drama therapy are being evaluated. These interventions can improve therapeutic alliance, communication, engagement and risk reduction.

In collaboration with A/Prof Tim Lambert (OPEN, The University of Melbourne) we have investigated medical comorbidity in patients with chronic schizophrenia including obesity, diabetes and high levels of cholesterol and other lipids. We have also investigated the adverse effects on the heart of treatment with clozapine and are now working with Prof Michael Berk and colleagues at Barwon Health who have also been examining these problems.

5.2

Clinical Neuropsychiatry at RMH

Dr Dennis Velakoulis is the Clinical Director of the Centre and is also the Director of the Neuropsychiatry Unit, which is a Victoria-wide service that is located at The Royal Melbourne Hospital (RMH). It is an 8-bed inpatient unit with an average length of stay of 10 days. Dr Velakoulis' main interest is clinical research, education in neuropsychiatry and excellence in clinical practice of neuropsychiatry.

Clinical Goals

The Neuropsychiatry Unit at RMH specialises in a range of clinical disorders and treatments including:

- Younger Onset Dementia (YOD)
- Huntington's disease
- Epilepsy and psychiatric disorders
- Creutzfeldt-Jacob disease
- Movement disorders
- Neurological disorders that present as psychiatric phenocopies
- Intellectual disability
- Treatment-resistant psychiatric disorders (particularly schizophrenia)
- Cognitive impairment in psychiatric disorders
- Electroconvulsive Therapy (ECT)
- Psychosurgery (RMH is the only site undertaking these medical procedures).

Education programs

The neuropsychiatrists and neuropsychologists at RMH run a regular seminar series for mental health clinicians interested in diagnosing and managing complex neuropsychiatric disorders. Workshops and seminars previously conducted include:

- Problem-solving rare, unusual and complex clinical neuropsychiatric dilemmas
- The assessment and management of brain impairment
- Neuropsychiatry in the aged
- Managing behaviour change
- Diagnosis and management of YOD.

Younger Onset Dementia has been an area of clinical and research interest at the Neuropsychiatric Unit, and several workshops and symposia have been presented at national conferences on this topic. In conjunction with Alzheimer's Australia, the Neuropsychiatry Unit has developed an information book for carers and clinicians working with patients suffering YOD.

More recently the Neuropsychiatry Unit has received a grant from the Mental Health Branch to archive and collate clinical video material into a Multimedia Clinical Archive. The archive includes past videos collected by Dr John Lloyd (Director Neuropsychiatry Unit 1973-2001) and ongoing video collection. This archive will ensure that educative and informative clinical material can be made widely available to clinicians and students.

Our group is one of the first to show how intellectual and thinking ability develops in adolescence and how this is affected as mental illness develops.

Neuropsychology

The neuropsychologists at RMH provide onsite supervision for rural psychologists, involving supervision and training over a two week period. Through telepsychiatry (a psychology rural outreach program) the team provides monthly supervision sessions for psychologists working in aged psychiatry and a monthly case discussion and professional development for other Southwest Healthcare Network psychologists.

Clinical students

The RMH environment is active in training students from Masters and Doctorate Clinical Neuropsychology programs, as well as students completing Advanced Medical Science, Occupational Therapy, and Social Work degrees.

Neuroimaging tools used in our clinical neuropsychiatric practice

Consultant Neuropsychiatrists in the Unit have expertise in integrating the findings from neuroimaging with clinical presentations of patients. This expertise derives from years of clinical and research experience with neuroimaging of neuropsychiatric disorders.

Patients benefit from the latest MRI scanning techniques, which:

- Have greater sensitivity to detect and monitor early brain changes in neurodegenerative disorders
- The on-site single-photon emission computed tomography (SPECT) scanner allows us to monitor changes in brain metabolism
- Electroencephalography (EEG) is also used in neuropsychiatric conditions, including delirium, epilepsy, and drug withdrawal states.

Research Areas & Approach

The Neuropsychiatry Unit has a long history of clinical collaboration with Clinical Neurosciences at The Royal Melbourne Hospital.

In close collaboration with A/Prof Terence O'Brien and Dr Raju Yerra of the Comprehensive Epilepsy Program a number of research projects in the neuropsychiatry of epilepsy have commenced. The studies include:

- A retrospective study examining co-morbid neuropsychiatric disorders in patients with focal epilepsy. This includes comprehensive neuropsychiatric, neuroimaging and neurological evaluations undertaken over the last ten years
- Dr Sophia Adams is undertaking her PhD in a prospective follow-up study of these patients that will provide important information about the course of epilepsy and the relationship between epilepsy and neuropsychiatric disorders
- The outcome of patients with first seizures compared with concurrently treated patients with non-epileptic seizures is also being investigated.

Phylis Chua is undertaking her PhD examining pre-onset Huntington's disease individuals identified by genetic screening. She has assessed them comprehensively using neuropsychological, clinical and brain imaging techniques.

Case Studies: The clinical populations at the Neuropsychiatry Unit include patients with rare or atypical conditions, which provide insights into the relationship between brain pathology and mental or cognitive symptoms.

Clinical tools designed by the RMH team

The clinical team at RMH has developed three useful screening tools, the Neuropsychiatry Unit Cognitive Screen (NUCOG), the Behavioural Assessment Tool for Cognition and Higher function (BATCH), and the CogRisk (see www.neuropsychiatry.org.au).

- The NUCOG is a bedside battery that has been used in neuropsychiatric populations to assess cognition in medical or psychiatric patients. It assists clinicians in their assessment of cognitive deficits
- The BATCH uses systematic observation and recording of ward-based behaviours to assess cognitive function in patients who cannot be formally tested
- The CogRisk is a carer questionnaire that provides information on the patient's demographics, cognitive risk factors and cognitive symptoms.

5.3

Adolescent Development of Brain & Behaviour

Dr Stephen Wood is investigating brain maturational changes occurring during early childhood and adolescence, and how these may affect the development of reasoning and decision-making skills. He aims to identify risk and resilience factors that may contribute or prevent the development of different mental illnesses.

Research Goals

Until relatively recently, adolescence was not regarded as an especially important time for brain development. Most focus was on the prenatal or early childhood period, when the brain is constructed and motor and language functions are brought online. However, we are now paying much greater attention to adolescence for the reason that morbidity and mortality rates increase 200% from early school age. This is not the result of cancer, heart disease or infection – instead, this is related to difficulties in the control of behaviour and emotion, resulting in accidents, suicide, depression, substance abuse and so on. The aim of the stream is to better understand the changes in reasoning and decision-making that occur from childhood through adolescence to adulthood, and to discover the alterations in brain structure and function that underpin them. In doing so, we hope to understand how the onset of mental illness impacts on the way the brain develops, and whether the normal trajectory of brain maturation is disrupted.

Research Areas & Approach

The approach we take considers both normal and abnormal development. By combining neuroimaging and neuropsychological methods, we are able to examine brain changes over time in healthy subjects, and compare these with the pattern of changes seen in mental illnesses such as schizophrenia, bipolar disorder, depression and substance abuse. Further, we can also apply these methods to neurological disorders where early damage to the brain has occurred, such as malformations of cortical development, prematurity or childhood onset epilepsy.

Research Highlights

- A collaborative study with Prof Vicki Anderson and Dr Rick Leventer at the Murdoch Children's Research Institute and the Royal Children's Hospital has investigated children experiencing neurodevelopmental lesions (malformations of cortical development). These anomalies in the migration of the brain's grey matter can result in children early in life having developmental delay, intellectual disability, epilepsy, or significant motor impairment
- PhD student, Cinzia de Luca has examined the cognitive, behavioural and social development of children with these malformations in an attempt to understand the contribution of abnormal brain formation to the development of psychopathology later in life
- The Adolescent Early Development Study: Prof Christos Pantelis, Dr Murat Yücel, Dr Stephen Wood, Dr Ben Harrison, Alex Fornito and other MNC researchers are involved in a large prospective, longitudinal study led by A/Prof Nick Allen following a unique cohort of over 150 12-13 year old pre-pubertal children. These children have been strategically selected from a community sample of 2500 children for this investigation, which is examining temperament as an investigative tool for the identification of both 'risk' and 'resilience' factors related to the development of mental disorder in adolescence.

5.4

Impulsive, Compulsive & Addictive Behaviour

Dr Murat Yücel is investigating the neural and psychological bases of impulsive, compulsive and addictive behaviour. Using the latest neuropsychological and neuroimaging techniques, he is investigating how prefrontal and cingulate brain networks mature through the life-span and how disruptions to them can lead to the maladaptive behaviours and symptoms that characterise psychiatric and addictive disorders.

Research Goals

The complex demands of everyday life require us to continually monitor and adjust our behaviour to ensure our actions generate favourable outcomes. This adaptive regulation of behaviour involves a dynamic interplay of cognitive, emotional and motivational processes. Disturbances in these interactions lead to maladaptive behaviours that often characterise psychiatric disorders. The goal of this research stream is to characterise how individual differences in key psychological and biological (including genetic) measures determine the individual's susceptibility to develop impulsive, compulsive and addictive behaviour.

Research Areas & Approach

The key psychological and biological measures of focus are:

- Brain maturation (especially during early childhood and adolescence)
- Cognition (e.g. attention, inhibition, intelligence)
- Emotion (e.g. anxiety, temperament, personality)
- Motivation (e.g. sensation seeking, reward/punishment sensitivity)
- Genetics (genetic traits and polymorphisms).

Our work combines (a) detailed behavioral characterisation, using experimental cognitive, psychophysiological, and standard psychological/neuropsychological tests; (b) multi-modal brain imaging, incorporating measures of brain anatomy, function, biochemistry, connectivity, and perfusion and; (c) molecular genetic information. The inter-relationships of these measures are characterised in healthy participants, as well as disorders such as:

- Schizophrenia
- Bipolar Disorder
- Major Depressive Disorder
- Obsessive-Compulsive Disorder (OCD)
- Borderline Personality Disorder
- Drug Abuse & Drug Dependence Disorders.

Additionally, we are testing the notion that adolescence represents a unique time-window during which individuals are especially sensitive to the effects of drugs of abuse on brain development, leading to cognitive, emotional and motivational disturbances later in life. Finally, we place a strong emphasis on translating our findings into practical strategies that are relevant to the clinical management of these patients.

Research Highlights

Our research is conducted with a number of national and international collaborators. The following lists some of the major studies currently underway.

The Adolescent Early Development Study

As part of this collaborative study (earlier discussed in the Adolescent Development of Brain & Behaviour stream), Dr Murat Yücel and collaborators are examining the way in which developmental processes predispose individuals towards impulsive, compulsive, and addictive behaviours, as well as psychopathology more generally. Children in this cohort will be assessed longitudinally as they grow through adolescence. This project is headed by A/Prof Nick Allen (ORYGEN) and involves multi-dimensional assessments of family dynamics, cognitive processes, and neuropsychological and neurobiological development. This work involves a range of measures including psychophysiology, neuropsychology and neuroimaging (156 MRI brain scans acquired at baseline) to assess different trajectories of brain maturation and their relationship to the emergence of symptoms as children grow.

The neuropsychology of risk-taking behaviour

Risk-taking behaviour increases dramatically during adolescence and is thought to increase vulnerability for the subsequent development of addictive disorders. We are currently examining reward and risk-processing in adolescents and young adults who engage in risk behaviours, as well as those who use drugs to better understand pathways into and out of drug addiction.

Anatomical, neurochemical and functional changes of the anterior cingulate and connected regions in psychiatric conditions

We have developed new methods for assessing the anatomical, biochemical and functional integrity of the anterior cingulate cortex and interconnected circuits critical for integrating cognitive and emotional processes. We have applied these to understand how this region is altered in patients with serious mental illness, particularly schizophrenia, OCD, major depression, addiction, bipolar disorder, and borderline personality disorder.

The neuropsychology and neurobiology of substance abuse and addiction

Through Dr Dan Lubman and other members of ORYGEN we have recently completed detailed neuropsychological and multi-modal neuroimaging assessments of individuals addicted to opiates to gain a better understanding of how risk-taking and problems with behavioural inhibition lead to addictive states. More recently and in collaboration with Dr Dan Lubman, we have begun to conduct similar assessments in young people using inhalants. We are also currently examining the neurobiological correlates of the complex, yet often neglected relationships between substance use, cognition and psychiatric illness in cross-sectional and longitudinal cohorts.

The social brain in depression

Together with A/Prof Nick Allen we are using structural and functional neuroimaging techniques to examine the neurobiological correlates of maladaptive responses to socially threatening situations that are potentiated by depressed mood states. Studying people who are actively depressed, in addition to those who have a history of depression but are currently in remission, will allow us to disentangle transient state-related effects from more-enduring trait-related dispositions.

The neurobiology of moral dilemmas in adolescence, OCD and psychopathy

Dr Ben Harrison recently completed his PhD, which examined anterior cingulate function in schizophrenia from illness onset and is now undertaking a NH&MRC CJ Martin overseas training fellowship. His training and projects over the next few years will attempt to understand the neural and psychological processes underlying adolescent brain development, adolescent OCD and psychopathy. He is working with Prof Jesus Pujol in Barcelona and will be returning to complete his fellowship with MNC in 2008.

Training in the application of neuroimaging techniques to psychiatric disorders

This training typically involves joint supervision from many MNC staff members.

- An Australian Government Endeavour Award for Turkey is allowing Dr Emre Bora to spend 12 months at MNC to take part in research activities and to be trained in the application of neuroimaging techniques to psychiatric disorders. He is gaining experience on novel techniques like functional magnetic imaging and Diffusion Tensor Imaging
- Dr Melissa Green was awarded an NH&MRC training grant to spend time at the MNC to gain expertise in conducting and analysing neuroimaging research in psychiatric populations including major depressive disorder
- Valentina Lorenzetti is soon arriving from Italy for similar training.

5.5

Brain Imaging Methods

The development of sensitive and sophisticated neuroimaging techniques is an important and central resource for many MNC investigations. These studies are focused upon measuring changes in the brain across adolescence to adulthood, which are related to the development of various types of mental illness. We have developed new imaging and research techniques, which allow us to map the progression of brain changes across all illness stages.

These various methods and other standard processes have been integrated and combined to produce an imaging analysis "Pipeline". The MNC researchers have developed and formalized the Neuropsychiatry Imaging Laboratory (NIL) Image Processing Pipeline to handle the large number of magnetic resonance images that the MNC processes. The Pipeline consists of the loading and pre-processing steps needed for analysis of brain scans, the various methodological protocols for analysing images, and the appropriate storing of data and metadata.

Research Approaches & Highlights

Recent developments include methods to assess brain change over time, automated analyses (incl. voxel based methods), Texture Analysis techniques, and Diffusion Tensor Imaging to assess white matter.

Automated analyses

A/Prof Geoff Stuart has developed methods to examine cortical surface changes in subjects scanned longitudinally. Using software developed in Oxford, in collaboration with Dr Mark Jenkinson (Department of Engineering Science, University of Oxford), he supervised Dr Daqiang Sun to develop this technique (see discussion under schizophrenia section).

A/Prof Geoff Stuart, Ms Bridget Soulsby and Mr Chris Adamson have also been improving the voxel-based analysis (VBM) technique for analysing brain scans automatically. While this has been a useful way to compare brain MRI scans, the methodological issues have been challenging. This work is in collaboration with Dr Paola Dazzan (Wellcome Travelling Fellow from the IOP, London), Prof Philip McGuire and colleagues from the IOP, London, as well as Prof Ed Bullmore and Dr John Suckling from Cambridge University.

Diffusion Tensor Imaging

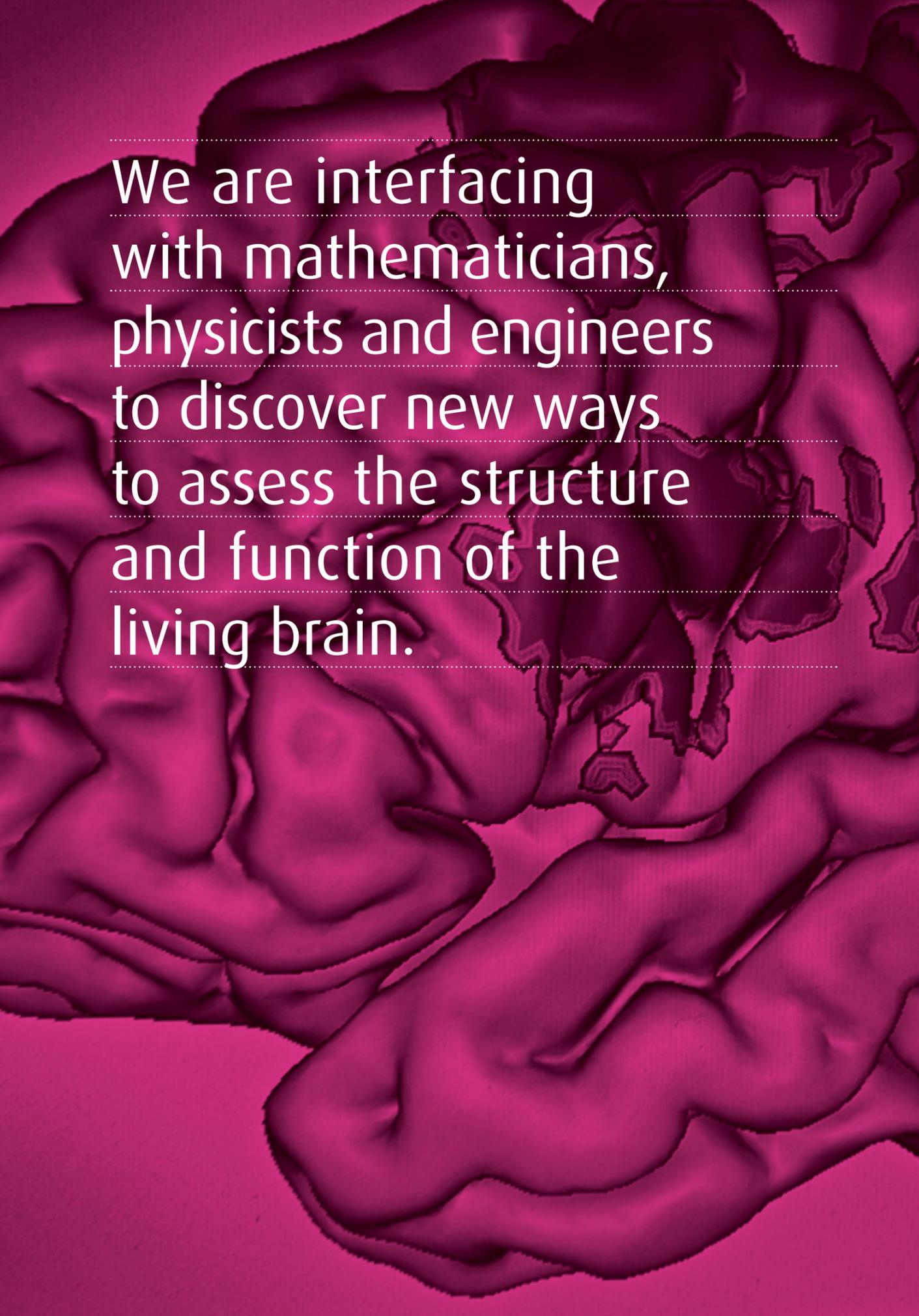
Diffusion Tensor Imaging (DTI) is a relatively new neuroimaging technique that provides an estimate of the health of white matter in the brain. This technique measures the flow or “diffusion” of water molecules through, around, and across different types of tissue in the brain. Briefly, around white matter fibers, the flow of water molecules is constrained so we can estimate the direction and strength of the connections. We have collected DTI data from individuals with a range of mental illnesses and also a large group of people from the general population.

Multimodal Imaging

In a recently completed NH&MRC funded project led by Dr Murat Yücel, we are using multiple brain imaging techniques acquired from the same individuals to map all the connections from the anterior cingulate cortex to other parts of the brain. This is the first time that anyone has had enough data and the methodological techniques to attempt this ambitious goal in living participants.

Texture Analysis

In contrast to the usual means of analyzing brain scans, we have been developing methods to examine differences in ‘texture’ across brain scans that may be informative about anomalies of brain development. We have been developing these methods in collaboration with Dr Joselito Chua from the Department of Computer Science and Software Engineering (CSSE), The University of Melbourne.



We are interfacing
with mathematicians,
physicists and engineers
to discover new ways
to assess the structure
and function of the
living brain.

There is a wide range of cognitive resources that are employed by MNC's research investigations. These resources are invaluable as they provide a means of measuring specific cognitive functions that can be linked to particular brain structures or pathways. Further, poor test performance can also provide an indirect means of demonstrating brain dysfunction. Aspects of cognitive functioning that are typically assessed by MNC investigators include intelligence, attention, language, memory and executive functions (problem solving and planning skills).

There are also resources specially designed for use in the functional Magnetic Resonance Imaging (fMRI) environment, which allow task requirements to be monitored and manipulated whilst individuals are participating in the fMRI investigations. A new and important resource recently acquired by the MNC for this purpose is a system designed to track eye-movements, which can be used to ensure that the participant is attending to and performing the task appropriately. Such resources include tasks used in studies where specific moods are induced or when emotional stimuli are presented.

The MNC is a major user of complex computer systems for the storage and analysis of brain images and associated data. One of the major achievements in 2004/2005 was the establishment of the Neuropsychiatry Imaging Laboratory at The University of Melbourne, with smaller nodes at Sunshine Hospital and The University of Melbourne, Parkville. MNC Imaging Laboratories have a user base of between 25 and 35 individuals that includes MNC permanent staff, visiting staff, research students and administrative staff. Ms Bridget Soulsby manages this growing resource.

The technical environment is situated across three locations: Sunshine Hospital, The Royal Melbourne Hospital and the National Neuroscience Facility at The University of Melbourne. These locations each comprise an information technology environment with imaging workstations, database and file servers, and standard desktop computers for office and administrative applications. A key feature is the capacity for 4TB of storage with a current library of approximately 2,500 MRI brain scans.

The continued growth of the MNC will place greater requirements on the capabilities of the IT environment, particularly in database design and management, and the need to support a growing number of research users. Planning for the expansion of the laboratories to accommodate these increasing needs is currently underway to ensure that the research work generated by the Centre and its collaborators can continue to be supported.

In collaboration with other research groups, the MNC plans to assemble a database of at least 5,000 brain scans and associated clinical data. This would then be linked with other biobank facilities currently being developed (e.g. the ORYGEN Biobank). This database could be accessed and examined for morphological markers across disorders including schizophrenia, bipolar disorder, depression, substance abuse disorders, borderline personality disorder, obsessive-compulsive disorder, developmental disorders of adolescence, and other neuropsychiatric conditions.

Using this approach we have the potential to gain important new insights into the similarities and differences between these disorders, by examining factors such as:

- Brain structure and function
- Phenotype/genotype characterisation
- Developmental stage (of brain maturation) at illness onset
- Treatment history
- Progression over time
- Patient outcomes under different treatment regimes.

Building and data mining a large-scale database would enable a fundamental shift in how research is conducted into the genesis and development of serious mental illness. We would move from small-scale patient studies of specific regions of interest in the brain (typical cohort size between 20 to 100 subjects), to large-scale analyses of data across thousands of participants.

Significant progress was made in 2005/06

Over \$250,000 has been invested in establishing MNC's Neuropsychiatry Imaging Laboratory neuroimaging facilities, with capacity for growth.

The MNC has attracted \$139,000 through the Clinical Neurobiology of Psychiatry Platform. Dr Katherine Manson, an astrophysicist who previously worked on 'databasing the stars', was recruited as a database design expert. Dr Manson will develop a sophisticated relational data model to map and integrate the various brain indices with clinical and genetic data. This will involve integration with the Biobank at ORYGEN Research Centre.

Mr Andrew Zalesky has been appointed as Technical Research Fellow to provide scientific programming expertise. Mr Zalesky is an electrical engineer who recently completed his PhD in applied mathematics.

The MNC has developed a collaboration with the Department of Computer Science and Software Engineering (CSSE) of The University of Melbourne. The Department of CSSE is funding Dr Joselito (Joey) Chua on 0.2 EFT to help identify the methodological issues related to machine learning and to provide advanced computational methods for analysis of our brain images.

The MNC has begun discussions regarding possible linkages with Bio 21 Molecular Medicine Informatics Model (MMIM) platform. This is a platform for clinical and scientific research teams to access and share clinical, bio-technical and genomic data across multiple organisations.



MNC and ORC researchers were the first to identify that smell deficits are found in young people at high risk of developing schizophrenia.

The MNC have been actively involved in television, print and radio media, providing comments and discussion on a wide range of topics including schizophrenia, addiction, brain structures and intelligence, adolescent brain development, and cannabis use. Two prominent features that were presented on the ABC's scientific television program Catalyst were "Teen Spirit" (2005) and "Smell and Schizophrenia" (2004). Both programs had a significant impact in the community and were well received.

- "Teen Spirit" provided insights into the development of the adolescent brain and discussed research by the MNC, which questioned the age at which teenagers' cognitive skills reach adult levels of maturity
- "Smell and Schizophrenia" discussed new findings that may assist in the identification of schizophrenia in its early stages. A/Prof Brewer and Prof Pantelis have found that our sense of smell may assist in determining who will likely develop schizophrenia in a cohort of individuals at high risk
- Other media that the MNC have been involved in include ABC TV News, New York Times, The Age, Sydney Morning Herald, The Australian, Sydney Morning Herald, Nine MSN, Canberra Times, The Adelaide Advertiser, Daily Telegraph, The West Australian, MX Geelong Advertiser, Ballarat Courier. Radio stations include ABC, BBC, US radio, ABC Radio National, 2GO FM – Gosford, ABC Ballarat, ABC Newcastle, 3RRR-FM radio, 2UE.

Mr Jim Murray was appointed as business manager of MNC in 2005. Ms Barbara Stachlewski was appointed to the position of Office Manager and Ms Thetis Sardo was recruited as Administrative Assistant. The MNC Management group has provided important support that has assisted the Centre to grow. Mr Murray provides the following report.

The MNC is a small, close-knit group that is making advances in our understanding of the origin and development of serious mental illnesses from a relatively small resource base.

The MNC has been able to rapidly build a portfolio of research programs and produce very high standard and high impact research in its first two full years of operation. The number of publications continues to grow and the generation of research funding is also growing. The Centre is well on the path to demonstrating both its academic and its clinical impact, which will be important in securing its long-term sustainability.

There are three tiers to the funding of the MNC:

1. Platform funding to provide a stable base for its core research capabilities, managed directly by MNC
2. Externally generated research funding, managed by MNC and its close research collaborators
3. The clinical base, which is managed directly by Melbourne Health.

In 2003 and 2004 Melbourne Health facilitated a series of negotiations to establish the MNC and provide a stable platform of funding. Operational funding has been provided on a reducing basis over three to five years to help the Centre move towards self-sustainability. The package comprised a set of mutual commitments made by the following organisations:

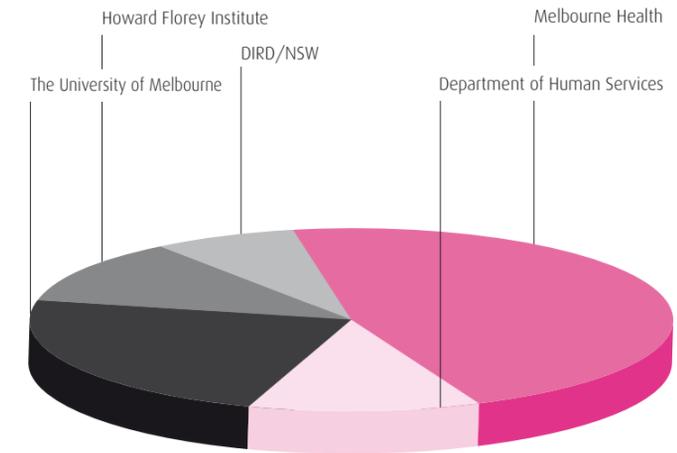
- a. Melbourne Health; funding over 5 years in the first instance
- b. The University of Melbourne; funding over 5 years
- c. The Howard Florey Institute; cash and in-kind support over 5 years
- d. Department of Human Services; funding over 3 years
- e. Department of Innovation, Industry and Regional Development (via Neurosciences Victoria); initial support to establish the Neuropsychiatry Imaging Laboratory.

Externally generated research funding

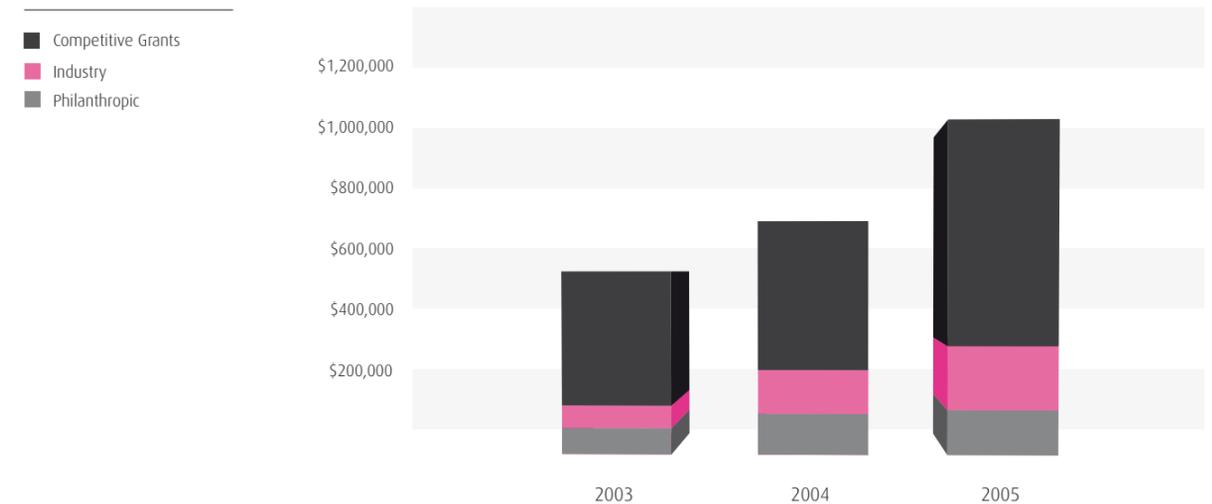
The MNC attracts research funding from a range of sources including the NH&MRC, ARC, US-based organisations, philanthropic organisations and industry. The research activity has grown dramatically since 2003. The outlook for 2006 and beyond is for continued growth in research funding.

- In the period between 2003 and 2005 the MNC directly led research projects to the value of over \$2.2 million and provided significant support to collaborative projects to the value of another \$2 million. That includes a major role in the \$7.4 million NH&MRC Program Grant, which was the first such grant in mental health awarded in Victoria
- The competitive funding component of MNC's direct research activity between 2003 and 2005 will produce research infrastructure grants to The University of Melbourne of over \$400,000. This, in part, will go towards supporting the case for sustainable funding for the Centre in future years.

MNC Core Funding: Approximately \$900,000 per annum



Funding Sources for MNC driven Research Projects



Clinical base

The MNC has important clinical links to The Royal Melbourne Hospital and Sunshine Hospital. This represents a total operating budget of over \$5 million per annum. The clinical funding is managed directly by Melbourne Health.

8.2

Governance, Administration and Business Development

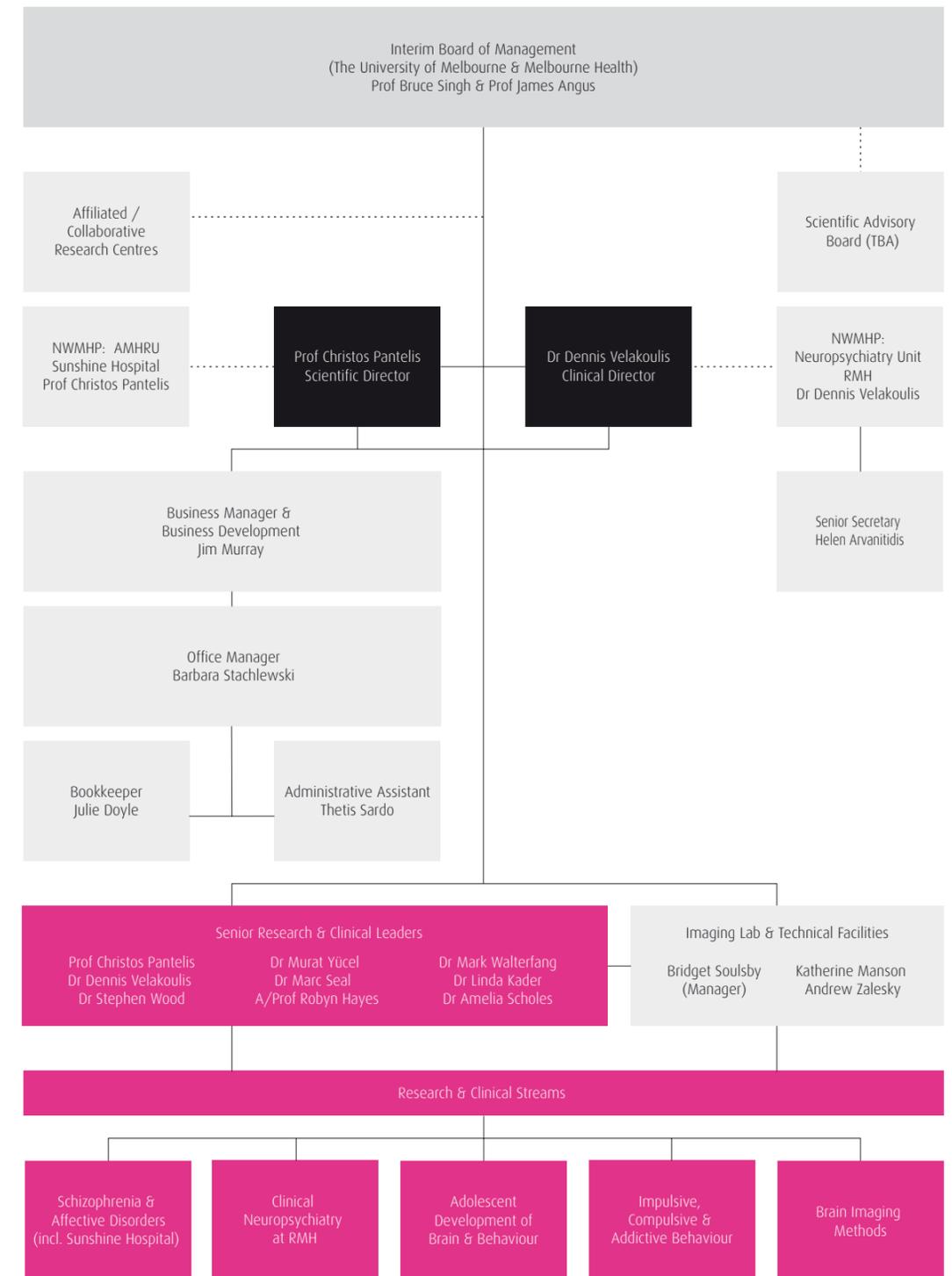
The MNC was established as a joint centre of The University of Melbourne and Melbourne Health. Staff are employed either by The University or by Melbourne Health. The MNC utilises both The University and Melbourne Health's financial systems.

The objectives for 2006 in terms of Governance, Administration and Business Development are:

- Complete the formalisation of the legal status of MNC
- Invite prominent scientific leaders to join the MNC Scientific Advisory Board
- Clearly define and communicate the identity, role and direction, as well as the strengths and outcomes that the MNC delivers to its major stakeholder audiences (including The University of Melbourne and Melbourne Health, research collaborators, clinicians, patients, families, industry and philanthropists)
- Pursue continued growth in research projects and research funding, with an emphasis on large scale collaborative projects
- Invest in projects that utilise the MNC's strengths in its understanding of brain structure, its unique library of longitudinal data and historical MRI images, and its access to patient populations
- Develop stronger relationships with philanthropic organisations and industry
- Further develop methods to translate new knowledge generated by this research into clinical practice through education activities and other forms of knowledge transfer
- Complete the detailing of the operations, human resources, finance and administration of the MNC
- Streamline the financial reporting and project tracking systems
- Pursue a financial sustainability strategy based on:
 - Continued increases in the MNC research activity and related funding income
 - Maintain high levels of researcher productivity (esp. high quality / high impact publications) that place the MNC in a strong position under the Research Quality Framework (RQF)
 - Actively negotiate with The University of Melbourne to secure an appropriate share of the research infrastructure funding generated by the work of the MNC
 - Refine our systems for project costing and include appropriate allocations for cost recovery.

8.3

Organisation Chart of the Melbourne Neuropsychiatry Centre



MNC Staff & Students**Senior Staff and Post-doctoral Fellows**

Christos Pantelis
Dennis Velakoulis

Ben Harrison
Robyn Hayes
Marc Seal
Geoff Stuart
Stephen Wood
Murat Yücel

Research Staff*Clinical staff at Sunshine Hospital*

Hussain Alshakhoori
Deidre Bradshaw
Linda Kader
Norman Moore (2003-2006)
Louisa Patrikios (2002-2004)

Clinical staff at RMH

Sophia Adams (PhD candidate)
Jo-Anne Bevilacqua
Phyllis Chua (PhD candidate)
Simon Jones
Evrin March (2005)
Kathryn Miller
Ramon Mocellin
Joanna Neith
John O'Donovan
Amelia Scholes
Daniel Varghese (PhD candidate)
Mark Walterfang (PhD candidate)

Research Assistants

Shelda Alcock
Anthony Ang
Carli Bartholomeusz
Deidre Bradshaw
Jo Buchanan
Kerrie Clarke
Anita Condello/Morlacci
Catherine Croft
Gayle Franklin
Lauren Hoiles
Susanne Jones
Liz Leeton
Sally Li
Carlyn Muir

Belinda Newman
Casey O'Brien
Eleanor Page
Bridget Ryburn
Nicole Sandhouse
Karen Shaw
Jerildene Smith

Administration Staff

Helen Arvanitidis (Senior Secretary)
Julie Doyle (Accountant)
Jim Murray (Business Manager)
Thetis Sardo (Administrative Assistant)
Barbara Stachlewski (Office Manager)
Renee Testa (Technical Writer)

Information Management & Laboratory Research Staff

Chris Adamson
Katherine Manson (Research Fellow)
Bridget Soulsby (Manager)
Andrew Zalesky (Research Fellow)

Students*Awarded 2003*

Louisa Bilske, MOccThy
Jo-Anne Buchanan, MSc

Awarded 2004

Belinda Garner, PhD
Stacey Hemphill, Honours
Noriko Kawasaki, AMS - MMedSci
Hua Loon Ling, AMS - MMedSci
Pat Reed, BLitt (Hons)
Judith Riffkin, DPsych
Leonie Simpson, DPsych
Daqiang Sun, PhD

Awarded 2005

Jude Bulten, MOccThy
Linda Gonzalez, PhD
Ben Harrison, PhD
Helen Higgins, PhD
Byung-Ook Lee, AMS - MMedSci
Natasha Nointin, AMS - MMedSci
Sharan Randhawa, AMS - MMedSci

Current Students

George Aranda
Andreia Azevedo
Yasmin Baliz
Anna Barrett
Simon Baxter
Laurelle Bland
Antoinette Boima
Elizabeth Bowman
Allison Cox
Cinzia de Luca
Christopher Davey
Joanna Fitzsimons
Alex Fornito
Clare Hamer
Katrina Hannan
Suzie Keller
Penny Koutsouradis
Simone Kurlender
Ashleigh Lin
Evelyn Lindsay
Belinda Newman
Sayed Shah
Loretta Sheppard
Kerrie Shiell
Wilaiwan Maneechak Snow
Michael Tagaki
Po-Yin Tang
Robin Valentine
Chris Watson
Jane Weaver-Cargin
Sarah Whittle
Gina Woodhead

Visitors*Visiting Collaborators*

Larry Abell (VIC)
Thomas Barnes (London)
Philipp Baumann (Switzerland)
Bill Blessing (SA)
Ibrahim Emre Bora (Izmir, Turkey)
Vaughan Carr (Newcastle, NSW)
Xavier Chitnis (London)
John Csernansky (USA)
Paola Dazzan (London)
Sophia Frangou (London)
Melissa Green (NSW)
Mark Griffin (QLD)
Dominique Hannah (QLD)
Ian Hickie (NSW)
Evangelos Karanikas (Salonika, Greece)
Richard Keefe (North Carolina, USA)
Dan Lieberman (Boston, USA)
Gin Malhi (NSW)
Ute Marx (QLD)

John McGrath (QLD)
Patricia Michie (Newcastle, NSW)
Robin Murray (London)
Hazel Nelson (Devon, UK)
Adrian Owen (Cambridge, UK)
Carmine Pariante (London)
Mary Phillips (London, UK)
Lye Yin Poon (Singapore)
Michio Suzuki (Toyama, Japan)
Tsutomu Takahashi (Toyama, Japan)
Konstatina Vassilopoulou (Athens, Greece)
Swapna Verma (Singapore)
Lei Wang (Washington State, USA)
Mark Wellard (QLD)
Zhou ShiYu (Toyama, Japan)
John Waddington (Dublin, Ireland)
Daniel Weinberger (Washington DC, USA)

International Students Visiting

Denise Chang (USA)
Anja Heims (Germany)
David Janelle (Germany)
Valentina Lorenzetti (Italy)
Alvaro Mancilla (Colombia)
Birgit Mathes (Germany)

Other Visitors

Japanese Delegation Visit
Malaysian Delegation Visit
Michael Brammer (UK)
Tony David (UK)
Cherrie Galletly (Adelaide, SA)
Bernd Gallhofer (Germany)
Shôn Lewis (UK)

8.5

MNC Collaborators

National

Alzheimer's Australia Vic
 Austin & Repatriation PET Centre
 Barwon Health
 Black Dog Institute
 Brain and Mind Research Institute
 Brain Research Institute
 Cogstate
 Department of Human Services, Vic
 Department of Psychiatry,
 Austin Hospital
 Department of Psychology, Department
 of Computer Science and Software
 Engineering & Department of Optometry
 and Vision Sciences,
 The University of Melbourne
 Department of Psychology,
 Deakin University
 Department of Psychology,
 Monash University
 Department of Psychology,
 Victoria University
 Department of Psychology & Department
 of Psychiatry,
 The University of Queensland
 Drug and Alcohol Services,
 Howard Florey Institute
 Huntington's Disease Association
 La Trobe University
 Mental Health Research Institute
 Menzies School of Health Research
 Monash University Centre for Brain and
 Behaviour
 Macquarie University
 Murdoch Children's Research Institute
 Neuroscience Institute for Schizophrenia
 & Allied Disorders (NISAD)
 Neurosciences, RMH
 Neurosciences Victoria
 North Western Mental Health
 ORYGEN Research Centre

Prince of Wales Medical
 Research Institute
 Queensland Centre for Schizophrenia
 Research
 Queensland University of Technology
 Royal Children's Hospital, Vic
 Swinburne University
 The Royal Melbourne Hospital
 University of Newcastle
 University of Wollongong
 WESTCARE and Salvation Army
 Westmead Hospital

International

Cambridge University, UK
 Clinical Neuroscience Lab, University of
 California, Los Angeles, USA
 Barcelona Biomedical
 Research Park, Spain
 Imperial College, London, UK
 Institute of Mental Health, Singapore
 Institute of Psychiatry, London, UK
 Lab of Neuro Imaging, UCLA, USA
 Massachusetts General Hospital /
 Harvard Medical School, USA
 National Institute of Mental Health,
 Washington DC, USA
 Oxford University, UK
 Toyama Medical and Pharmaceutical
 University, Japan
 University College, London, UK
 University of Athens, Greece
 University of Bremen, Germany
 University of Hamburg, Germany
 University of Pittsburgh, USA
 Washington University School of
 Medicine, St Louis, USA

9.0

PUBLICATIONS (2003 - 2006)

Journal Publications

- Addington, D. E., Pantelis, C., Dineen, M., Benattia, I., & Romano, S. J. (2004). Efficacy and tolerability of ziprasidone versus risperidone in patients with acute exacerbation of schizophrenia or schizoaffective disorder: an 8-week, double-blind, multicenter trial. *Journal of Clinical Psychiatry*, 65(12), 1624-1633.
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- Bellgrove, M. A., Collinson, S., Mattingley, J. B., Pantelis, C., Fitzgerald, P. B., James, A. C., & Bradshaw, J. (2004). Attenuation of perceptual asymmetries in patients with early-onset schizophrenia: evidence in favour of reduced hemispheric differentiation in schizophrenia? *Laterality*, 9(1), 79-91.
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- Castle, D. J., & Pantelis, C. (2003). Comprehensive care for people with schizophrenia living in the community. *Medical Journal of Australia*, 178(11), 592.
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