Prince of Wales

Medical Research Institute

Annual Report 2008

INNOVATION + DISCOVERY

INNOVATION + DISCOVERY

"Our science is steeped in innovation. Changing the health outcomes of the world has never been a job for the conventional or easily discouraged. And the medical challenges of our time demand a determined breed of researcher. Recognising this, our researchers are finding new ways to take on old medical problems – and new ways to take on new ones. They are the innovators. They are battling problems that have no simple cause or solution – innovation, leading to new medical research discoveries, is the key."

Professor Peter R Schofield
Executive Director and CEO

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CHAIRMAN'S REPORT

The role of the POWMRI Board is to create an environment that allows our team of talented neuroscientists to conduct medical research that is of value to humankind through the generation of knowledge that will help prevent, treat or cure brain disorders. We all stand to benefit from such a collaboration.

The biggest barrier to achieving these medical breakthroughs is a lack of funding for research and its translation to improved health. Many research projects of significant potential never reach fruition because we cannot afford to investigate their potential and many existing programs could greatly improve healthcare, if only the resources were available to refine them.

External Scientific Review

This year, the Institute Board asked an independent panel of experts to conduct a Scientific Review of the quality of the Institute's overall research, the way in which we undertake this research and the quality and feasibility of our future research directions. Held over three days in August, the review involved all of the Institute's senior scientists.

The Review Panel, chaired by Professor Phil Robinson of the Children's Medical Research Institute, Sydney, comprised national and international experts including Professor Marie-Francoise Chesselet, Chair of the Department of Neurobiology at the University of California Los Angeles; Professor Roger Lemon, Director of the University College London Institute of Neurology; Professor Ian Cameron of the University of Sydney; and Professor Tony Jorm of the University of Melbourne. The Panel was ably assisted by Professor Roger Dampney of the University of Sydney, who is the NHMRC representative on the POWMRI Board.

The Panel's report highlighted the high esteem that its members have for the Institute and its staff as highlighted in the various quotes below:

"The Panel found POWMRI to be a vibrant and exciting research machine. It has a treasured collection of talented scientists with multiple common goals and shared visions."

"It is evident that the output of POWMRI adds real value to the total Australian health research system."

"A particular strength of the Institute is its excellent balance between lab-based research and clinical research. Most other medical research institutes focus on one or the other, and POWMRI is distinguished by establishing a good balance between them. POWMRI takes a lifespan approach to brain health and has a clear commitment to strengthening the translation of basic research into the clinical setting."

"POWMRI adds considerable value to the overall Australian medical research scene…This includes providing a nurturing and supportive environment to allow outstanding scientists to develop their maximum potential at an early stage of their careers."

The Board was delighted with the review report which provided an outstanding endorsement of the relevance and significance of our research programs. The Review also made some valuable and constructive suggestions for further improvements. The Board has sanctioned the Institute's plans to implement the Panel's recommendations to further lift our hard-earned but well-deserved reputation for research excellence, and its translation, into the clinical setting.

The Board

My fellow Board members and I welcome the advice and expertise provided by two new Directors appointed in 2008. In September, Andrew Bernard was nominated to the POWMRI Board by one of the Institute's founding stakeholders, South Eastern Sydney & Illawarra Area Health Service. Andrew is General Manager, Northern Hospitals Network, SESIAHS.

Also in September, Mike Quigley was appointed an independent Director of POWMRI. Mike was the former President and COO of Alcatel, a global telecommunications company and is currently an independent Director of Leighton Contractors and Senior Visiting Fellow, Australian School of Business, UNSW. Mike's input to Board governance is proving invaluable.

Judi Hausmann, Principal of Hausmann Communications, resigned from the Board in February after four years' service as an independent Director. Judi has contributed much to the work of the Institute, especially in relation to our fundraising activities.

In December, Professor Roger Dampney concluded his term of service as Board nominee of the National Health & Medical Research Council. Roger's contribution over the last 13 years has been most significant, particularly his advocacy on behalf of the Institute's scientists and, this year, his liaison role in the External Scientific Review. The Board has elected Roger an Honorary Life Governor in recognition of his dedication to the Institute over his long tenure.

Acknowledgements

My personal thanks are extended to my fellow Directors for their continuing enthusiasm and dedication to the work of the Institute and the Board. I would also like to express my appreciation to those Directors who serve on our Board Subcommittees, including the Audit Committee, Investment Committee, Building Committee, and the MRI Committee, which culminated in POWMRI purchasing from Primary Health Care Ltd its own high-resolution MRI for research purposes.

I congratulate POWMRI researchers for their outstanding achievements over the last year. In particular, I thank Professors Peter Schofield and Simon Gandevia and the research group leaders of the Institute. With our extraordinarily dedicated group of scientists and clinicians, we remain resolute in our pursuit of excellence in the neurosciences.

The Board thanks those Institute friends and donors in the wider community who have supported our research projects and activities. Of particular note is the $1 million grant to the Institute from the Prince Henry Hospital Centenary Research Fund. In recognition of this major donation, an extension of the Institute's current building will be named the *Prince Henry Wing.*

We acknowledge the crucial role played by individuals, trusts and foundations in helping the Institute achieve its mission. Our Foundation was formally established in 2008 and, while I recognise that the years ahead will be a challenge, I look forward to your support in extending the success of the Institute and in developing the Neuroscience Research Precinct to full potential.

With your help, POWMRI will enhance its reputation as one of Australia's foremost institutes dedicated to brain research and its application in health and disease. Please take the time to find out more about the Institute and support our research in neuroscience.

Paul Brassil
Chairman

EXECUTIVE DIRECTOR REPORT

Our research into the major disorders of the brain is driven by both the excellence and tenacity of our scientists in successfully competing for research grants from national and international agencies. We continued to have outstanding success in securing competitive research grants including 19 NHMRC and ARC Project Grants and Fellowships, awarded in 2008 with a success rate nearly double the national average.

Likewise, we have continued to successfully compete and communicate this research with a record 153 publications in 2008, considerably more than many larger medical research institutes.

Research themes

Following our last Strategic Planning Day, scientific activities have been organised in five research themes and this has helped to provide further cohesion and collaborative opportunities. The themes are detailed in the research summaries of this Annual Report.

The Institute's Research Committee, which provides strategic leadership and advice under the chairmanship of Professor Stephen Lord, together with its various subcommittees, has made a major contribution to the current success of the Institute.

In 2008, there were two areas of infrastructure support that were a major focus of the Institute. For several years, the Institute had conducted a highly-successful joint venture with Symbion Health Ltd in which a 3 Tesla MRI provided both clinical and research brain scans. However, following Primary Health Care Ltd's hostile takeover of Symbion in March 2008, Primary withdrew its services and no MRI scans could be conducted at the Institute for more than six months. In December, the Institute purchased the MRI from Primary and re-established its scanning research activities.

The Brain Bank has been a key element of the Institute's research capability for many years, underpinning many of our projects. The Institute and the University of New South Wales both made substantial commitments in 2008 to further enhance the level of support required for the Brain Bank. With an average of two donor brains received each

week, there is a markedly increased level of activity, and substantially greater support for our research.

Building future capacity

In the 2007 Federal Budget, the Institute was awarded a capital grant of $30 million to expand its research facilities. Together with the Institute's own funds, for the first time there was an opportunity to design a purpose-built medical research facility. Planning has been underway for some time, comprising the immediate construction of Stage 1 improvements while undertaking the more detailed design of the new $35 million Stage 2 building.

The Stage 1 works have included a range of temporary improvements such as the West Wing, a two storey 300m^2 annex that has provided desperately needed space. With generous support from the Prince Henry Hospital Centenary Research Fund, work on the Prince Henry Wing has been undertaken to provide both additional laboratories and offices. The Prince Henry Wing, built by Fugen Constructions, is due for occupancy in May 2009.

Our vision is of a large, collaborative work environment where expensive research infrastructure is shared, opportunities for collaboration are maximised and the translation of medical research to improved health care is a core focus. Our plan has therefore been to ensure that we can maximally leverage our investment in medical research and create, over time, a larger and more integrated Neuroscience Research Precinct.

The proposed Stage 2 building was determined to be a Major Project by the NSW Minister for Planning and, subject to final planning approval, will provide substantial new research capacity by the end of 2010. Designed by Cox Richardson Architects and with Winton Associates as the project manager, the design has received extensive staff input to ensure maximal flexibility and adaptability to both the current and anticipated future needs of our researchers. The building reflects the Institute's belief that creativity in science is best fostered by creating an environment that is conducive to interaction and innovation. And a brilliant building helps to attract and retain brilliant minds and allows us to house state-of-the-art facilities needed to pursue top quality medical research.

Staff promotions, awards and recognition

Our staff members are our key asset and it is with great pride that three of our current group leaders, Drs James Brock, Kay Double and Janet Taylor were promoted to Associate Professor by the University of New South Wales. Kay Double was also promoted to a POWMRI Principal Research Fellow.

Dr Olivier Piguet, a senior postdoctoral fellow, was appointed as a Research Fellow and Dr Americo Migliaccio was recruited to the Institute as a Research Fellow from Johns Hopkins University in Baltimore. Dr Lorimer Moseley, who had previously undertaken a portion of his PhD studies at the Institute, was recruited back from Oxford University in the UK as a Senior Research Fellow. Americo was subsequently awarded an NHMRC Career Development Award and Lorimer was awarded an NHMRC Senior Research Fellowship.

Institute researcher, Dr Arun Krishnan was awarded an NHMRC Career Development Award, while Dr Tim Karl, who was recruited to the Institute to establish a new capacity in animal behavioural research, was also awarded an NHMRC Career Development Award.

Dr Rhoshel Lenroot was also offered appointment as a Research Fellow to coincide with her UNSW offer as Professor of Child & Adolescent Psychiatry and will relocate from the USA in mid-2009.

Supporters and donors

Our fundraising efforts for the 2008 financial year were the best ever achieved by the Institute, with $3.1 million being raised. In particular, I wish to thank the Trustees of the Prince Henry Hospital Centenary Research Fund for their $1 million donation. This donation and ongoing annual pledges from several generous trusts, families and individuals have helped the Institute meet its commitment to providing $5m for the capital program.

We were most grateful to receive two new donations to support postgraduate student scholarships. Ms Laurie Cowled, founder of the Cowled Foundation, established The Cowled Postgraduate Research Scholarship in Brain Research, with the first recipient being Rebecca St George, and Mrs Elizabeth (Betty) Fyffe established the International Collaboration PhD Scholarship, with Marcella Kwan as the first recipient.

In July, we conducted another successful Food for Thought Gala Dinner at the Four Seasons Hotel, and, in October, the Creative Madness Art Exhibition was held at Orson & Blake. Both events raised valuable funds to support our research into mental illness.

Members of the Phyllis Luker Society, which was established to formally acknowledge people who have advised the Institute that they have left a bequest in their will, were invited to tours and morning teas throughout the year. Regular tours and cocktail functions were also held for invited guests after each Board meeting, providing an opportunity to meet Directors and senior staff in an informal setting.

Acknowledgements

My personal thanks go to the Board of Directors, especially the Chairman Paul Brassil and the members of the various Board subcommittees for their continued support. I also wish to acknowledge the support of Professor Simon Gandevia, our Deputy Director, and Professor Steve Lord, Chairman of the Research Committee who form the Management Executive. Finally, I thank all my scientific colleagues and our operations staff for helping to achieve the successes of 2008.

Professor Peter R Schofield
Executive Director and CEO

BOARD OF DIRECTORS


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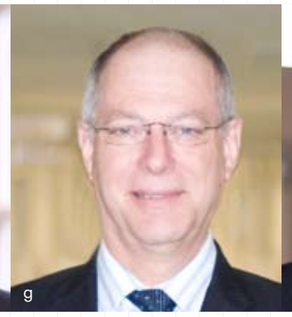
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a. Mr Paul Brassil,
BEc LLB ACA FTIA
Director, POWMRI Limited, 1997–present
Chairman of the Board, 2004–present
Chairman, Audit Committee, POWMRI Limited, 2003–present
Chairman, Investment Committee, POWMRI Limited, 2007–present
Member, MRI Committee, POWMRI Limited, 2008 Independent Director

Paul is a Partner of PricewaterhouseCoopers, Chartered Accountant and a Fellow of the Taxation Institute of Australia, specialising in advising local and international clients on income tax and related matters.

b. Mr Andrew Bernard,
BSc MPH
Director, POWMRI Limited, September 2008–present
Nominee of South Eastern Sydney & Illawarra Area Health Service

Andrew is General Manager, Northern Hospitals Network, SESIAHS since December 2007. Formerly he was General Manager of Area Clinical Services, Sydney South West Area Health Service (2005–07) and Acting Director, Clinical Governance (2007).

c. Professor Roger Dampney,
BSc PhD DSc
Director, POWMRI Limited, 1995–December 2008
Board Liaison, External Scientific Review, 2008
Nominee of National Health & Medical Research Council

Roger is Professor of Cardiovascular Neuroscience at the University of Sydney and an Honorary Consultant Physiologist at Royal North Shore Hospital. He is also a member of a number of Societies and Advisory Committees and has served on a number of NHMRC Grant Review Panels.

d. Ms Judi Hausmann,
MPRIA
Director, POWMRI Limited, 2003–February 2008
Independent Director

Judi is Principal of Hausmann Communications in Sydney and a Member of the Public Relations Institute of Australia.

e. Mr Peter Kemp,
LLB
Director, POWMRI Limited, 2006–present
Member, Investment Committee, POWMRI Limited, 2007–present
Member, Building Committee, POWMRI Limited, December 2008–present
Chairman, MRI Committee, POWMRI Limited, 2008
Independent Director

Peter is Principal of Macpherson & Kelley Lawyers. He has been involved in commercial legal practice for over 30 years, mainly in his role as one of the founding partners of Kemp Strang Lawyers. He is also a member of the Business Law Section of the Australian Law Council and a founding member of its Insolvency Section.

f. Mr Michael Quigley,
BSc BE
Director, POWMRI Limited, September 2008–present
Independent Director

Mike is a Company Director and Consultant. Former President and COO of Alcatel, a global telecommunications company. He is currently an independent Director of Leighton Contractors; Senior Visiting Fellow, School of Strategy & Entrepreneurship, Australian School of Business, UNSW; Director of Audinate; and Independent Advisor to Innovation Capital.

g. The Hon Dr Andrew Refshauge,
MBBS FAICD
Director, POWMRI Limited, 2005–present
Member, Audit Committee, POWMRI Limited, 2006–present
Member, Building Committee, POWMRI Limited, 2007–present
Member, MRI Committee, POWMRI Limited, 2008
Nominee of NSW Minister for Health & Medical Research

Andrew is the former Deputy Premier of NSW, former Treasurer and Minister for Health, and a medical practitioner with extensive skills and experience in the political, financial and health sectors.

h. Mr Barry Shepherd,
PSMedal, GradDip PSM
Director, POWMRI Limited, 2005–present
Member, Building Committee, POWMRI Limited, 2007–present
Nominee of South Eastern Sydney & Illawarra Area Health Service

Barry is the former Director of Corporate Services, SESIAHS and Deputy CEO, SESIAHS. He served as POWMRI Director during the Institute's formative years and was renominated to the Board by the Area Health Service. He hasextensive expertise in the health and medical research sector and the delivery of major projects and continues to provide consultancy services for major health projects in NSW, Victoria and Queensland.

i. Professor Peter Smith,
RFD MD FRACP FRCPA FAICD
Director, POWMRI Limited, 2005–present
Nominee of University of New South Wales

Peter is Dean, Faculty of Medicine, UNSW. He specialised in cancer medicine and research following study in Australia, USA and Germany. He has held senior hospital management posts in Brisbane and Melbourne, senior academic appointments at the Universities of Queensland, Melbourne and Auckland. He has served in a consulting role to Government, including as Chair of the recent Inquiry into Vietnam Veterans Cancer Incidence and Mortality. He is currently a Director of St Vincent's and Mater Health Sydney, NewSouth Innovations, MedSys Assurance (NZ and a number of research centres and institutes.

j. Mr David Thomas
Director, POWMRI Limited, 1997–present
Independent Director

David is a key member of the Sydney Hotel Industry and has owned several well known Hotels in and around Sydney over the years. In 2008, he was inducted into the Australian Hotel Industry Hall of Fame for services to the Industry, with particular reference to his training and teaching of younger members of the Industry over his career.

k. Ms Gabrielle Upton,
BA LLB MBA FAICD
Director, POWMRI Limited, 2007–present
Nominee of University of New South Wales

Gabrielle is Deputy Chancellor, UNSW. A lawyer and banker, she is currently Legal Counsel at the Australian Institute of Company Directors and member of the Corporations & Markets Advisor Committee, the Federal Government's advisory committee on corporations and securities law. She is Deputy Chair of the Duke of Edinburgh Awards and serves on the General Sir John Monash Foundation NSW Awards Committee.

l. Mr John Walton,
AM MBA BEc FCPA FAIM FAICD
Director, POWMRI Limited, 1991–present
Member, Investment Committee, POWMRI Limited, 2007–present
Member, MRI Committee, POWMRI Limited, 2008
Independent Director

John was an inaugural Director of POWMRI and nominee of SESIAHS (1991-June 2008). He was Chairman of Eastern Sydney Area Health Service when POWMRI was founded. He has served as Chairman or a Director of many public companies, industry associations, and community based organisations. He was awarded the Queen's Silver Jubilee Medal in 1977 and the Medal of the Order of Australia in 1998.

m. Professor Peter Schofield,
BScAgr PhD DSc
Executive Director and Chief Executive Officer, POWMRI, 2004–present
Member, Building Committee, POWMRI Limited, 2007–present
Member, Investment Committee, POWMRI Limited, 2007–present
Member, MRI Committee, POWMRI Limited, 2008

Peter studied genetics at the University of Sydney and graduated with the University Medal. He obtained a PhD in genetics from ANU. He has worked in the biotechnology industry and in academic medical research institutes in the US, Germany and Australia. In 1998, he was awarded the degree of Doctor of Science by UNSW where he is appointed as a Professor of Medicine. His research has been recognised by several prestigious awards and he has provided community service to a number of professional organisations and committees.

n. Mr Andrew Dermott,
BEc CA
Company Secretary and Finance Manager, POWMRI, 1999–present
Member, Audit Committee, POWMRI Limited, 2003–present

Andrew has been in the role of Finance Manager and Company Secretary of the Institute for the last 10 years. Previously he was Chief Accountant for a European trading company and he has held accounting positions in a variety of industries including the mining sector and professional services.

RESEARCH

Dr Michael Hornberger, Research Officer, investigates memory and emotion processes in dementia patients

Stefanie Reyes, PhD student, investigates tyrosine hydroxylase isoforms and the role they may play in Parkinson's disease

AGEING + NEURODEGENERATION

Neurodegeneration is the process by which a part, or parts, of the brain progressively die. Common brain diseases in which neurodegeneration occurs include Alzheimer's disease, and other forms of dementia, which affect memory and the ability to think, and Parkinson's disease and related disorders in which the ability to move is affected.

Alzheimer's disease and other dementia disorders currently affect 220,000 people in Australia, while a further 60,000 Australians suffer from Parkinson's disease. Neurodegenerative diseases cannot be cured or prevented and our ability to treat these conditions is limited. These disorders impose a severe burden on the quality of life for persons suffering these disorders, as well as their families. The financial costs of these disorders to affected families and the Australian health system is significant.

Research into neurodegenerative diseases at the Institute is identifying the causes of these disorders and is working towards developing better diagnostic methods and improved treatments for patients. The ultimate goal of this research is to contribute to the worldwide effect to prevent these disorders.

BROE GROUP

ARC/NHMRC Ageing Well Network Project
Led by Professor Tony Broe, this project is aimed at building and developing the links between ageing-related researchers with a particular focus on Aboriginal Ageing. The network has been recruiting researchers from both Indigenous and non-Indigenous backgrounds and promotes Aboriginal ageing research through a number of networks including the Australian Association of Gerontology, and through specific workshops and presentations. This is a four year project receiving funding support from the NSW Ageing Well Network based at the University of Sydney. In addition, it has matched funding support from the Faculty of Medicine at the University of New South Wales.

Cognition, dementia and ageing in Australian Aboriginal and Torres Strait Islander peoples: A review of the literature
Developed over the past two years, this project has become a comprehensive survey of research that has been conducted on cognition, dementia and ageing in broad terms and specific work on cognition, dementia and ageing in Aboriginal communities in Australia. The key aim of this review has been to clarify the current knowledge base on these issues in Australia. As well, some work was conducted on international and cross-cultural settings including what is known about other indigenous peoples and the links to their health and wellbeing across the life span. This research has been supported by the Dementia Collaborative Research Centres (DCRC) and the ARC/NHMRC Ageing Well Network.

What is the burden of dementia in urban dwelling Indigenous Australians?
Identifying the prevalence of dementia and its sub-types in urban dwelling Aboriginal people in NSW is the aim of this NHMRC funded project under Professor Tony Broe and colleagues. The research will recruit and assess approximately 700 Aboriginal people aged 45 and over across NSW in early 2009. The rationale for this particular project is that very little is known about dementia in non-remote Aboriginal communities. The urban population is growing and so, too, is the number of older Aboriginal people (those aged 45–64). The project aims to clarify and quantify these important issues and also to build capacity in Aboriginal people by employing and training Aboriginal researchers and by feedback and information provision for local Aboriginal communities.

A modified cognitive assessment tool for Urban Aboriginal Populations
A modified Kimberley Indigenous Cognitive Assessment (KICA) tool will be trialled in an urban Aboriginal community. The reason for this is that a literature search and review indicates a lack of suitable tools for working with urban dwelling populations. This pilot will involve the redesign of a KICA for an urban sample and assessment of a sample of adults with data analysis and reporting. This research is supported by the Dementia Collaborative Research Centres (DCRC).

A modified dementia assessment tool for Urban Aboriginal Populations
This project aims to trial a modified Rowland Universal Dementia Assessment Scale (RUDAS) in an urban Aboriginal community. As with the KICA, the literature indicates a lack of suitable tools for working with urban dwelling populations. The pilot study will redesign RUDAS for an urban sample and assess a sample of adults with data analysis and reporting. This research is supported by Alzheimer's Australia Research.

DOUBLE GROUP

Lipid changes in Parkinson's disease
Assoc Professor Kay Double and colleagues Professor Glenda Halliday and Assoc Professor Brett Garner are investigating changes in lipids in Parkinson's disease. Interestingly, work by PhD student Khuen Yen Ng identified a marked decrease in cholesterol in cells in persons with a particular type of genetic Parkinson's disease. Ongoing work is investigating the underlying reason for this difference and the consequences of this change for cell function and survival.

Metals in the brain in Parkinson's disease
Collaborative studies with Dr Sylvain Bohic at the European Synchrotron Radiation Facility in Grenoble, France characterised changes in metal within the healthy brain over the human lifespan. Subsequent work is investigating metals in the brain in Parkinson's disease. The data presented by Assoc Professor Double and her team suggest that concentrations of copper are decreased in the brain in this disorder. This finding is the subject of further work which aims to identify the mechanistic basis of this change and how it affects the function of copper-binding proteins.

Dopamine production in the human brain
In a collaboration with colleagues at the University of Newcastle, Assoc Professor Double's laboratory is investigating the enzyme tyrosine hydroxylase, the rate-limiting enzyme for dopamine production. The researchers have demonstrated that the four different forms of the enzyme vary in their localisation within the human brain. This finding may have important implications for the way dopamine production is regulated in different areas of the brain. They are also investigating changes in tyrosine hydroxylase in Parkinson's disease and PhD student Stefanie Reyes is investigating how other factors in the brain may increase the vulnerability of certain brain cells in this disorder.

Misincorporation of L-dopa
In collaboration with Dr Ken Rodgers at the Heart Research Institute, Assoc Professor Double is investigating how L-dopa, a protein widely used as a treatment to manage the symptoms of Parkinson's disease, can be mistakenly incorporated into a range of proteins in the brain. She and her researchers are investigating the extent of this phenomenon, how the incorporation of L-dopa into proteins affects their structure and function and the consequences of this for patients prescribed this medication.

Diagnosis of Parkinson's disease
Developing methods to diagnose Parkinson's disease earlier and more accurately than currently possible is a particular focus of Assoc Professor Double's team. The approaches being used include a patented blood test for this disorder in a commercial collaboration with the Queensland-based diagnostic firm Anteo. A further project is investigating an imaging method based upon ultrasound in collaboration with Dr Gabrielle Todd from the University of Adelaide and POWMRI's Assoc Professor Janet Taylor and Dr Jane Butler.

Stem cell research
Modulation of neurogenesis, or the birth of new brain cells, is hoped to be a new avenue for the development of treatments for neurodegenerative disorders but, as yet, the regulation of these processes in the human brain are not well understood. Assoc Professor Double's collaborative work with Professors Glenda Halliday and Cynthia Shannon Weickert in this area is investigating changes in the rate and regulation of new brain cell birth with age, undertaken by Brain Sciences UNSW Postdoctoral Fellow Dr Eryn Werry, and in Parkinson's disease.

GARNER GROUP

Regulation of neuronal cholesterol and amyloid-beta production by ABC transporters
Researchers in the Garner laboratory have shown that certain proteins called ABC transporters are expressed in human neurons and other cells. They are undertaking a detailed analysis of the function of these transporters in the brain with a focus on the control of lipid balance and the Alzheimer's disease-causing amyloid-beta peptide production. With key contributions from Dr Scott Kim, PhD student Sharon Chan and Surabhi Bhatia, their studies have identified which of the ABC transporters are involved in the regulation of neuronal cholesterol efflux to apoE, a key cholesterol transport protein in the brain, as well as the impact of specific transporters on amyloid-beta production in the brain. This research has provided exciting advances that increase understanding of the cause of Alzheimer's disease.

Impact of membrane lipids on neuronal amyloid-beta peptide formation
Investigations have shown that cellular glycosphingolipid (GSL) accumulation promotes cholesterol storage. Other work indicates that these lipids may promote the production of amyloid-beta peptide. With key contributions from Dr Scott Kim and Dr Henry Li, the researchers have discovered that a new prototype drug, that they call P4, inhibits GSL synthesis and prevents formation of neurotoxic amyloid-beta peptides that are known to cause Alzheimer's disease. Researchers are currently testing these prototype drugs in mice that produce the amyloid-beta peptide. This research may, in the future, offer a novel treatment for Alzheimer's disease.

Understanding the function of apoE in neurobiology and neurodegeneration
ApoE plays an important role in brain lipid transport and neurodegenerative diseases. The apoE4 "isoform" is a major risk factor for Alzheimer's disease but the mechanisms underlying this risk are unclear. With key contributions from Dr David Elliott, the Garner team has shown that apoE fragmentation in the brain is highly dependent on the apoE isoform. They are currently defining the pathways that result in isoform-selective apoE fragmentation in the brain and examining the biological activity of specific apoE fragments.

Regulation of neuronal alpha-synuclein expression
Lewy bodies are neuropathological inclusions found in Parkinson's disease brain and are composed of aggregated proteins including alpha-synuclein. Alpha-synuclein is a neuronal protein that is found at increased levels in neurodegenerative diseases. With key contributions from PhD student Danni Cheng, investigators have discovered a novel pathway that leads to increased expression of alpha-synuclein in neurons that involves the nuclear hormone receptor LXR. This research helps to understand the factors that are involved in producing dangerously increased levels of alpha-synuclein in Parkinson's disease.

Lysosomal function and amyloid-beta mediated neurodegeneration
Neurons, and other cells, contain "organelles" called lysosomes. Previous research indicates that the lysosomal compartment is an important site for amyloid-beta mediated neuron death. With key contributions from Dr Katarina Kagedal, PhD student Hanna Mild and PhD student Lotta Hellstrom, the Garner group has brought together two research areas to define the molecular details underlying the regulation of amyloid-beta production via ABC transporter regulation of lysosomal membrane lipid composition. The research helps indentify new therapeutic targets that may in the future be utilised to treat Alzheimer's disease.

Targeting the sphingolipid pathway to treat atherosclerosis
Atherosclerosis is a major cause of heart attack and stroke and accounts for ~50% of all deaths in developed countries. Under Assoc Professor Brett Garner, researchers have shown that members of the sphingolipid family may promote atherosclerosis. With key contributions from PhD student Elias Glaros, they have tested novel therapeutic approaches, inhibiting synthesis of specific sphingolipids, to prevent atherosclerosis in mice. They have shown that a sphingolipid inhibitor prototype drug called Myriocin inhibits both the early development of atherosclerosis and also the progression of established atherosclerotic lesions and this is associated with increased production of a protective protein called apoA-I. This approach provides the proof of principle required to develop a new and potent means to treat atherosclerosis in humans.

Dr Michelle Hill, Research Assistant, studies the role of inflammation in Alzheimer's disease

HALLIDAY GROUP

Genetic influences on Parkinson's disease

Professor Glenda Halliday and her team assessed how common dominant genetic mutations for Parkinson's disease were in Australia and found that more than 2% of Australians with Parkinson's disease have known mutations. This differs from European, Arabic and American populations, and suggests that alternate dominant genes influence Parkinson's disease in Australia. They assessed whether common variations (rather than mutations) in genes known to cause Parkinson's disease, or known to produce dopamine (transmitter lost in Parkinson's disease) or affect mitochondrial function (energy producing organelle for cells) increased the risk of developing Parkinson's disease and found that most do not, but polymorphisms do in a minority. This highlights that levels of the proteins, enzymes and transmitters that these genes produce are important for common forms of Parkinson's disease.

Progression of symptoms and pathology in Parkinson's disease

Clinical and pathological features that occur over 20 years of Parkinson's disease, showing that dementia is common in long-term survivors, were published by the Halliday research group. They found that age was the most significant factor influencing progression and outcome for patients–those with disease onset over 70 had more rapid and severe disease with additional cognitive symptoms and multiple pathologies in their brain. In contrast, those with earlier onset had much slower disease and only one type of brain pathology (Lewy bodies). The scientists studied whether Lewy bodies were a consequence of the cell loss over time in long-term survivors by assessing parkinsonian monkeys, and found no evidence of Lewy bodies. This suggests that Lewy bodies are the key feature to the disease process.

Progressive supranuclear palsy and multiple system atrophy

Dopamine treatment does not work in progressive supranuclear palsy or multiple system atrophy. The Halliday team showed that greater loss of dopamine occurs in progressive supranuclear palsy compared with Parkinson's disease. In multiple system atrophy, they found that proteins identified through genetic studies in Parkinson's disease affect non-neuronal cells in multiple system atrophy. These cells are important for insulating the electrical impulses in the brain and researchers have identified important proteins found in these cells that are involved early in the pathology.

Inflammation in Alzheimer's disease

Inflammation is closely associated with the cell loss that underlies Alzheimer's disease, and researchers have found that a protein that plays a crucial role in the inflammatory cascade, called monocyte chemoattractant protein-1 (MCP-1), appears to play an important role in initiating and sustaining inflammation in Alzheimer's disease. This finding, by Professor Halliday and Dr Claire Shepherd, gives a target to manipulate and modify to determine whether the course of the disease can be changed.

Sharon Savage, Research Assistant, conducts cognitive assessments of patients with neurodegenerative disorders such as frontotemporal dementia

HODGES AND PIGUET GROUPS

FRONTIER – a clinical research group dedicated to the study of frontotemporal dementia (FTD) and related disorders

Emotion processing in frontotemporal dementia

Processing of emotion is commonly impaired in frontotemporal dementia (FTD). How this deficit evolves with time, whether all types of emotional information (auditory or visual) are equally affected, and whether subtypes of frontotemporal dementia show different patterns of deficits are some of questions that remain unanswered. Examination of emotion integrity has relied mostly on visual stimuli – pictures of faces, objects or short video vignettes – and little has been done in the auditory domain, particularly with music. Music is dynamic, non-verbal and has the potential to become a therapeutic tool. This project, led by Dr Olivier Piguet and Professor John Hodges, investigates emotion processing integrity in FTD patients using tasks that include auditory, as well as static and dynamic visual stimuli. Testing will be repeated at yearly intervals and combined with brain MRI to understand the nature and progression of these deficits.

Brain imaging in frontotemporal dementia

Frontotemporal dementia predominantly affects two regions of the brain: the frontal and temporal lobes. Presence of progressive change to these brain structures is an important feature of the disease and helps towards an accurate diagnosis. Using structural MRI with diffusion tensor imaging (DTI), and cutting-edge functional imaging (PiB-PET and FDG-PET), this project, led by Professor Hodges and Dr Piguet and Dr Michael Hornberger, investigates the extent and severity of changes taking place in the frontal and temporal lobes as the disease progresses. The study, which includes collaborations with the University of Queensland, Westmead Hospital, and the Austin Hospital in Melbourne, will contribute to understanding the progression of the disease and improve diagnostic accuracy.

Hypothalamus integrity in frontotemporal dementia

The hypothalamus is a small brain structure that plays a critical role in regulating a number of body functions, such as body temperature, appetite, and sleep. A relatively large number of patients with frontotemporal dementia show disturbance in their appetite and sleeping patterns but no studies have examined this region of the brain in this disease. Under Dr Piguet and Professor Halliday, this research investigates changes in hypothalamus integrity using high-resolution magnetic resonance imaging and postmortem tissues.

Progressive aphasia: new assessment methods and therapy

Deficits of speech and language are an important component of frontotemporal dementia and in a proportion of patients constitute the primary presenting feature. Two major variants are recognised: semantic dementia and progressive nonfluent aphasia, although there is emerging evidence of a third clinical variant called logopenic aphasia. Professor Hodges and colleagues have been developing a new battery designed to differentiate these syndromes. The pathological basis of these variants may differ with a greater representation of tau pathology in those with progressive nonfluent aphasia, TDP-43 in semantic dementia and Alzheimer pathology in logopenic aphasia. To investigate clinico-pathological correlations, the scientists have embarked on a collaboration with the PET group at the Austin Hospital in Melbourne using an amyloid specific ligand (PiB). They are also working closely with speech and language therapists to develop more effective language retraining methods. All families are approached regarding possible brain donation and the study's researchers work closely with Professor Glenda Halliday.

Cognition in Motor Neurone Disease (MND)

Classically, motor neurone disease (MND) has been considered a pure motor syndrome which spares aspects of cognition, behaviour and emotional processing. Recent evidence has established that a proportion of patients with frontotemporal dementia (FTD) develop features of MND. Moreover, some patients with classic MND also go on to manifest features of FTD. Under Professor Hodges and his team, this project focuses on cognition in MND. They are developing a neuropsychological battery to assess patients with MND that will correlate with neuroimaging findings. The primary aim is to identify the prevalence and pattern of cognitive changes in MND patients, and the potential impact on activities of daily living, decision making and on carer burden.

Identifying biomarkers in frontotemporal dementia

In order to develop treatments and effective interventions for patients with frontotemporal dementia (FTD), the underlying process of brain degeneration needs to be identified early in the disease course. FTD patients may have one of several different underlying brain pathologies which cannot at present be predicted by either the type of symptoms exhibited, or by a genetic profile. Cellular studies of the brain have shown that there are two types of protein ("tau" and the more recently discovered "Tar DNA-binding protein 43") which accumulate in neurons in FTD. These pathologies are associated with different inflammatory responses, and so may require very different approaches to treatment. The project, led by Professors Hodges and Halliday, use blood of patients with FTD to develop an easily identifiable biological marker for the type of cellular changes associated with each brain pathology.

Autobiographical memory in frontotemporal dementia

Disorders of memory are increasingly recognised as part of the clinical presentation in frontotemporal dementia (FTD). The nature and severity of these deficits are not well studied as they are often masked by more prominent clinical manifestations such as behavioural changes or language deficits. How these deficits evolve with time is also not well understood. This project, led by Dr Piguet, is a collaboration with RPAH and the University of Queensland and investigates autobiographical memory integrity for different life periods in patients with FTD at yearly intervals. Because this type of memory is not affected by possible encoding deficits, it is an ideal instrument to measure memory processing. These findings will be correlated with measures of cognitive function, emotional processing and with brain imaging.

Severity rating scales and everyday life impact in frontotemporal dementia

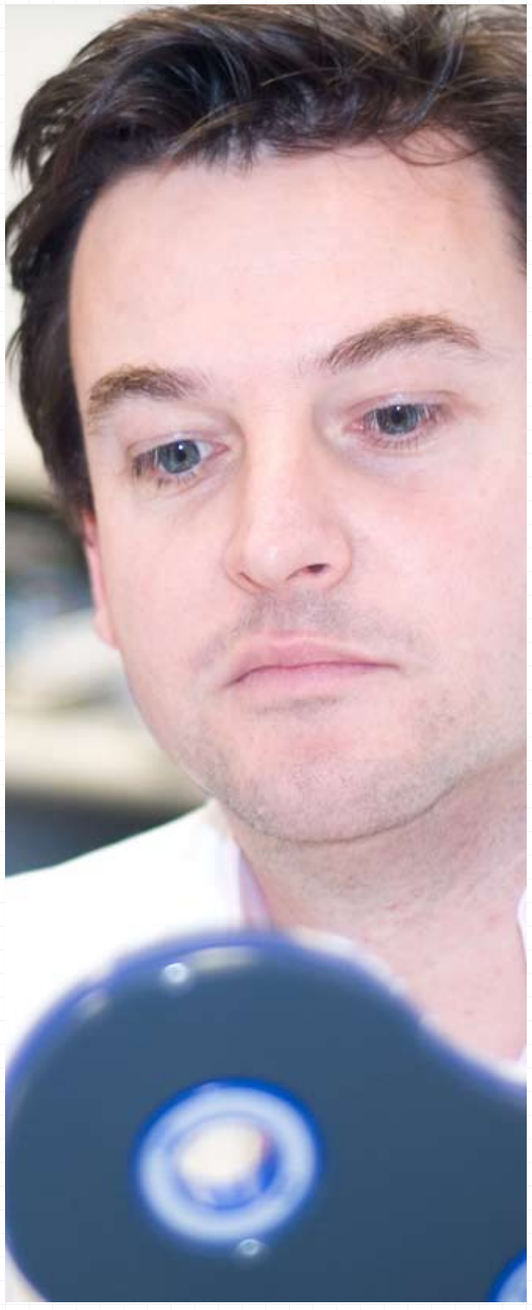
Frontotemporal dementia (FTD) is associated with progressive behavioural and cognitive difficulties, as well as changes in the ability to perform daily activities. No standardised instrument currently exists to measure such changes with disease progression in FTD. This creates difficulties in predicting the course of the condition, and can cause anxiety in families because of the lack of knowledge of disease progression. Professor Hodges and colleagues will develop an instrument aimed at measuring such changes. This rating scale will allow professionals to give better advice to families and patients, and will permit patients and families to make adjustments to their living arrangements.

Caregiver burden in frontotemporal dementia

Dementia is the cause of significant stress and distress, especially for family members closely involved with a patient. In frontotemporal dementia (FTD), however, little research has been done to understand the nature and severity of caregiver stress. Under Professor Hodges, this study will establish the relations between measures of caregiver stress and burden and patients' clinical presentations and patterns of deficits – cognitive, behavioural, emotional – in order to understand the aspects of the condition that are creating more distress for their families. The project will enable professionals to give better advice and support for caregivers and families affected by FTD, and also to work on the prevention and alleviation of stress whenever possible.

Memory in transient epileptic amnesia (TEA)

Transient epileptic amnesia (TEA) is a clinical syndrome characterised by short, recurrent amnesic periods, more common in middle-age or later years. Individuals present with complaints of focal memory loss, while other cognitive functions remain intact. The memory deficits are characterised by accelerated forgetting, over days and weeks, of newly acquired information and a loss of autobiographical memories. Importantly, however, these memory deficits are rarely picked up by standard neuropsychological tests. This project, led by Professor Hodges, investigates the profile of the accelerated forgetting and autobiographical memory disturbance in TEA patients and will explore the neural basis of these deficits using neuroimaging. This research will also investigate how pharmacological intervention may improve the patients' ability to retain personal memories of the recent past.



Assoc Professor Matthew Kiernan, Principal Research Fellow, whose research focus is the investigation and development of new therapeutic strategies for neurological disorders

KIERNAN GROUP

Motor neurone disease

Following recent discoveries in motor neurone disease (MND) that identified abnormalities in patients before disease manifestations appeared, translational studies incorporating new clinical trials have commenced, with the support of the NHMRC. These studies are directed from POWMRI and, as part of this process, researchers have developed a clinical trials consortium to enrol patients from across Australia.

The first investigator-driven studies have focused on a novel 'neuroprotective' medication that aims to slow the destruction of the motor neurone and thereby stop or slow the progressive paralysis experienced by MND patients. In addition, researchers have been exploring physical therapies, including a respiratory muscle training device, attempting to maintain function in MND patients. These studies are being undertaken by PhD student Ben Cheah and postdoctoral Fellows Dr Jennica Winhammar and Dr Steve Vucic, with coordination support by Sr Margie Zoing.

Australian Motor Neurone Disease Registry

The successful collaboration that established the Australian Motor Neurone Disease Registry is now filtering through large amounts of clinical information from more than 700 MND patients enrolled in the registry from sites across Australia. This transcontinental registry forms part of a growing worldwide trend to obtain epidemiological and natural history information for MND, and provides a hub for collaborative approaches. Through this approach, Assoc Professor Matthew Kiernan hopes to improve the multidisciplinary care of MND patients.

Motor neurone disease and cognitive function

In collaboration with the Institute's Frontier group, the Kiernan research team is exploring the processes of memory problems that seem to develop in a significant proportion of MND patients. In addition to understanding the processes of cognitive dysfunction in these patients, PhD student James Burrell hopes to develop simple diagnostic tools and biomarkers for distinguishing trademark features of the cognitive impairment that may accompany MND. In separate studies in paediatric patients who develop a childhood form of the disease known as spinal muscular atrophy, Dr Michelle Farrar has recently commenced studies to explore the pathophysiology of this devastating neurodegenerative disease.

Neurotoxicity and chemotherapy

Studies from the NHMRC project grant investigating nerve function in patients treated with chemotherapy to determine the patho-physiology of nerve dysfunction and development of neuropathy, have identified a biomarker to establish which patients may be at risk of neurotoxicity. This biomarker was developed from over 500 studies undertaken in cancer patients by PhD student Susanna Park and postdoctoral students Dr Cindy Lin and Dr Arun Krishnan. These studies have identified involvement of Na+ channels in the development of neuropathy due to chemotherapy. They have been using nerve biomarkers to provide feedback to oncologists regarding nerve function in their treated patients, attempting to preserve nerve function and thereby reduce the incidence of neuropathy. In addition, research focus groups have been developed through collaboration with the NSW Cancer Institute to explore the functional impact of neurotoxicity on patients.

Pathophysiology of uraemic neuropathy

Chronic kidney disease is a major public health problem with ~16% of Australians having some evidence of kidney damage. Currently over 9,000 Australians receive dialysis treatment and, of these, 90–100% have developed nerve complications, in most cases neuropathy. Following his successful PhD studies at the Institute that identified potassium as a cause of the neuropathy, Dr Arun Krishnan returned to undertake a clinical trial to establish whether the effects of strict dietary potassium restriction will prevent the development of neuropathy in kidney failure patients. These studies will be supported by a NHMRC career development award to Dr Krishnan.

Dr John Kwok, Research Fellow, investigates the biochemistry and genetics of hereditary dementias

KWOK GROUP

Cloning of a chromosome 9 Dementia/ Motor Neurone disease gene

Dr John Kwok and Professor Peter Schofield have been studying familial dementias and, together with PhD student Agnes Luty, have identified a new gene on Chromosome 9 that causes frontotemporal dementia and motor neurone disease. Their experiments have confirmed that altered expression of the new dementia gene can lead to perturbations in the molecular markers of the neurodegenerative diseases found in the pedigree. They have demonstrated that commercially available and therapeutically relevant drugs are able to modulate the biological activity of the same molecular markers. This project has the potential to revolutionise the diagnosis and treatment of two neurodegenerative disorders.

Positional cloning of a splicing factor on chromosome 15 that modulates splicing of key dementia genes

Alzheimer's disease and Parkinson's disease are the two common causes of dementia and neurodegeneration. Through positional cloning, Dr Kwok's research team has identified a gene on chromosome 15 as a modulator of alternative splicing, a process that controls the biological activity of the majority of genes. They propose to study the genetic and biochemical role of the gene in neurodegeneration in terms of its effect in splicing.

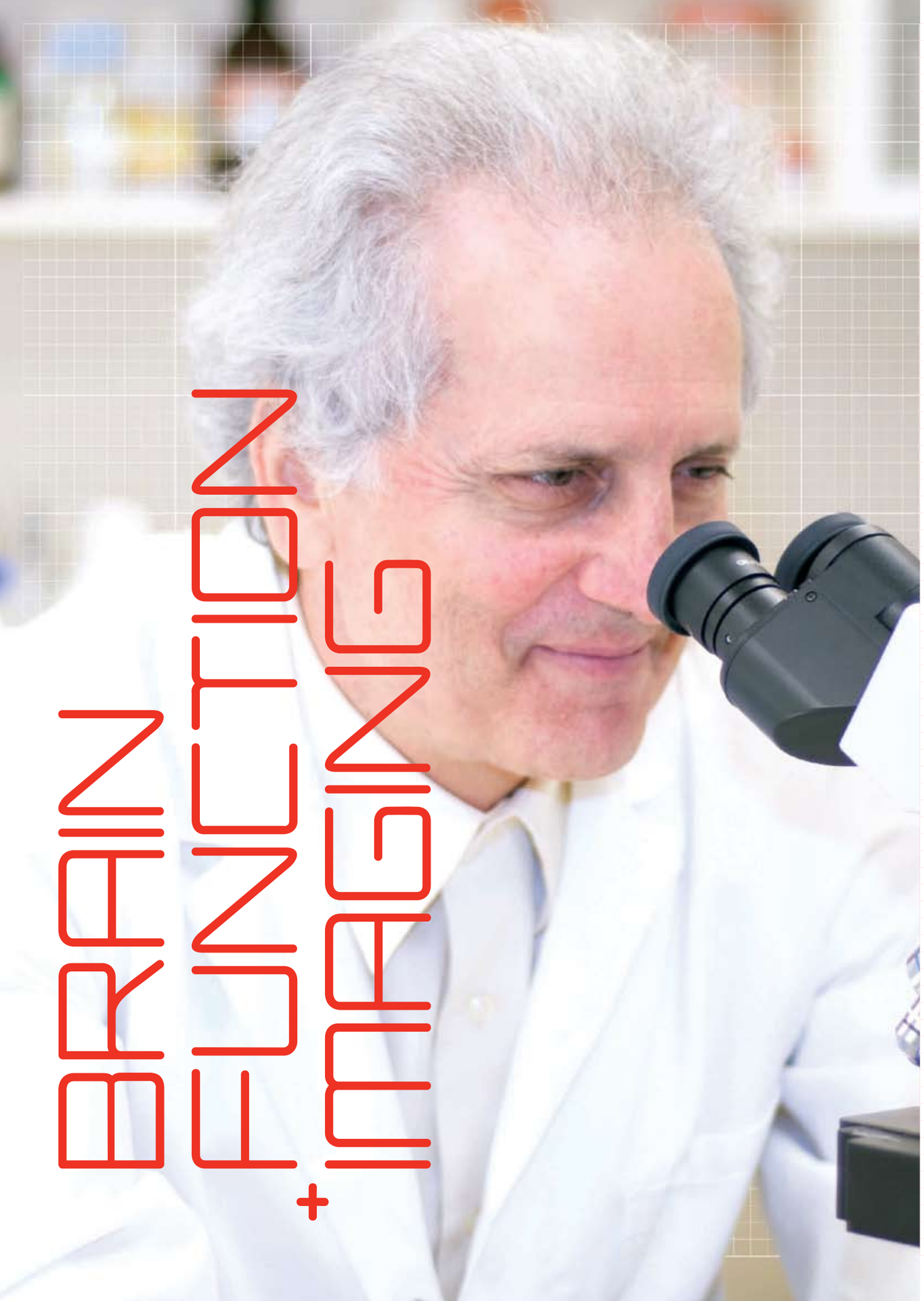
Role of the glycogen synthase kinase-3 (GSK3B) and microtubule associated protein tau (MAPT) genes in neurodegeneration

Both GSK3B and MAPT genes control crucial processes in the cell. Researchers in Dr Kwok's laboratory have shown that genetic polymorphisms in these two genes interact to increase risk for late-onset, idiopathic neurodegeneration. They aim to discover whether the two genes will have an effect in other diseases and to determine the biological mechanisms in the genes interact to increase disease risk. Future research will include the collection of a large, clinically well-defined case-control cohort. This cohort, combined with epidemiological data, will enable them to examine how environmental factors, such as diet and exposure to chemicals, can interact with genes to alter risk of disease.

Genetics of early onset Alzheimer's disease

Dementia is usually thought of as a disease of ageing. However, the burden of young onset dementia, with symptoms occurring before age 65, has recently been identified as an important area not well supported by the health care system.

In a new international collaborative study funded by the US National Institutes of Health, Professor Schofield and Drs Brooks and Loy will lead one of eight sites studying the clinical progression and biomarkers to better define and understand Dominantly Inherited Alzheimer's Disease. The DIAN study will follow participants for the next six years.



BRAIN FUNCTION + IMAGING

Professor George Paxinos AO, Senior Principal Research Fellow, is the author of 35 books, including atlases, on the brain of humans and animals which assist scientists to study human disease

The brain is a secretive organ. It hides deep within the bony plates of the skull and is so intrinsically bound up with the person to whom it belongs that study of the organ itself can be problematic. Non-invasive imaging technology, such as the Institute's new 3T Philips Achieva MRI scanner, has made it possible for researchers to study the brain in situ. They can see live changes in brain activity and blood flow; determine brain chemistry and structure – all while the subject is lying down!

Brain researchers, no less than geographers, need maps and coordinate systems to navigate the brain and communicate their observations to each other. On a map of the brain, scientists can superimpose types of neurons, neuro-transmitters, enzymes, and connectivity and functional data. Institute scientists are continuing to develop and refine brain atlases which are used internationally as the standard guides for scientific work and are also used by neurosurgeons to target small deep lying structures in the brain.

PAXINOS GROUP

Identification of rhombomeres in mammals on the basis of avian homologies and transgenic mice

This project involves the use of developmental data to decipher the organisation of the brainstem. There have been major advances in gene targeting which have significant implications for understanding brain structure. Professor George Paxinos and his team are collaborating with scientists in the laboratory of Nobel Prize winner, Professor Mario Capecchi, at the University of Utah in the US. Their studies of genetically modified mice have opened the way to a new system of subdivision of the mammalian brainstem.

Atlases of the rat and human spinal cord

With support from the Christopher and Dana Reeve Foundation and the NSW Office for Science and Medical Research, Professor Paxinos and colleagues completed atlases of the rat and mouse spinal cord. They used the distribution of chemicals (immunohistochemistry) to find the neurons in the spinal cord that animate muscles or control the autonomic system. They also commenced work on the human spinal cord, establishing the areas that correspond with the cord of experimental animals.

Homologies between the cortex of humans and other primates

With support from the US National Institutes of Health, Professor Paxinos and colleagues are constructing an atlas of the marmoset brain. The marmoset is the size of a rat but it has a primate brain that resembles that of humans. Preliminary data indicates that, while rats have quite different cortex, the marmoset cortex and the human cortex is quite similar. Their ultimate aim is to construct an atlas of the human cortex.

The organisation of the human hypothalamus

The Paxinos group is studying the hypothalamus of the normal human so that it will provide a baseline for comparisons with pathological tissue. The hypothalamus is involved with regulations of functions such as eating, drinking, aggression, copulation, thermo-regulation and arousal.

Development of the mouse brain

The mouse is increasingly being used as a model for many human conditions such as Alzheimer's disease, Parkinson's disease and epilepsy. Of most interest are developmental events which may be responsible for these abnormalities. Scientists need atlases at various time points in the development of the mouse and it is these atlases that the Paxinos laboratory is constructing.

3D reconstructions of the brain of the mouse and rat

Recently, brain atlases are being transformed from passive paper guides to dynamic organising principles at the core of databases. In collaboration with global publisher Elsevier and the Allen Institute, the Paxinos laboratory is reconstructing their 2D atlases into 3D. They are also segmenting MR images of mouse brains that have been scanned at the National Imaging Facility in Queensland.

Timecourse of brain metabolite and BOLD changes studied by magnetic resonance following anodal transcranial direct current stimulation in healthy volunteers

In collaboration with Assoc Professor Colleen Loo of the Black Dog Institute and Patrick Arul-Anandam, Professor Caroline Rae and her research team undertook a placebo controlled study of the effect of direct cortical stimulation on the brain in healthy volunteers. Direct current stimulation is an emerging treatment used in disorders such as major depression and schizophrenia and is known to increase brain activity. Here, they measured changes in brain metabolites and the blood oxygen level dependent (BOLD) signal which is used to measure brain activation in fMRI experiments. They found that direct current stimulation caused a significant increase in-brain metabolic activity that lasted for half an hour following stimulation, as well as a large increase in the cortical BOLD response which remained elevated for at least an hour. This study has shown the timecourse in which measurements monitoring treatment of patients must be performed, as well as identifying possible biomarkers for treatment, and brain networks affected by the treatment.

Brain morphology in Duchenne muscular dystrophy

Mei-Fang Chew, a BSc(Med) honours student working in the Rae laboratory has been obtaining structural MR images of the brains of boys with the degenerative disorder Duchenne muscular dystrophy, or DMD. DMD is caused by lack of a single, large protein, which is normally expressed in the brain where it is involved in anchoring and clustering neurotransmitter receptors such as the $GABA_A$ receptor. Mei studied eight boys with DMD and found structural changes in the cerebellum and hippocampus of these boys. This work is being carried on in 2009 by Louise Killen, another medical student.

Yash Tiwari, Research Assistant, studies the function of susceptibility genes ST8SIA2 and NRG1 altered in brains affected by bipolar disorder and schizophrenia

There has been a rapid realisation that mental illness is responsible for one of the largest disease burdens in Australia. The major psychiatric disorders schizophrenia and bipolar disorder each affect around 1% of the population, and the Institute now has active programs in each of these areas. Other mental health conditions, such as depression, will affect up to 20% of the community. Individual and family costs of these disorders are substantial and this is further reinforced by the high financial costs of these disorders.

SCHOFIELD GROUP

Genetics of bipolar disorder

Both genetic and environmental factors are involved in the development of bipolar disorder, a severe mood disorder characterised by oscillations from normal mood to periods of elevated mood (mania) or low mood (depression). Dr Jan Fullerton and Professor Peter Schofield are investigating the genetic contributors to bipolar disorder using Australian families with multiple individuals who have been diagnosed with the disorder. Together with PhD student Erica McAuley, the group has recently identified a new bipolar disorder susceptibility gene located on chromosome 15. The sialyltransferase gene is involved in developmental regulation of neurons and controlling the contacts that neurons make with each other. They are now aiming to understand how these alterations translate into an increased genetic susceptibility by characterising the biological pathways involved.

Bipolar disorder has a complex pattern of genetic transmission, so the researchers expect that multiple genes will contribute to susceptibility to develop the illness. Combinations of genes may be stronger risk factors for developing bipolar disorder than individual genes, so the researchers are examining gene-gene interactions (genetic epistasis) throughout the genome to identify genes which, in concert, may increase susceptibility. This analysis has led to the identification of multiple interacting regions. Dr Fullerton is now seeking to identify the specific genes involved in these interactions.

Genes, ethics and mental illness

Work on genes involved in predisposing an individual to mental illness has allowed Professor Schofield's research group to undertake a range of collaborative studies examining community and patient understanding and attitudes to modern issues surrounding genetics. This has included studies with Professors Mitchell and Wilhelm, Assoc Professor Bettina Meiser and PhD student Alex Wilde in which they have evaluated who wants to know their risk, and perhaps more importantly, why. Current studies are examining public perceptions about the role of genes and mental illness, with a strong focus on the role of stigma and ways in which it can be addressed.

Animal models of mental illness

While genetically or pharmacologically altered animals do not show the full spectrum of symptoms of mental disorders such as schizophrenia (SCZ), they still enable research on specific aspects of the disorder. Dr Tim Karl's team, Dr Leonora Long and Rose Chesworth, has investigated the effects of different environmental SCZ risk factors using mice, which are genetically predisposed for this disorder. These animals showed an increased sensitivity to the effects of cannabis confirming potent interactions between genetic and environmental risk factors. Importantly, cannabis had also short-term beneficial effects on SCZ-like symptoms. Thus, current research aims to identify how major constituents of cannabis might have a differential impact on the development of schizophrenia.

Neurotransmitter receptors
Over many years, Professor Schofield and his UNSW colleagues have been investigating the detailed biology of a key class of neurotransmitter receptors, the ligand gated ion channels, through studies on the glycine receptor. This work has continued with studies examining the role of the receptor in the mechanism of neurotransmitter induced activation and in determining how ions permeate the receptor channel. Mouse models with inherited deficits in their glycine receptors have been studied in collaboration with Professor Robert Callister at Newcastle University and have shown the role of reduced glycine receptor function on the excitability of neurons that affect movement and balance.

Genetics of normal brain function
In a collaborative study with Professor Lea Williams from the University of Sydney at Westmead Hospital, Dr Carol Dobson-Stone and Professor Peter Schofield have investigated how polymorphisms within genes may give rise to variations in normal brain functions. Using cognitive, psychological and neuroimaging data on a large collection of normal individuals, they have investigated the role of several genes known to be involved in brain disorders. They have demonstrated how genetic polymorphisms in brain derived neurotrophic factor can impact brain function and memory and how this correlates with depressive features in a normal population. These collaborative studies have also demonstrated an association between monoamine oxidase A polymorphisms with emotional and behavioural brain markers and their relationship to antisocial and psychopathic personality traits.

SHANNON WEICKERT GROUP

Clinical trial of selective estrogen receptor modulator in schizophrenia
Of all the various systems associated with schizophrenia, impairments to cognition function are generally resistant to full remission and are the most lasting and debilitating as they interfere with the ability to function independently. This study aims to provide a means to determine if the estrogen receptor type 1 genotype can be linked to specific cognitive deficits in patients with schizophrenia and a means to reverse cognitive deficits in patients with schizophrenia. This research project will be in partnership with the Kiloh Centre at the Prince of Wales Hospital and future work with the clinical population is planned to enhance the translational work from the laboratory.

Neuregulin dependent neuronal migration and schizophrenia
Genetic and environmental factors combine to increase risk for developing schizophrenia. The key neurobiological events in which risk genes participate during development are not understood. Without this important information, we do not know which pathological events are primary to the disease, nor do we know where to aim therapy. The path to developing therapies to prevent schizophrenia involves research on how risk genes influence brain development and structure.

Deficits in interneuron populations in schizophrenia
Although a primary pathology of schizophrenia remains unclear, some of the most consistent findings in the disease implicate a deficit in inhibitory interneurons and their signalling. In an attempt to characterise which cells may be the most affected in schizophrenia, and following this the level of signalling at which inhibition may be deficient, Professor Shannon Weickert's* team is examining expression and localisation of markers of subtypes on interneurons in a cohort of patients and controls. The researchers also plan to determine whether the inhibitory connections of any particular subclass of interneuron are altered in the disease, which may aid development of targeted treatments.

Dr Richard Morris, Research Officer, studies neural and cognitive deficits in schizophrenia

The effects of sex hormones during puberty on neurocognition in an animal model of schizophrenia
This research will determine the role of pubertal testosterone in the development of cortical volume and cognitive function during adolescence. Removal of the effect of testosterone on pubertal development was the independent variable used to examine the effect. Reversal learning and prepulse inhibition tests (PPI) were administered during puberty and 16 months later (PPI only). The data will tell researchers whether removing testosterone affects these important measures of orbitofrontal cortex functioning and dopaminergic transmission, both of which are implicated in the pathology of schizophrenia. The study also analysed data from 3T MRI scans of the brain taken across the pubertal period to identify and correlate changes in cognitive function with reductions in cortical volume. One of the major developmental changes found to date is an overall reduction in brain size during adolescence. Manual tracing methods will determine if grey matter, white matter or ventricular decreases are the source of this reduction. This project will also validate the method used to obtain volumetric estimates from the MRI scans, by comparing and correlating the volume measurements for a previously determined region of interest (the amygdala) with histological stains of the same region.

Alterations in brain-derived neurotrophic factor and TrkB alternate transcript expression in schizophrenia
Brain-derived neurotrophic factor (BDNF) is a neurotrophin important for neuronal differentiation and survival. BDNF undergoes a number of alternate splicing events and the transcript variants generated give rise to the same protein as all transcript variants contain the same common coding exon. Reductions in BDNF at the level of mRNA and protein have been reported in the prefrontal cortex of schizophrenic patients. TrkB is the membrane bound receptor for BDNF and is expressed as a variety of transcripts which give rise to different proteins. In the same vein as BDNF, trkB expression is also altered in schizophrenia. This study aims to determine how BDNF and trkB alternate transcripts are altered in schizophrenia and from which promoter these reductions occur. Moreover, changes in protein expression will also be investigated. Determining how expression of this key neurotrophin-neurotrophin receptor pathway is altered in schizophrenia will open up novel avenues to reverse some of the molecular deficits in schizophrenia.

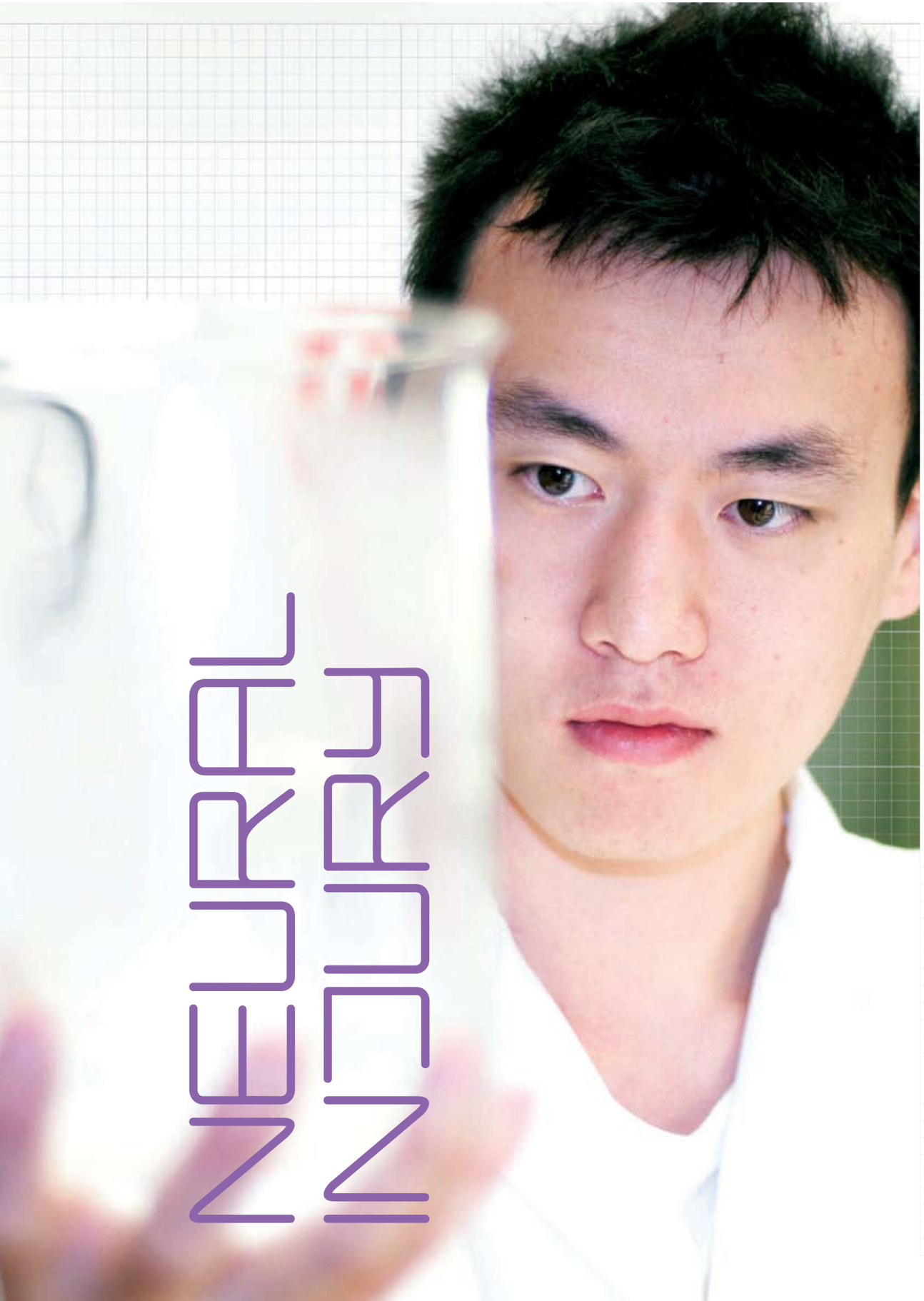
* Professor Shannon Weickert is the Macquarie Group Foundation Chair of Schizophrenia Research, a joint initiative of the Prince of Wales Medical Research Institute, University of New South Wales, Schizophrenia Research Institute and the Macquarie Group Foundation. It is supported by NSW Health.

WEICKERT GROUP

Brain stimulation studies to assess cortical role in category learning and reverse deficits in schizophrenia
The unique contribution of different brain regions to category learning remains unclear and represents a critical gap in our current knowledge base. Knowledge of the contribution of these brain regions is beneficial to the development of therapy to treat this and other cognitive impairments in schizophrenia. Reversal of this impairment may also lead to improvement of daily function and independent living in people with schizophrenia; thus improving their quality of life and reducing the burden to their families and society.

Ultra-high risk, prodromal, and early intervention studies of cognitive and genetic predictors of the development of schizophrenia
The study of children and young adults who are at an 'ultra-high risk' to develop schizophrenia (during late childhood through late adolescence) and may be in the prodromal (pre-symptomatic) phases of illness will open up the possibility for medical intervention before illness onset and would improve the prognosis of people likely to develop schizophrenia. The goal of this research is to establish accurate early detection measures and discover new and effective early treatments that are tailored to the individual on the basis of their genetic constitution.

Australian Schizophrenia Research Bank (ASRB)
The aim of the ASRB, a national collaboration led by the Schizophrenia Research Institute, is to collect and link genetic, neuroanatomical, cognitive and clinical information from 2,000 healthy adults and 2,000 people with schizophrenia nationwide. The information stored by the ASRB will be used in genetic research with the aim of developing better diagnosis, treatments and preventative strategies for people with schizophrenia. During part of 2008 we were part of the Sydney-based data collection team for the ASRB.



NEURAL INJURY

Eric Qin, PhD student, is working toward developing novel methods for detecting changes in soft tissue microstructure and biomechanical properties using multi-modality MR imaging

Injury is the leading cause of death for people under 45 years of age. Injuries to the nervous system, such as brain and spinal cord injuries, are particularly devastating, often leading to lifelong disability. These injuries affect the remaining undamaged nervous system so that even finding how best to make damaged cells regenerate may not be successful in producing functional recovery. Peripheral nerve injury may also lead to chronic "neuropathic" pain which does not respond to current treatments.

The institute's research includes a range of studies from basic research into the mechanisms of injury, to developing improved treatments for injured people and to developing strategies to prevent injuries.

BILSTON GROUP

Injuries to children in car crashes are exacerbated by incorrect use of restraints

Assoc Professor Lynne Bilston's group is studying how road trauma injuries occur in children, and how changes to the types and design of restraints used by children can reduce serious injuries and death. Building on their previous research that has shown that many children are not using the most appropriate restraint for their age and size, they have recently shown that up to 40% of children aged 12 and under are using their restraints in ways that undermine their restraint's ability to protect them in crashes. Rates of incorrect use are higher among younger children using dedicated restraints, suggesting that changes to restraint designs to minimise misuse are needed, and also that parents need to be educated about key errors in restraint installation and usage to make sure their children receive maximum protection.

Non-invasive measurements of brain and muscle tissue properties

The Bilson laboratory has been undertaking research into using MRI scanning methods to estimate tissue stiffness and viscosity (the fluid character of tissues) to detect changes in tissue behaviour in the presence of disease by vibrating the tissue and measuring how this vibration moves through the tissue. This gives the researchers a non-invasive method of "palpating" or feeling the stiffness of tissues. Their research has refined techniques for estimating these properties in the brain and muscle tissues of the leg and upper airway. Using these new techniques, they have commenced studies of disease conditions of the brain, lower leg muscles and upper airway muscles.

Paediatric spinal cord injury

Continuing the work into the mechanisms of paediatric spinal cord injury, in 2008 Assoc Professor Bilston's team completed key studies that showed that it is not until 12 years of age that the risk of spinal injury for children travelling in cars reduces to the same as the risk for adult occupants. Laboratory studies have shown that there are significant differences in the mechanical behaviour of the infant spinal cord which, together with previous studies, suggest that mechanical differences between the spines of adults and young children may underlie the increased severity of spinal injury seen in paediatric patients.

Upper airway biomechanics

Using MRI and electrophysiological methods, the Bilston group has been studying the activity and motion of the muscles that surround the upper airway, both in healthy volunteers and patients with sleep apnoea. Recent findings include demonstrating that specific regions of the tongue muscle (genioglossus) act in a coordinated way to keep the upper airway open during normal breathing, by contracting and moving the tongue forward just before and during the early part of inspiration.

BROCK GROUP

Injury-induced changes in nervous control of blood vessels

A major focus of Assoc Professor James Brock and his team's work is determining how injuries to the nervous system change the way in which nerves control blood vessels. Changes produced by spinal cord injury that result in episodes of high blood pressure (autonomic dysreflexia), greatly increasing the risk of stroke or death, are being investigated. Researchers are also studying nerve injury-induced changes in blood vessels supplying skin. Many people who recover from traumatic injury, or who have chronic conditions such as diabetes, suffer from poor circulation in skin, resulting in impaired wound healing, cold hands and feet and ongoing pain. These people must face a life with progressively increasing disability. The primary goal of this work is to identify drug targets that can be used to improve control of blood flow and thereby alleviate the symptoms.

Changes in neurovascular function following spinal cord injury

Dr Nicole Rummery demonstrated that neural activation of veins was increased following spinal cord injury. Interestingly, this change was associated with a large reduction in the size of the veins. A reduction in the dimensions of veins has previously been documented in people with spinal cord injury and may be an adaptation that contributes to restoring blood pressure control following injury. Findings suggest that loss of neural control of veins is the trigger that causes them to change their size.

Nerve injury induced changes in blood vessel function

Following loss of nerves, blood vessels develop increased responsiveness to chemicals that are normally released from the nerves. This change is believed to cause the reduction in blood flow in skin following nerve injuries. The cause of the increased responsiveness of blood vessels has not been established. In the Brock laboratory, Diana Tripovic has demonstrated that a manipulation that acts simply by increasing calcium entry into the vascular muscle mimics all the effects of nerve loss. This finding suggests that selectively reducing calcium entry in skin blood vessels may improve control of skin blood flow and thereby alleviate the symptoms produced by nerve loss.

Ben Beck, PhD student, is investigating the biomechanics of occupant protection in motor vehicle accidents through improving the safety of occupants in the rear seat

Mechanisms controlling the excitability of 'pain' sensing nerves

The Brock laboratory is also investigating the mechanisms regulating the ease with which sensory stimuli elicit activity (action potentials) in 'pain' sensing nerves (nociceptors). This work uses a technique that allows the electrical activity in the sensory nerve terminals of nociceptors to be recorded. Assoc Professor Brock has used this technique to map, for the first time, the site(s) in the nerve terminal where the pain-generating stimulus is converted into action potentials. Importantly, the study demonstrates that this site is mobile and that the favoured site of action potential generation depends on the numbers of sodium channels that are available for activation. This finding is likely to explain why changes in sodium channel behavour play a central role in increasing the excitability of nociceptive sensory nerves in inflamed tissues.

MACEFIELD GROUP

The role of sensory information from the finger pads in fine motor control of the hand

While the brain has exquisite control of the muscles that act on the wrist and fingers, the sensory feedback provided by specialised sensory endings in the skin of the finger pads is critical for fine motor control. Using fine needle electrodes inserted through the skin into the median nerve at the wrist, Professor Vaughan Macefield and Dr Ingvars Birznieks (supported by the ARC/NHMRC Thinking Systems Grant), together with Professor Tony Goodwin and Dr Heather Wheat from the University of Melbourne, are recording from single cutaneous nerve fibres to determine how the encoding of compressive and rotational forces is associated with manipulation of held objects. This knowledge will allow the design of biologically-inspired sensors for teleoperated robotic surgery which will improve the capacity of the robotic manipulators, and ultimately of robotic surgeons themselves, to sense the shape and softness of the tissues on which they are working.

Functional identification of the sites of the brain involved in blood pressure regulation

How is blood pressure controlled in health, and what goes wrong in disease? In a set of unique experiments, Professor Macefield, together with Dr Luke Henderson from the University of Sydney, is recording from the *muscle sympathetic nerves* that control the diameter of blood vessels, via fine needles inserted into nerves of awake human subjects, while scanning the brain in the 3T MRI facility at POWMRI. They are using the pattern of sympathetic nerve activity to identify regions within the brain that covary with this activity and hence are functionally coupled to the generation of the sympathetic outflow. This will improve their understanding of the circuitry involved in the generation of sympathetic nerve activity and improve understanding of the underlying disturbances in sympathetic control that manifest themselves in different cardiovascular pathologies.

Cortical and subcortical processing of muscle and skin pain in human subjects

Pain differs in quality according to the tissue from which it originates: muscle pain is dull and aching, and often refers to sites remote from the origin, while skin pain is sharp and burning and is well localised. Using the Institute's 3T MRI facility, Professor Macefield and Dr Henderson are examining differences in how the brain treats these different types of pain, and how males and females differ in how the pain is processed by the brain. The researchers are also exploring how referred pain develops: is it established in the brain, the spinal cord, or both? Their work is important in developing a better understanding of the transition from short-lasting (acute) to long-lasting (chronic) pain.

Developing better assessments of autonomic function in spinal cord injury

In addition to motor and sensory loss, spinal cord injury can interrupt the spinal pathways that transmit information from the brainstem to the blood vessels, such that those below the lesion are now deprived of control and blood pressure plummets. In addition, sensory inputs

below the lesion can reflexly excite vasoconstrictor neurones in the spinal cord which, when activated, cause sudden and sustained increases in blood pressure (autonomic dysreflexia) that can lead to stroke and sudden cardiac death. The Macefield group has developed two new means of assessing the integrity of these pathways such that the clinical management of people with spinal cord injury can be improved.

McLACHLAN GROUP

Neuroinflammation

The overall theme of Professor Elspeth McLachlan's work is that inflammation beyond the sites of injury in the spinal cord and peripheral nervous system is involved in the generation of chronic pain after nerve injuries and in the progressive degeneration of vulnerable nerve cells, leading to permanent deficits in nervous function.

Mechanisms underlying chronic neuropathic pain in people with spinal cord injury

Dr Gunnar Wasner, a visiting Research Fellow from Kiel in Germany showed, for the first time, that pain that appears to come from below a spinal injury in people who have no sensations according to conventional sensory tests is often associated with residual connections from pain sensing nerve cells (neurones) that pass through the lesion site. This finding was achieved by stimulating the nerve endings in the skin excessively with capsaicin (from chilli peppers) and histamine and was published in the top ranking neurological journal *Brain*. Dr Wasner also completed a project showing that sympathetic nerve activity was not involved in the generation of pain from such connections.

Death of pathways that project to the brain after spinal cord injury

A researcher in the McLachlan group, Dr Lauren Staples, has identified in models that half the neurones in the lower spinal cord that have their processes (axons) damaged by a spinal cord injury die within two months after the lesion. This slow, ongoing death would explain the progressive loss of function seen in some people with spinal injuries. Clem Lau found that the inflammatory response within the damaged cord involves increased T-cell invasion over this period, suggesting a relationship with the neuronal death. The loss of these neurones means that attempts to regenerate descending connections are unlikely to be successful in the recovery of normal functional responses in the lower limbs and pelvic organs.

Atrophic changes in disused sensory axons below a spinal cord injury

Dr Sabine Krofczik, a researcher in the McLachlan team, recorded from single unmyelinated axons (<0.002 mm thick) in leg nerves that supply the skin below transection of the upper thoracic cord and found that the velocity at which impulses travel along sensory axons is already significantly reduced by two months after the injury. In collaboration with Dr Susan Luff at Monash University, Research Assistant Rathi Ramasamy has found, using the electron microscope, that these axons shrink by about 20% over this period. The changes in conduction velocity can be explained by these changes in dimensions, suggesting the membrane channels responsible for electrical signalling are not defective. Axon shrinkage may follow decreased neurotrophin receptor within the epidermis after spinal cord injury.

Dr Tertia Purves-Tyson, Senior Research Officer, investigates the cellular mechanisms contributing to diabetes-induced nerve damage underlying bladder incontinence and erectile dysfunction

Distinct patterns of degeneration in the distal stump of damaged nerves after different types of injury

Ping Hu, a Senior Research Assistant in the McLachlan group, has examined the immune cells (macrophages and lymphocytes) that invade the stump of a damaged peripheral nerve using specific staining for protein antigens. The inflammatory changes in the nerve trunk a long way below the lesion differ whether or not the damaged axons can regenerate. If only some of the axons are damaged, but others survive the injury, such as after compression, inflammation is more than predicted by the number of damaged axons. The findings point to a new type of interaction between growing axons and the immune system and have implications for the regeneration of nerves over very long distances in human limbs.

Inflammation after peripheral nerve injury is modified by sympathetic activity

As well as the loss of growth factors important for maintenance of neurones, activation of non-neuronal cells, including immune cells, may play a role in triggering the progressive death of damaged neurones. Ping Hu has found that T-cells invade sensory ganglia and damaged nerve trunks to a greater extent as the neurones die. Removal of sympathetic nerve activity reduces the invasion of T-cells, implying a novel interaction between these nerves and the immune system. These results may lead to new treatments to modify the beneficial and/or destructive effects of the immune response and its role in the generation of abnormal (neuropathic) pain and in functional recovery after nerve injuries.

The effects of diabetes on the autonomic pathways to the male pelvic organs

Pelvic autonomic nerve cells are damaged by diabetes and this can result in impotence and bladder incontinence. To develop targeted interventions that promote survival and regeneration of these nerves, it is crucial to determine the causative molecular mechanisms. Senior Research Officer, Dr Tertia Purves-Tyson, is investigating the signalling mechanisms that control degeneration and regeneration of these nerves by manipulating hormones and metabolic pathways. Steroid hormones (testosterone) act as neurotrophic factors that maintain pelvic autonomic nerves by activating neuroprotective pathways, whereas diabetes-related stressors such as high glucose and oxidative stress activate neurodegenerative pathways. These mechanisms are being investigated in pelvic ganglion neurons grown in culture and in their normal location in an animal model of diabetes.

STOODLEY GROUP

Mechanisms of spinal cord cyst formation

Assoc Professor Marcus Stoodley's current projects are investigating various aspects of syrinx development, focusing on mechanisms of fluid inflow, pathways for fluid outflow, and properties of the spinal cord tissue around cysts that could influence their development. Assoc Prof Stoodley and his team are collaborating with Assoc Professor Lynne Bilston on projects examining the effect of Chiari malformations and scarring around the cord on fluid pulse transmission, and the effect this has on fluid flow from the subarachnoid space into the spinal cord. A project in collaboration with Professor Anne Cunningham is examining the effect of syrinxes on surrounding nerve fibres and the feasibility of stem cells to promote remyelination of damaged axons.

Enhancing the response of brain arteriovenous malformations to radiation treatment

After developing an animal model that can be used to investigate the effects of focused radiation on brain blood vessel abnormalities, researchers in the Stoodley group have studied the molecular changes in this model and proposed various strategies to enhance the effect of radiation. Their recent work has demonstrated significant success occluding abnormal vessels using a strategy to increase thrombosis within the vessels. Current projects are aiming to refine this strategy to determine the longer term thrombosis rates and durability. They are also continuing work examining the molecular response to radiation, both in the animal model and in cells cultured from humans.

KIERNAN GROUP

Spinal cord injury

Longitudinal studies to investigate nerve function after spinal cord injury undertaken by Dr Rob Boland have gathered data from patients throughout the course of their admission to the Acute Spinal Unit, Prince of Wales Hospital. These studies are supported by a program grant awarded by the NSW Office of Science and Medical Research. Some patients have been studied in follow-up for more than 12 months. Data from these patients have identified that spinal cord injury has significant downstream effects on nerves in the arms and legs of spinal patients. To address the potential therapeutic and rehabilitation implications of the novel findings, a further series of studies in acute spinal patients is currently underway in which mild electrical stimulation is being applied to paralysed limbs to determine whether the acute deleterious changes observed in earlier studies can be improved or perhaps even prevented.

SPINAL INJURIES RESEARCH CENTRE

The Spinal Injuries Research Centre (SIRC) incorporates work on spinal cord injury by more than ten laboratories in the Institute. The research ranges from experimental studies of the effects of spinal transection on the responsiveness of blood vessels and on inflammation (responsible for spinal hyperexcitability and progressive neurone death) to better understanding how spinal cysts develop in the long term after spinal injuries and the design of improved child restraints in motor cars.

Projects studying people with spinal cord injury included measurements of the excitability of motor and sensory axons, the evaluation of nerve-muscle units in atrophied muscles, the development of stimulation techniques for generating more effective muscle force to assist coughing and coordinated walking during rehabilitation, and the role of residual connections in chronic pain. An atlas of the spinal cord in the rat and mouse has been published, supported by the Christopher and Dana Reeve Paralysis Foundation.

Several SIRC researchers are funded by Program and Project Grants from the NSW Ministry of Health and Medical Research Program for Spinal Cord Injury and Related Neurological Conditions. In 2008, grants were awarded to Assoc Professors Marcus Stoodley and Lynne Bilston by the Column of Hope Foundation in the USA for studies of spinal cyst formation, and to Drs Jane Butler and Penelope McNulty by the NHMRC for the use of electrical muscle stimulation (FES) to improve standing. Assoc Professor James Brock and Professor Simon Gandevia are each involved in successful Program Grants recently announced by the Victorian Neurotrauma Initiative.

SENSATION + MOVEMENT

BALANCE + FALLS

Professor Stephen Lord, Senior Principal Research Fellow, studies a wide range of falls research, from epidemiology to randomised controlled trials

Sensory receptors reside in virtually every part of the body. They respond to different stimuli and provide the brain with important information about our internal environment and about the world around us. Institute scientists are using a range of techniques to understand how the sensory system works, how it affects the motor output from the brain, and how it gives an accurate "sensory" map of the external world. Sensory nerves and their connections in the central nervous system and the motor pathways can be damaged in a range of pathologies.

Control of balance is vital to everyday life. Maintaining balance involves highly complex processing of peripheral sensory information and precise coordination of motor responses. Institute research aims to enhance understanding of human balance and involves investigations of sensory and motor contributions, particularly how sensory signals from the proprioceptive, vestibular and visual systems are integrated to produce coordinated motor activities, orientation and balance. Current studies are designed to investigate the physiology and biomechanics of standing, walking, stepping reactions, trips and slips. Risk factors for falls and injuries and strategies for prevention of falls in different populations are being examined in large-scale population studies.

The movement of breathing requires co-ordinated contractions of many muscles and special control systems in the brain to ensure that it can be maintained. Institute research examines the way that the brain controls the output to the breathing muscles in health and in diseases such as chronic obstructive pulmonary disease, spinal cord injury and obstructive apnoea.

Anna Hudson, Research Assistant, investigates respiratory muscle activation in humans

GANDEVIA GROUP

Studies of proprioception

How the position, movement and size of limbs are judged is being investigated by Institute researchers. This sensation, known as proprioception, is critical to move accurately and maintain posture. Recent studies have revealed how the different signals for proprioception (from muscle and skin receptors) are modulated by other sensory inputs. Professor Simon Gandevia, Assoc Professor Janet Taylor and colleagues induced pain acutely in skin regions and muscles involved in a movement to show that the impairment of proprioception produced by pain depends on a specific interaction with the muscle and skin signals that tells the position and movement of limbs. The work has also shown that different aspects of proprioception are affected differently by pain. This research should improve understanding of how the brain synthesises information to allow accurate voluntary movement.

Plasticity in the motor pathway

Voluntary movements of the limbs are controlled by signals conveyed by nerve cells from the motor areas of the brain to the spinal cord. These cells then connect (synapse) with other nerve cells which convey the signals to the muscles. In human subjects, Assoc Professor Taylor and colleagues have demonstrated, for the first time, that increases and decreases in the strength of the connections in this pathway can be produced over 10–20 minutes by appropriately timed stimulation. When the connections were made stronger (or weaker), the same signal from the brain produced more (or less) voluntary muscle force. This technique of strengthening connections in the motor pathway may prove useful in rehabilitation.

Human sensory function

Each input to proprioception provides the brain with a different and incomplete “view” of the world and the body. The brain merges the signals coming from these sensory systems to produce an accurate internal representation of the position and movement of the body relative to the external world. Dr Richard Fitzpatrick and colleagues are studying how the brain combines these different inputs to form a single perceptual image of the body and its orientation. Using new techniques to stimulate the vestibular organs electrically while also moving the visual surrounds and ground underneath subjects, they have shown that the vestibular signal continuously calibrated to the real or the “mind’s eye” image of the visual world. This vestibular sense is normally turned up and down rapidly by the level of ongoing movement. Their research is exploring how this system is altered with ageing and in clinical conditions associated with movement and balance problems.

Motor function after stroke

There are over 60,000 new strokes in Australia annually. Most who survive have major weakness and half are severely disabled. After the initial damage, secondary changes in the motor pathway can have serious additional deleterious consequences. Dr Penelope McNulty aims to understand these changes in the brain, spinal cord, nerve and muscle and to use the knowledge to improve rehabilitation. She is aiming to study functional ability before and after a novel rehabilitation strategy based on commercially-available video games. Stroke patients may spend more time in these activities than other rehabilitation tasks. Increased physical activity should improve recovery and make stroke patients more independent, reducing the burden of care on families, carers and the community.

Breathing reflex is critical

There is a powerful reflex when the airway is transiently blocked which stops inspiration. This acts to stop inhalation of something blocking the air passages. Scientists are studying the neural mechanisms that underlie this potent protective reflex. So that further studies can be conducted in patients who have shown that this reflex is disturbed, Dr Jane Butler, Professor Gandevia and Dr Nicolas Murray have assessed the best way to monitor the reflex. This involved repeated studies on healthy subjects. Researchers now have a robust and reliable method to assess quickly how this reflex system operates and how it changes with interventions. They will be applying this to study factors such as airway inflammation which may modify this breathing reflex.

LORD GROUP

Prediction of falls and disability during and after rehabilitation ward stays

This study, being undertaken by Dr Cathie Sherrington, Professor Stephen Lord, Assoc Professor Jacqui Close, Dr Anne Tiedemann, Elizabeth Barraclough, Morag Taylor and colleagues, aims to develop screening and assessment tools for prediction of falls and disability during and after rehabilitation ward stays.

Data collection has recently finished in a prospective cohort study involving 435 older people. This involved assessment of patients and medical records reviews and falls outcome data collection. The research team will use the data to test the ability of existing falls screening tools to predict falls and develop new screening tools, if necessary. They will also develop a tool which can predict disability three months after hospital discharge.

The potential impact of this study is significant. Health professional have been asking for a valid in-hospital screening tool which includes objective measurement of physical ability to enable identification of very high-risk individuals. Such a tool will help guide intervention strategies. Development of a pre-discharge screening tool for falls and disability in the month following discharge will help in referral to appropriate rehabilitation and community services after hospital discharge.

Development of safe footwear

By altering somatosensory feedback to the foot and ankle and modifying frictional conditions at the shoe-sole/floor interface, footwear influences postural stability and the subsequent risk of slips, trips and falls in older people. However, little is known about what constitutes safe footwear for older people when undertaking activities in and around the home. Because footwear appears to be an easily modifiable falls risk factor, it is imperative to identify the specific shoe features that might facilitate or impair balance in older people so as to design targeted falls prevention interventions and provide evidence-based recommendations. As part of her PhD project, Jasmine Menant has been conducting a series of studies which examined the effects of common shoe features on functional tests of balance as well as on walking and stopping on various surfaces in young and healthy older community-dwelling people.

Protective stepping

Protective stepping is crucial for balance control and recovery. A step made to restore balance must have the right timing, direction and size for it to succeed. Initial studies have shown that inappropriate step responses are significantly more prevalent in older, compared to younger, people. Impaired stepping is even more common in older people at risk of falls and those with balance impairments, suggesting that appropriate stepping responses are crucial for falls prevention. However, no studies have comprehensively examined stepping performance as a risk factor for falls in a prospective study.

Dr Daina Sturnieks, Professor Lord and Dr Richard Fitzpatrick have begun work to systematically investigate sensory, motor, neural, mechanical and psychological determinants of appropriate and impaired responses to postural perturbations to determine the role that impaired stepping plays in falls. Much of this work will be addressed in a large prospective cohort study. This study is currently underway, with over 70 participants recruited and completed their baseline assessments. Two targeted experimental studies will also be undertaken to identify the effects of fatigue and divided attention on stepping performance and balance control. The final study will comprise a randomised controlled trial to evaluate the effects of a training intervention to improve balance and stepping performance in older adults.

Betty Ramsay, Research Physiotherapist, investigates strength and balance exercises to prevent falls in older people

Visual intervention strategy incorporating bifocal and long-distance eyewear

Presbyopia is a visual condition in which the crystalline lens of the eye loses its flexibility, making focusing on close objects difficult. To correct for presbyopia, older people are either prescribed separate single lens glasses for distant and near vision or, for convenience, a single pair of multifocal (bifocal, trifocal or progressive lens) glasses. Multifocal glasses have benefits for tasks that require changes in focal length. However, multifocals also have disadvantages. Many anecdotal reports have recorded that multifocals constitute a 'danger' for older people, particularly when walking on stairs, and in those with disabilities that affect gait. Professor Lord and his team are conducting a randomised controlled trial in 600 older people to determine whether the provision of single-lens distance glasses to elderly multifocal glasses wearers, together with recommendations for wearing them for standing and outdoor activities, can reduce falling rates over a 12 month period. The team anticipates that the study results will be implemented into public health falls prevention strategies with tangible benefits.

Falls in cognitively impaired older adults

Over the past decade, a number of controlled trials have been published which show it is possible to prevent falls in older people. However, a major disappointing outcome of research in this field is that trials that have included or specifically focused on older people with cognitive impairment have been unsuccessful in preventing falls. As a result, Professor Lord, Assoc Professor Close, Morag Taylor and Stefanie Mikolaizak are conducting a study which aims to develop an understanding of the important factors that contribute to risk of falling in older people with cognitive impairment and dementia. They anticipate that they will be able to identify which risk factors and underlying mechanisms are most strongly associated with falling in cognitively impaired older people. They then hope to use the information to design targeted and tailored intervention strategies to reduce falls and fractures in this high risk population. They are currently conducting a longitudinal cohort study with a one-year follow-up period. To date, over 100 subjects have been recruited and completed baseline assessments. Follow-up and re-assessment has been completed for 24 participants. Assessments include detailed medical history questionnaires, neuropsychological tests, physical assessments and an optional MRI of the brain. Subjects are recruited from local hospitals, hostels, day-care centres and retirement villages.

Fear of falling and risk taking behaviours

Falls are prevalent in older people, and often result in injuries that impose limitations upon daily activities and threaten autonomy. Older people are often aware of these potentially devastating consequences and report being afraid of falling. Although fear of the consequences of falling is often thought necessary to raise awareness and to encourage people towards participation in falls prevention programs, there is a growing consensus that fear of falling may be maladaptive and can lead to the avoidance of fall-related activities. The resulting reduction in activity leads to physical deconditioning, poor quality of life, and increased falls risk. Few studies of falls, fear of falling, anxiety, and depression have been able to unravel the 'chicken and egg' question regarding the interrelationships among these measures, since most studies are cross-sectional. Furthermore, the problem of inappropriate fear, either too much or too little, has been neglected in the current literature. The current study, being conducted by Professor Lord, Assoc Professor Close and Dr Kim Delbaere, aims to investigate prevalence and associated factors of fear of falling in older people. They are currently conducting a longitudinal cohort study with a one-year follow-up period in approximately 500 community-dwelling older people aged over 70.

Falls risk assessment for ambulance officers

The Ambulance Service of NSW attends many older people who have suffered a fall and around 10–25% of these people are not subsequently conveyed to the hospital Emergency Department. A study from the UK has reported that those not conveyed are a high risk group for not only falls, but also other health outcomes, yet existing support and onward referral services are limited for this particular group. This study aims to develop a screening tool to allow for safe non-conveyance and the means of identifying people requiring more detailed assessment and follow-up. Assoc Professor Close, Dr Anne Tiedemann, Professor Lord and Kerrie Atkins are conducting the cohort study with a six-month follow-up period. 60 ambulance service clients aged 70 years and over have been recruited from eight ambulance stations in Sydney so far. The study aims to recruit 250 participants in total.

Falls risk assessment for emergency departments (ED)

The ED represents a defined geographical area which allows for the easy identification of fallers. The evidence to date suggests that these people benefit from a multi-disciplinary assessment in a Falls Clinic type setting. However, the number of fallers presenting to the ED would generate an enormous case load for most Falls Clinics. This study aims to develop a validated screening tool which will allow for a more streamlined approach to managing falls in this high risk population and allow a more cost-effective approach to intervention and prevention. People aged 70 years and over who attend the ED at either the Prince of Wales Hospital or the Royal North Shore Hospital as a result of a fall, and are subsequently discharged, or those who are aged 70 years and over and have had two or more falls in the past 12 months, and are subsequently discharged, will be invited to take part in the study. Assoc Professor Close, Dr Tiedemann, Professor Lord and Teresa Orr are conducting the cohort study with a six-month follow-up period. The recruitment aim is 500 people and, to date, 332 people have been enrolled.

Stepping training for reducing fall risk in older people

This study is being undertaken by Dr Stuart Smith, Professor Lord, Dr Sherrington and Professor Stephanie Studenski, University of Pittsburgh, and aims to develop an enjoyable, interactive home-based step training intervention for older adults. The study also aims to determine the effects of this intervention on key indicators of fall risk in a randomised control trial. The project is in its initial stages of identifying the characteristics of dance mat game play that are appropriate for the functional level of older adults.

Video games for maximising balance in children with ataxia

This study is being undertaken by Dr Stuart Smith, Dr Sherrington, George Institute and Professor Louise Ada, Dr Cath Dean and Dr Colleen Canning, University of Sydney. It aims to investigate the effect of Nintendo Wii training on gait in a child following cerebellar tumour resection. The project is ongoing and should be completed by the end of April 2009.

In-home monitoring of neuromotor function in Parkinson's disease

This project has been funded by Parkinson's NSW and is being undertaken by Dr Smith, Professor Lord, Assoc Professor Rick van der Zwan, Southern Cross University and Assoc Professor George Mellick, Griffith University. It aims to evaluate the use of a recently-developed device for monitoring a number of indices of neuromotor function in people living with Parkinson's disease.

MOSELEY GROUP

Why do some people not recover from wrist fracture?

Most people recover from wrist fracture and have no ongoing problems. However, about 2% of people don't. Instead, they develop a very debilitating disease called Complex Regional Pain Syndrome, or CRPS. This project is investigating whether changes in the way the immune system, the sympathetic nervous system or the brain elevate the risk of developing CRPS after wrist fracture. By measuring these things straight after the fracture, and using a predictive model developed in earlier work, Dr Lorimer Moseley and colleagues hope to understand why some people get CRPS and then work out a method of preventing it. Dr Moseley leads a group of Australian and German researchers in this project.

How can other senses be used to modulate pain?

Pain occurs when the brain judges body tissue to be in danger and that the owner of the body needs to know about it. It is a complex process that occurs outside of consciousness but one that is open to modulation from many factors, including what the visual and other senses are contributing. This series of studies is investigating whether pain can be reduced by manipulating visual information, for example through magnifying lenses, or by manipulating one's sense of ownership over the body part that hurts, for example via the rubber hand illusion. Dr Moseley leads a team of researchers in Australia, the UK, Italy and Sweden on this line of research.

The mind in the body

For centuries it has been known that the body and the mind are well linked. There is a large amount of attention at the moment towards the effects of the body on the mind – leading to theories of the 'embodied mind'. Dr Moseley leads an international team of researchers investigating the link the other way – the effects of how the body is perceived on the regulation and health of the tissues.

Training the brain for chronic pain

When pain persists, the brain undergoes functional and structural changes. There is some evidence that changes actually become part of the problem, in so far as they contribute to the symptoms of chronic pain disorders. This project is pursuing better ways of training the brain to reduce this contribution to pain disorders. This includes training the brain's normal ability to inhibit unhelpful brain activity without reducing helpful brain activity.

Explaining pain

The age-old mantra that 'education to behavioural change is like spaghetti to a brick' has been challenged recently by a series of studies that show that providing patients in pain a clear understanding of the biological processes that underpin their pain improves outcomes. This project continues in this vein by testing new and better ways to explain pain biology. The studies involve investigation of the process by which patients change their understanding of pain and the effects that this has on their pain and functional capacity.

RESEARCH FACILITIES

Brain Bank

The POWMRI Brain Bank became part of the Australian Brain Bank Network in July 2004, and in 2008 partnered with UNSW to further expand from one to four full-time staff positions with the appointment of a new Senior Research Officer, Dr Claire Shepherd, who will function as an overall Facility Manager, a new Liaison Officer to interact with our brain donors and other clinical studies wishing to sign their research subjects up as brain donors, and a new Tissue Resource Manager to oversee the collection, storage and distribution of donated tissue for research. This is in addition to the existing Research Assistant who receives and processes the brain tissue and maintains the laboratory.

Currently the Brain Bank has 692 brains and 220 DNA samples extracted from donated brain tissue in storage. Almost 200 of the brains, and a large proportion of the DNA samples, are available for distribution to other researchers throughout the world upon request. The number of tissue requests has risen steadily with tissues from the Brain Bank being used in some important and large-scale international studies.

The main challenge in 2009 is to integrate the new staff and formalise the new structure and processes of the facility so that everything runs smoothly and efficiently to ensure optimal tissue quality for future research.

Genetic Repositories Australia

With the support of a $2 million National Health and Medical Research Council (NHMRC) Enabling Grant, Genetic Repositories Australia (GRA) was established at the Institute in 2006 under the direction of the Facility Manager, Steve Turner. GRA is a national genetic repository for DNA and cell lines, providing researchers with a central facility for processing, long-term secure storage and distribution of human genetic samples derived from appropriately consented disease-specific and population-based studies.

In 2008, GRA became the first laboratory in Australia to acquire a fully automated large volume DNA purification system, the QIAGEN Autopure LS. Costing over $300,000, the acquisition of the Autopure has increased GRA's productivity and research efficiency, resulting in consistent high quality DNA purification through the ability to fully automate processing of research specimens. A significant number of NHMRC and ARC-funded research projects throughout Australia continue to be supported by GRA's research enabling capacities, with the facility receiving samples from 14 different research projects. A total of 1100 samples were processed in 2008, a 30% increase over the previous year.

The vision for the future is to continue expanding to create GRA as an ongoing national research enabling facility providing a critical core service to enhance medical research in molecular and clinical genetics. The operations of GRA will thus underpin significant biomedical and public health discoveries.

Information Technology

IT at the Institute continues to be a rapidly evolving endeavour. The continued aim is to provide top-quality support for research at every level within the Institute, from the bare bones of the network up to the specialised scientific applications which drive research.

A continual challenge for IT is keeping up with the pace of the expansion within and throughout the Institute. The major building works currently underway require a large growth in the capacity of the IT "backbone" – the core services available to research staff. Items to support the new growth include an enterprise-grade voice-over-IP telephone system, massive expansions in the data network range and capabilities, and the introduction of a centrally based redundant freezer and equipment monitoring system.

A wide range of research interests exists within the Institute and, through the use of standards-based technologies, IT is dedicated to ensure that all laboratories are properly supported at their individual levels, whilst maintaining a cohesive framework to enable co-operation and dialogue between laboratories.

The IT group will continue to support and foster ongoing research excellence and innovation.

POWMRI Imaging

The clinical imaging facility at POWMRI continues to provide researchers working on more than 30 different projects with an open-access, merit-based opportunity to obtain magnetic resonance imaging (MRI) scans. As a result of the commercial takeover of Symbion Health, the new owners ceased operating the MRI facility from May to December. The unplanned stoppage led to unavoidable impacts on research projects and negotiations to resolve the matter were vigorously pursued.

The successful resolution to the provision of MRI imaging occurred in December when the institute purchased the existing 3T Philips Achieva MRI and associated elements of the facility. The facility reopened in January 2009 and has been busy servicing the majority of the studies that were interrupted in 2008. Based on past track record, and increased time available for research scanning, a further nine new studies have commenced since the POWMRI Imaging facility reopened.

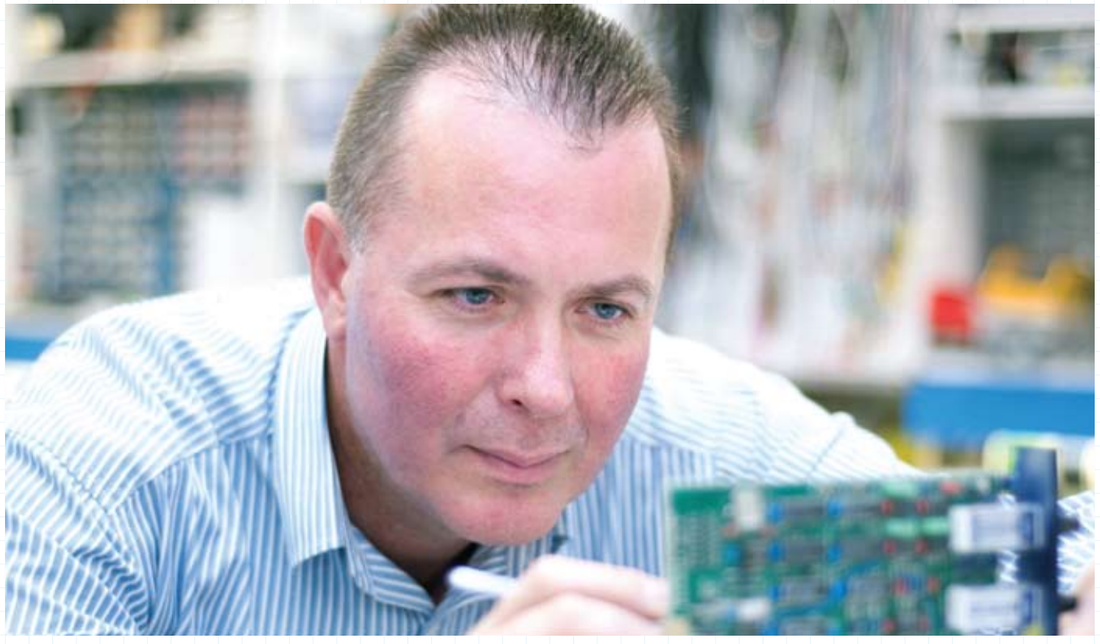
Electronic and Mechanical Workshops

The Institute's workshops provide essential infrastructure support to scientists and students and were the first infrastructure module to be established shortly after the Institute opened in 1993. The unique nature of research carried out at the Institute means that the equipment needed for the experiments cannot be bought "off the shelf"–instead must be constructed to individual specifications.

Workshop staff, Lajos Weisz in the Electronic Workshop and Hilary Carter and Dave Menardo in the Mechanical Workshop, collaborate with scientists to design, prototype and manufacture the equipment–either in-house or by CAD drawings–which are then turned into parts by subcontractors. The workshop team is also on-call to repair breakdowns or calibrate equipment during experiments involving volunteer subjects with spinal injuries or respiratory illness.

The equipment manufactured in the Mechanical Workshop ranges from large-scale frames which support an entire person assisting investigation into human movement and balance, to small tissue baths which record electrical signals from individual nerve cells. In the Electronic Workshop, the equipment required ranges from simple strain gauge amplifiers to Hi DC voltage stimulators and from position measurement to data acquisition for accurate analysis.

Equipment designed and manufactured by the workshops is used in other institutions such as The Black Dog Institute, University of Sydney, UNSW, Cumberland College and University of Western Sydney. Various components for Professor Stephen Lord's "Falls Kit", prototyped in the workshops, have been distributed world-wide.



Lajos Weisz, Electrical Workshop Manager, attends to all electronics requirements for Institute projects including repair and maintenance of existing laboratory and office

Dr Claire Shepherd,
Senior Research Officer, is researching the
role of inflammation in neurodegeneration

OUR PEOPLE

Dr Lorimer Moseley, Senior Research Fellow, was recently named outstanding mid-career clinical scientist by the International Association for the Study of Pain

TRAINING & RECOGNITION

BLAINE ALLEN
ACSR Spinal Research Symposium VI, Adelaide – best oral presentation

GEORGE PAXINOS
Awarded Doctor Honoris Causa by University of Athens

RAJ REDDY
Neurosurgical Society of Australasia Peter Leech Memorial Prize – best oral presentation

REBECCA ST GEORGE
Brain Sciences UNSW Symposium – best postgraduate presentation

LORIMER MOSELEY
Ulf Lindblom Young Investigator Award for Clinical Science awarded by the International Association for the Study of Pain (research undertaken at the University of Oxford)

The Institute hosts PhD, Masters and Honours students, mostly enrolled through the University of New South Wales. During the year, the following PhD degrees were conferred.

POSTGRADUATE DEGREES CONFERRED IN 2008

Student	Degree	Project Title	Supervisor(s)
Dr Svetlana Cherepanoff	PhD	Age-related macular degeneration: histopathogical and serum antibody studies	S Sarks
Dr Steve Vucic	PhD	Transcranial magnetic stimulation in ALS	M Kiernan/G Nicholson
Julie Brown	PhD	Spinal injuries to child occupants in car crashes	L Bilston
Elizabeth Clarke	PhD	Biomechanical aspects of animal models of spinal cord injury	L Bilston
Carlotta Duncan	PhD	Genetics and genomics of mental illness	P Schofield/C Shannon Weickert/ A Chetcuti
Phu Hoang	PhD	Changes in the length tension properties of individual human muscles in health and following muscle damage or disease	S Gandevia/R Herbert
Jasmine Menant	PhD	Effect of footwear on balance and gait in older people	S Lord
Julian Saboisky	PhD	Human respiratory neurophysiology	J Butler/S Gandevia

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Kim WS, Hill AF, **Garner B.** Impact of human neuronal ABC transporters on cholesterol efflux and amyloid-beta production. In: Hanin I, Windisch M, Poewe W, Fisher A (Eds). *New Trends in Alzheimer and Parkinson Disorders.* Medimond. Bologna. pp 43–47, 2008

Knibb J, **Hodges JR.** Semantic dementia: The story so far. In: Mariën P, Abutalebi J (Eds). *Neuropsychological Research: A Review.* Psychology Press. Hove. UK. pp 471–490, 2008

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McLachlan EM, Hu P. Inflammation of dorsal root ganglia: satellite cell activation and immune cell recruitment after nerve injury. In: DeLeo J, Sorkin L, Watkins L (Eds). *Immune and Glial Regulation of Pain.* IASP Press. Seattle. USA. pp 167–185, 2008

Piguet O, Corkin S. Memory: structure, function, and dysfunction. In: Mariën P, Abutalebi J (Eds). *Neuropsychological Research: A Review.* Psychology Press. Hove. UK. pp 411–436, 2008

Sturnieks D, Lord SR. Biomechanical studies for understanding falls in older adults. In: Hong Y, Batlett R (Eds). *Routledge Handbook of Biomechanics and Human Movement Science.* Routledge. New York. pp 495–509, 2008

Sturnieks D, Tiedemann A. Falls. In: Heggenhougen K, Quah S (Eds). *International Encyclopedia of Public Health. Vol 2.* Academic press. San Diego. pp 563–569, 2008

Taylor JL, Komi PV, Nicol C. Central and neuromuscular fatigue. In: Taylor N and Groeller H (Eds). *Physiological Bases of Human Performance During Work and Exercise.* Elsevier. Oxford. Chapter 5. pp 91–114, 2008

Velayos-Baeza A, Lévecque C, **Dobson-Stone C,** Monaco AP. The function of chorein. In: Walker RH, Saiki S, Danek A (Eds). *Neuroacanthocytosis Syndromes II.* Springer. Berlin. pp 87-105, 2008

PROFESSIONAL SERVICE

TO THE SCIENTIFIC COMMUNITY AND RELATED ORGANISATIONS

Lynne Bilston
- **Member,** NSW Products Safety Committee
- **Board Member,** College of Biomedical Engineers, Engineers Australia
- **Member,** Engineers Australia National Panel on the Biomechanics of Impact Injury
- **Member,** Australian Standards Committee for Child Restraints in Motor Vehicles (CS-085), including drafting panel
- **Member,** Kidsafe NSW
- **Member,** Australasian College of Road Safety

Ingvars Birznieks
- **Member,** Latvian Scientific Council (Human biology, Medicine), international popular science journal, Ilustrētā Zinātne

James Brock
- **Chair,** Grant Review Panel 4D, Autonomic, Peripheral and Sensory Nervous Systems
- **Member,** NHMRC Grant Advisory Group
- **Presiding Member,** UNSW Animal Care and Ethics Committee
- **Member,** Local organising committee for the International Society for Autonomic Neuroscience meeting in September 2009
- **Treasurer,** Australia and New Zealand Microcirculation Society
- **Member,** Editorial Board of *Autonomic Neuroscience: Basic and Clinical*
- **Teacher,** International Brain Research Organization Schools

Jane Butler
- **Member,** Local Organising Committee, 2010 meeting of the Australian Neuroscience Society
- **Editorial Board** – *Journal of Applied Physiology*

Kay Double
- **Member,** Management Council, Parkinson's NSW Inc and Scientific Editor of newsletter
- **NSW Representative,** Australian Association of Alexander von Humboldt Fellows
- **Secretary,** National Association of Research Fellows of the NHMRC
- **Founding Member,** Forum for European-Australian Science and Technology (FEAST), Germany
- **Editorial Board,** *Journal of Neural Transmission; Parkinson's Disease and Allied Conditions*

Richard Fitzpatrick
- **Editorial Board,** *Journal of Physiology*
- **Editorial Board,** *Journal of Applied Physiology*
- **Editorial Board,** *Gait and Posture*

Paul Foley
- **Book Reviews Editor,** *Journal of the History of the Neurosciences*
- **Board Member,** International Society of the History of the Neurosciences
- **Member,** Organising Committee, 2007–2009 Meetings of the International Society for the History of the Neurosciences (ISHN)
- **Organiser and Chairman** of symposium on scientific writing and book reviewing at ISHN meeting (2009)

Brett Garner
- **Member,** NHMRC Grant Review Panel – Molecular Neuroscience
- **Member,** Grant Review Panel, Wellcome Trust
- **Member,** Grant Review Panel, Juvenile Diabetes Research Foundation Projects
- **Editorial Board,** *Future Lipidology*
- **Editorial Advisory Panel,** *Biochemical Journal*
- **Editorial Advisory Panel,** *Clinical Science*

Simon Gandevia
- **Section Head,** Faculty of 1000 in Biology
- **Chair,** NHMRC CDA Panel
- **Deputy Chair,** NHMRC Grant Review Panel
- **Professorial Associate,** Centre for the Advancement of Cardiopulmonary Physiotherapy
- **Member,** Scientific Advisory Committee, The Bosch Institute
- **Associate Editor,** *Journal of Applied Physiology*
- **Editorial Board,** *Acta Physiologica*
- **Advisory Board,** *Australian Journal of Physiotherapy*
- **Field Editor,** *Encyclopedic Reference in Neuroscience*
- **Editorial Board,** *Journal of NeuroEngineering and Rehabilitation*

Glenda Halliday
- **Executive Member,** NHMRC National Network of Brain Banks
- **Executive Member,** NHMRC Australian Brain Donor Programmes
- **Director,** POWMRI/Parkinson's NSW Brain Bank
- **Member/Chair,** POWMRI Research Committee/ Finance Subcommittee
- **Chair,** UNSW Faculty of Medicine Postgraduate Review Panel C
- **Member,** UNSW Faculty of Medicine Research Committee
- **Member,** Coast Medical Association Tow Research Committee
- **President Elect/President/President Past/Executive,** Australian Neuroscience Society
- **Executive Member,** NHMRC Australian Parkinson's Project
- **Member,** NHMRC Academy
- **Member,** NHMRC Project Grants Variation Committee
- **Chair,** Grant Review Process for the Sir Zelman Cowen Universities Alzheimer's disease research fund for the University of Sydney
- **Chair/Member,** NHMRC Neuroscience Discipline Grant Review Panel
- Scientific Advisory Board of *Brain*
- **Scientific Advisory Boards,** Kolling Research Institute, Royal North Shore Hospital & the University of Sydney
- Centre for Brain & Mental Health Research, University of Newcastle
- **Governing Council Member,** International Brain Research Organisation
- **Member,** International Brain Research Organisation Membership Committee
- **Member,** International Brain Research Organisation Asya Pacific Regional Committee
- **Member,** Scientific Advisory Committee, Parkinson's NSW
- **Editorial Board,** *Acta Neuropathologica*
- **Editorial Board,** *Journal of Neural Transmission*
- **Editorial Board,** *Movement Disorders*

John Hodges
- **Editorial Board,** *Cognitive Neuropsychiatry*
- **Editorial Board,** *Cognitive Neuropsychology*
- **Editorial Board,** *Nature Clinical Practice Neurology*

Matthew Kiernan
- **Chair,** Specialist Advisory Committee in Neurology, Royal Australian College of Physicians
- **Chair,** Neurology Curriculum Writing Group, Royal Australian College of Physicians
- **Chair,** Scientific and Programme Committee, Australian and New Zealand Association of Neurologists
- **Member,** Committee for Physician Training, Royal Australian College of Physicians
- **Member,** Conjoint Committee, Memorandum of Understanding between Specialty Societies and the Royal Australian College of Physicians
- **Council Member,** Australian and New Zealand Association of Neurologists
- **Member,** Education and Training Committee, Australian and New Zealand Association of Neurologists
- **Postgraduate Coordinator,** Prince of Wales Clinical School, UNSW
- **Member,** Higher Degree Committee, UNSW
- **Member,** Examination Committees, Medicine, UNSW
- **Member,** Human Research Ethics Committee, Prince of Wales Hospital
- **Vice President,** Australian Brain Foundation
- **Chair,** Scientific Committee, Australian Brain Foundation
- **Board Member,** Australian Brain Foundation
- **Medical Advisor,** Motor Neurone Disease Association of NSW
- **Board Member and Member of the Scientific Committee,** Motor Neurone Disease Research Institute of Australia
- **Member,** Greater Metropolitan Transition Taskforce (GMTT) committee to address the needs of transitional care patients
- **Editorial Board,** *Journal of Neurology, Neurosurgery and Psychiatry*
- **Editorial Board,** *Journal of Clinical Neuroscience* (Associate Editor)
- **Editorial Board,** *Clinical Neurophysiology* (Associate Editor)
- **Editorial Board,** *Amyotrophic Lateral Sclerosis*
- **Editorial Board,** *Current Medicinal Chemistry*
- **Editorial Board,** *British Medical Journal* (case reports)

Stephen Lord
- **President,** Australia and New Zealand Falls Prevention Society
- **Member,** Osteoporosis Australia Medical and Scientific Committee
- **Founding Member and Scientific Advisor,** New South Wales Falls Prevention Network
- **Member,** National Association of Research Fellows of NHMRC
- **Associate Member,** Prevention of Falls Network, Europe (ProFaNE) (2004–)
- **Member,** Scientific Program Committee, International Society for Postural and Gait Research, 19th biannual conference, June, 2009, Bologna, Italy
- **Member,** Scientific Program Committee, Fourth Biennial Australian Falls Prevention Conference, Dunedin, New Zealand, November, 2010
- **Invited Presentation** – Evidenced-based fall prevention strategies for older people. NSW Area Health Services Health Promotion Directors Meeting
- **Chair,** Expert Advisory Group, Australian Commission on Safety and Quality in Healthcare National Falls Prevention Guidelines

Elspeth McLachlan
- **Chair,** International Brain Research Organization (IBRO) Brain Campaign – Public Education Committee
- **Member,** IBRO Committee on By-Laws and Procedures
- **Member,** Nuffield Foundation Medical Fellowship Committee
- **Member,** Scientific Advisory and Executive Committees, Victorian Neurotrauma Initiative
- **Chair,** NSW Regional Group, Australian Academy of Science
- **Member,** Assessor Selection Panel, NHMRC Project Grants
- **Honorary Senior Research Fellow,** Faculty of Biomedical & Life Sciences, University of Glasgow
- **Member,** Editorial Board, *Clinical Autonomic Research*
- **Member,** Editorial Board, *Clinical and Experimental Pharmacology and Physiology*

Lorimer Moseley
- **Editorial board,** *Reviews in Pain*
- **Associate Editor,** *PAIN*
- **Associate Editor,** *British Journal of Sports Medicine*
- **External course reviewer,** Masters of Pain Science, King's College London

Dr Samantha Fung, Research Officer, studies the role of testosterone in postnatal development of the brain and schizophrenia

George Paxinos
- **Editorial Board,** *Neuroscience and Biobehavioural Reviews*
- **Editorial Board,** *Journal of Chemical Neuroanatomy*
- **Editorial Board,** *Brain Structure and Function*

Olivier Piguet
- **Member,** Publication Board, *Brain Impairment*

Caroline Rae
- **Company Secretary,** Australian and New Zealand Society for Magnetic Resonance (ANZMAG)
- **NSW State Representative**, Council of the Australian Society for Biochemistry and Molecular Biology
- **Member,** Australian Academy of Science National Committee for Brain and Mind
- **UNSW Node Director,** Australian National Imaging Facility
- **Executive Committee,** Brain Sciences Institute, UNSW
- **Chair,** NMR Reference Group, UNSW
- **Review Editor,** *Frontiers in Neuroenergetics*

Peter Schofield
- **Member,** Inaugural Course Management Committee, Australian Course in Advanced Neuroscience
- **Chair Selection Committee,** Young Tall Poppies Campaign, Australian Institute of Policy & Science
- **Member,** Research Council, Schizophrenia Research Institute Australia – formerly NISAD
- **Panel Chair,** NHMRC Discipline Panel 4a
- **Member,** Scientific Review of kConFab (Kathleen Cunningham Foundation Consortium for Research into Familial Breast Cancer), Sydney
- **Co-Convenor,** 6th Australian GeneMappers Conference, Katoomba, April 2009
- **Director,** Neuroscience Australia Ltd
- **Member,** NHMRC Reference Group on Biobanks and Genetic Registers
- **Editorial Board,** *Psychiatric Genetics*

Cyndi Shannon Weickert
- **Co-Chair,** Developmental Neurobiology Panel (DNP) Schizophrenia Research Institute
- **Board Member,** Schizophrenia Research Institute
- **Committee Member,** Australian Psychosis Research Network
- **Committee Member,** Scientific Advisory Committee for Australian Brain Donor Programs
- **Member,** Schizophrenia International Research Society
- **Member,** Society for Neuroscience
- **Program Committee,** Society for Biological Psychiatry

Marcus Stoodley
- **Member,** Scientific Advisory Board, Cure for Life Foundation
- **Member,** RACS Board of Surgical Research
- **Member,** Brain Foundation NSW Committee
- **Board Member,** Australian Brain Foundation
- **Editorial Board,** *Pediatric Neurosurgery*
- **Board Member,** RACS Board of Neurosurgery

Charles Watson
- **Member and Chair,** Research Advisory Committee, Cancer Council of WA
- **Chair,** Neurological Council of WA
- **Editorial Board,** *Australian and New Zealand Journal of Public Health*
- **Editorial Board,** *Communicable Disease Intelligence*

Thomas Weickert
- **Member,** Executive Committee, School of Psychiatry, UNSW
- **Member,** Society for Neuroscience
- **Member,** Scientific Research Committee, Australian Schizophrenia Research Bank
- **Member,** Cognition and Connectivity Panel, Schizophrenia Research Institute

OUR PEOPLE

LEADERSHIP

Schofield, Prof Peter
Gandevia, Prof Simon

AGEING & NEURODEGENERATION

Halliday Group

Halliday, Prof Glenda
Shepherd, Dr Claire
Foley, Dr Paul
Reid, Dr Wayne
Huang, Dr Yue
Cartwright, Heidi
Hill, Dr Michelle
Dalton, Marshall
Yen, Annie
Amaral, Fabricio
Brooks, Daniel
Song, Christine
Warden, Lolita
Truong, Linda

Hodges Group

Hodges, Prof John
Piguet, Dr Olivier
Hornberger, Dr Michael
Schofield, Dr Emma
Mioshi, Eneida
Savage, Sharon
Hsieh, Sharpley
Foxe, David (from Aug 08)
Lillo, Dr Patricia
Garcin, Beatrice

Broe Group

Broe, Prof Tony
Jackson Pulver, Assoc Prof Lisa
Grayson, Dr David (from Aug 08)
Mack, Dr Holly (from Jul 08)
Arkles, Rachelle
Hill, Jay

Double Group

Double, Assoc Prof Kay
Dedov, Vadim (to Jan 08)
Werry, Dr Eryn
Carew-Jones, Francine
Smoothy, Veronica (from Mar 08)
Reyes, Stefanie
Ng, Ian

Garner Group

Garner, Assoc Prof Brett
Kim, Dr Scott
Kagedal, Dr Katerina
Bhatia, Surabhi (from Jun 08)
Glaros, Elias
Elliott, David
Chan, Sharon
Cheng, Danni

Kiernan Group

Kiernan, Assoc Prof Matthew
Boland, Dr Robert
Lin, Dr Cindy (to Feb 08)
Vucic, Dr Steve
Krishnan, Dr Arun
Winhammar, Dr Jennica [from Feb08)
Han, Eric
Park, Susanna
Cheah, Ben

Kwok Group

Kwok, Dr John
Dobson-Stone, Dr Carol
Hallupp, Marianne
Gorissen, Sarsha (from May 08)

Sarks Group

Sarks, Dr Shirley (to Aug 08)
Cherepanoff, Dr Svetlana
Jafri, Sadaf

BRAIN FUNCTION & IMAGING

Rae Group

Rae, Prof Caroline (Lindy)
Courcot, Dr Blandine (to Jul 08)
Abeshouse, Miriam
Nasrallah, Fatima
Chew, Mai Fang
Graham, Bronwyn
Sim, Ben
Cassidy, Ben

Paxinos Group

Paxinos, Prof George
Watson, Prof Charles
Fu, Dr Yuhong
Heise, Dr Claire (to May 08)
Zhao, Peter
Liang, Dr Andy

MENTAL ILLNESS

Shannon Weickert Group

Shannon Weickert, Prof Cyndi
Sivagnanasundaram, Dr Sinthuja (to Oct 08)
Wong, Dr Jenny
Duncan, Dr Carlotta
Catts, Dr Vibeke (from Apr 08)
Rothmond, Debora
Fung, Samantha
Rothwell, Alice
Woon, Heng Giap (from Aug 08)
Tsai, Shan-Yuan
Turner, Diana (from May 08)
Sinclair, Duncan

Schofield Group

Schofield, Prof Peter
Brooks, Dr William
Karl, Dr Tim (from Oct 08)
Fullerton, Dr Jan
Cederholm, Dr Jennie
Long, Dr Leonora (from Oct 08)
Pierce, Kerrie
Heath, Anna
Agahi, Giti (from Sep 08)
Chesworth, Rose (from Oct 08)
Tiwari, Yash (from Jun 08)
Sugiharto (from Apr 08)
McAuley, Erica
Assareh, Arezoo

Weickert Group

Weickert, Dr Thomas
Rushby, Jacqueline
Morris, Dr Richard
Dunlop, Kristy (to Oct 08)
Lim, Yen (to Nov 08)
Quinn, Siobhan (to Nov 08)
Youssef, Caroline (to Jun 08)
Gendy, Rasha
Short, Dr Brooke
McNamara, Dr Rebecca

NEURAL INJURY

McLachlan Group

McLachlan, Prof Elspeth
Purves-Tyson, Dr Tertia
Krofczik, Dr Sabine (to Sep 08)
Staples, Dr Lauren
Hu, Ping
Ramasamy, Rathi (to Dec 08)
Lee, Grace
Burton, Danielle

Bilston Group

Bilston, Assoc Prof Lynne
Green, Dr Michael
Cheng, Dr Shaokoon
Brown, Dr Julie (from Jun 08)
Clarke, Dr Elizabeth
Amatoury, Jason
Brown, Elizabeth
Tian, Maoyi
Ho, Anita
Dhondee, Donovan
Tammareddy, Sriram

Brock Group

Brock, Assoc Prof James
Pianova, Svetlana (to Jan 08)
Rummery, Dr Nicole
Tripovic, Diana

Stoodley Group

Stoodley, Assoc Prof Marcus
Tu, James
Hemley, Sarah
Goy, Christine (from Jun 08)
Fairhall, Dr Jacob
Allen, Blaine
Chan, Ronald
Hacibekiroglu, Sabiha
Koenig, Brigitte

Macefield Group

Macefield, Prof Vaughan
Birznieks, Dr Ingvars
Brown, Rachael
Burton, Alex
Henderson, Luke

SENSATION, MOVEMENT, BALANCE & FALLS

Gandevia Group

Gandevia, Prof Simon
McNulty, Dr Penelope
Nickolls, Dr Peter
Hoang, Dr Phu
Weerakkody, Dr Nivan (to Sep 08)
Walsh, Lee
Boswell-Ruys, Claire
Bowden, Jocelyn
Murray, Dr Nick
Yu, Dr Wei Shin
McNeil, Dr Chris
Lee, Andrew
Whyte, Morgan
Krishnananthan, Thanuja

Lord Group

Lord, Prof Stephen
Close, Assoc Prof Jacqueline
Smith, Dr Stuart
Sherrington, Dr Cathie
Sturnieks, Dr Daina
Delbaere, Dr Kim
Tiedemann, Dr Anne
Menant, Jasmine
Barraclough, Elizabeth
Vance, Dr Esther
O'Rourke, Sandra
Atkins, Kerrie (from Apr 08)
Foster, Cathy (to May08)
Porwal, Mamta
Martin, Jodie
Orr, Teresa
Ramsay, Betty
Taylor, Morag
Roberts, Layla (to Jun 08)
Kvelde, Tasha
Kwan, Marcella
Zheng, Jacqui
Wong, Alfred
Mitchell, Sarah
De The, Ming
Gschwind, Yves
Pijnappels, Mirjam

Fitzpatrick Group

Fitzpatrick, Dr Richard
Luu, Billy
Butler, Anne
St George, Rebecca
Offord, Joanne
Rahman, Tanjim
Grenet, David
Eisenberg, Yoel

Butler Group

Butler, Dr Jane
McBain, Rachel (to Mar 08)
Hudson, Anna

Taylor Group

Taylor, Assoc Prof Janet
Van Duinen, Dr Hiske
Martin, Dr Peter
Giesebrecht, Sabine

Moseley Group

Moseley, Dr Lorimer (from Oct 08)

Migliaccio Group

Migliaccio, Dr Americo (from Aug 08)

Colebatch Group

Colebatch, Prof James

RESEARCH FACILITIES

Tissue Resource Centre

McCann, Heather
Murphy, Karen

Genetic Repositories Australia

Turner, Steve
Stevens, Julia (to Jan 08)
Curphey, Lauren
Hawthorne, Sally (from Apr 08)
Wu, Wendy (from Oct 08)
Evans, Annie

Mechanical & Electrical Workshop

Weisz, Lajos
Carter, Hilary
Menardo, Dave

OPERATIONS

Finance

Dermott, Andrew
Wang, Ruby
Hilton, Lee
Dworjanyn, Rosalie
Davey, Randall (from Jul 08)
Xu, Lin

Information Technology

Cartwright, Dr Andrew
Cartwright, Michael
Tsang, Wai-Kit (from Jul 08)
Gunawin (to Jun 08)

Administrative Assistance

Nickolls, Ros
Riley, Andrea
Bebris, Inara
Homewood, Sarah
Smith, Vicky (from Jul 08)
Govindasamy, Laksmi
Severino, Connie
Temple, Dr Liz

Operations

McKay, Deborah
Wang, Kathy
Daniels, Ursula
Gobbe, Karen
Bryans, Bob
Thompson, Bill
Bryan, Adam

Facility Development

Freeman, Dr Jeffrey

THE FOUNDATION

Ellis, Margaret (from Sep 08)
Graham, Anne
Fury, Angela (to Oct 08)
Lilian, Ruth (from Nov 08)
Rienmueller, Cathy
Harle, Leonie

FINANCE

FINANCE

Statement of Financial Performance for the Year Ended 30 June 2008

	03/04	04/05	05/06	06/07	07/08
	$'000	$'000	$'000	$'000	$'000
Revenue					
Research Grants	4,147	3,828	4,592	5,213	7,478
Infrastructure	1,592	1,826	2,550	4,016	4,008
Donations and fundraising	211	1,000	1,298	1,579	3,095
Building Grant – Commonwealth					1,210
Financial	219	313	403	770	547
Other	345	509	304	953	721
Total	**6,514**	**7,476**	**9,147**	**12,531**	**17,059**
Expenses					
Salaries and employee benefits	4,953	5.012	5,947	7,418	9,041
Research operations	116	321	586	1,109	1,801
General operations	502	559	553	661	978
Depreciation and amortisation	478	467	454	534	677
Fundraising	7	176	151	203	243
Building	100	214	121	203	193
Other	213	155	317	188	142
Total	**6,369**	**6,904**	**8,129**	**10,316**	**13,075**
Operating Surplus	**145**	**572**	**1,018**	**2,215**	**3,984**

Statement of Financial Position as at 30 June 2008

	03/04	04/05	05/06	06/07	07/08
	$'000	$'000	$'000	$'000	$'000
Balance Sheet					
Current Assets	5,163	6,938	11,081	44,696	46,798
Building Development					1,210
Property, Plant & Equipment	6,945	6,552	6,703	7,315	6,985
Total Assets	12,108	13,490	17,784	52,011	54,993
Current Liabilities	885	1,655	4,831	36,729	35,628
Provisions	225	265	365	480	579
Total Liabilities	1,110	1,920	5,196	37,209	36,207
Retained Surplus	7,348	7,920	8,938	14,802	18,786
Reserves	3,650	3,650	3,650	0*	0
Total Net Funds	**10,998**	**11,570**	**12,588**	**14,802**	**18,786**

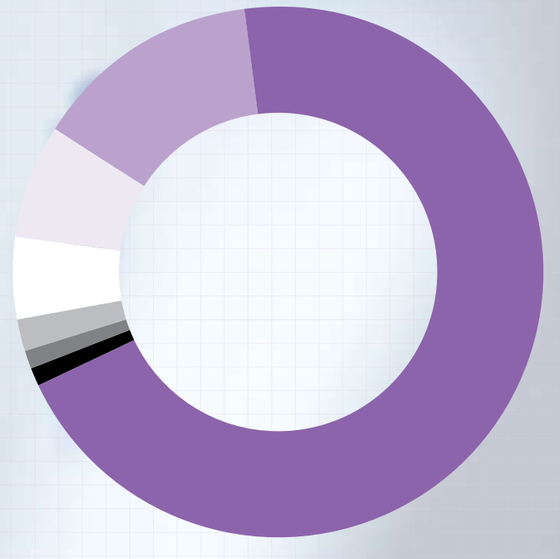
* Reserves transferred to Retained Surplus

Financial information was extracted from the audited Financial Statements of POWMRI Limited, the statutory entity of the Prince of Wales Medical Research Institute, for the year ending 30 June 2008 and is included here for information purposes only. A full copy of the audited Financial Statements, including Notes to the Financial Statements and the Audit Opinion, can be obtained free of charge on request to the Finance Manager, Prince of Wales Medical Research Institute, Barker Street, Randwick NSW 2031.

REVENUE

- Competitive Research Grants 45%
- Infastructure Support 23%
- Donations & Fundraising 18%
- Building Grant – Commonwealth 7%
- Financial 3%
- Other 4%

EXPENSES



- Salary & Employee Benefits 70%
- Research Operations 14%
- General Operations 7%
- Depreciation & Amortisation 5%
- Fundraising 2%
- Building 1%
- Other 1%

FUNDING

Research Grants

The Institute attracts competitive external grant funding from a number of national and international organisations every year. Total peer-reviewed funds for the 2008 calendar year were $9.75M. The most significant funding body is the National Health and Medical Research Council. In 2008, NHMRC income was $6.47M. While the NHMRC continues to be a major source of research funding, there has been a significant expansion in other funding bodies as Institute researchers continue to actively seek research funds from other sources.

NSW Medical Research Support Program

The Institute has been successful in securing funding of $4.41M for the 2006–2009 triennium from the NSW Medical Research Support Program. The Institute also received $1.35M of infrastructure funding from UNSW in 2008.

Research Funding 2008

Summary information on competitive peer-reviewed research grants, fellowships and scholarships, and other sources of external research grant income, applied for and awarded in 2007/08 (funds received) for expenditure through the calendar year 2008:

National Health and Medical Research Council

Bilston LE, Senior Research Fellowship A (2004–2008), 2008 amount $109,750

Bilston LE, Gandevia SC, McKenzie D, Novel neuromechanical measurements of the human upper airway in health and disease, NHMRC Project Grant (2007–2009), 2008 amount $173,692

Brock J, Senior Research Fellowship B (2005–2009), 2008 amount $109,750

Broe GA, Jackson Pulver L, Chalkley S, Grayson D, What is the burden of dementia in urban dwelling Indigenous Australians? NHMRC Project Grant, (2008–2010), 2008 amount $535,442

Bryant R, Williams L, Schofield PR, Raphael B, Richardson R, Dadds M, NHMRC Centre of Clinical Research Excellence in Anxiety and Neuroscience (2007–2011), $400,000 pa

Butler J, Senior Research Fellowship A (2008–2012), 2008 amount $109,750

Colebatch J, Vestibular reflexes evoked by brief lateral head accelerations: a new measure of utricular function, NHMRC Project Grant (2008–2010), 2008 amount $81,086

Dickson P, Dunkley P, Double K, Differential regulation of human tyrosine hydroxylase isoforms and the development of Parkinson's disease, NHMRC Project Grant (2007–2009), *administered by University of Newcastle*

Double KL, Senior Research Fellowship A (2006–2010), 2008 amount $109,750

Double KL, Garner B, Halliday GM, Isoprenoids, neuromelanin and neuronal vulnerability in Parkinson's disease, NHMRC Project Grant (2006–2008), 2008 amount $183,280

Eckert D, The role of arousal in the pathogenesis of obstructive sleep apnea and implications for novel therapeutic treatments, Overseas Based Biomedical Training Fellowship (2008–2011), 2008 amount $85,078

Finch CF, Stevenson MR, Norton RN, Zye AB, Lord SR, Williamson AM, Cameron DI, Addressing injury in a population health framework – an integrated approach to prevention, acute care and prevention, NHMRC Capacity Building Grant in Population Health (2005–2009), 2008 sub-contract amount $76,500

Fitzpatrick R, Human sensorimotor Physiology, NHMRC Biomedical Career Development Award – Level 2 (2008–2011), 2008 amount $102,250

Gandevia S, Senior Principal Research Fellowship + SEO (2005–2009), 2008 amount $165,250

Gandevia SC, Taylor J, Novel assessments of the central and peripheral control of the human hand, NHMRC Project Grant (2007–2009), 2008 amount $121,621

Garner B, Cholesterol efflux, apolipoprotein-E and glycobiology, NHMRC RD Wright Career Development Award (2005–2009), 2008 amount $92,500

Garner B, Kim W, Halliday G, Role of ABCA/G transporters in neuronal cholesterol regulation and Alzheimer's disease, NHMRC Project Grant (2008–2010), 2008 amount $202,760

Halliday GM, Principal Research Fellowship (2005–2009), 2008 amount $133,000

Halliday G, Gai W-P, Sue C, Huang Y, Cellular changes due to LRRK2 parkinsonism, NHMRC Project Grant (2008–2010), 2008 amount $192,300

Karl T, The role of cannabis in an Nrg1 animal model of genetic vulnerability to schizophrenia, NHMRC Project Grant (2008–2010) 2008 amount $150,405 *administered by Schizophrenia Research Institute,* 2008 POWMRI funds $23,899

Kiernan M, Pathophysiology of oxaliplatin-induced nerve dysfunction and neuropathy, NHMRC Project Grant (2006–2008), 2008 amount $87,112

Kiernan M, Motor neurone disease – pathophysiological insights into the site of origin and patterns of neurodegeneration, NHMRC Project Grant (2008–2010), 2008 amount $118,235

Kwok J, The leucine rich repeat kinase1 and 2 genes are modulators of alternative splicing – implication for neurodegeneration, NHMRC Project Grant (2008–2010), $192,485

Kwok J, Schofield P, Garner B, Biological characterisation of the opioid receptor sigma 1 gene in frontotemporal dementia and motor neurone disease, NHMRC Project Grant (2008–2010), $160,130

Lord SR, NHMRC Senior Principal Research Fellowship (2007–2011), 2008 amount $150,250

Lord SR, Close J, Identification and quantification of risk of falls in cognitively impaired older adults, NHMRC Dementia Research Grants Program Strategic Award (2007–2009), 2008 amount $182,279

Lord SR, Close J, Fitzpatrick R, Understanding fear of falling and risk taking in older people, NHMRC Project grant (2006–2008), 2008 amount $129,056

Lord SR, Sturnieks D, Fitzpatrick R, Rogers M, Sherrington C, Impaired stepping a risk factor for falls in older people, NHMRC Project Grant (2008–2010), 2008 amount $186,315

McLachlan E, Delayed neuronal death after peripheral nerve and spinal cord injury, NHMRC Project Grant (2006–2008), 2008 amount $155,586

McNulty P, Neurophysiological investigation of motor pathways in subjects with stroke, NHMRC Peter Doherty Fellowship (2004–2008), 2008 amount $85,008

Murray G, Henderson L, Macefield V, Klineberg I, An fMRI analysis of the functional organization within the central nervous system of experimental superficial and deep orofacial pain, NHMRC Project grant, *administered by the University of Sydney,* 2008 POWMRI sub-contract amount $20,750

Paxinos G, NHMRC Senior Principal Research Fellow (2006–2010), 2008 amount $150,250

Paxinos G, Watson C, The structure of the human cortex as revealed by gene expression, NHMRC Project grant (2007–2009), 2008 amount $175,435

Piguet O, Early identification of degenerative dementia syndromes, NHMRC Clinical Career Development Award – Level 1 (2008–2011), 2008 amount $92,500

Piguet O, Hodges J, Rose S, Miller L, Clinical and biological markers of disease presentation and progression in early frontotemporal dementia, NHMRC Project grant (2008–2010), 2008 amount $171,030

Purves-Tyson T, The effect of estrogen on signalling mechanisms of the pelvic autonomic nervous system underlying bladder and erectile dysfunction in diabetes, NHMRC Peter Doherty Fellowship (2004–2008), 2008 amount $50,438

Rae C, Coltheart M, McArthur G, The Rane and Spain routes in the brain: functional studies and remediation in dyslexia subtypes, NHMRC Project Grant (2006–2008), 2008 amount $117,366

Reutens D, Bartlett P, Galloway G, Paxinos G, Petrou S, Egan G, Australian mouse brain mapping consortium, NHMRC Enabling Grants – Model Biological Systems (2007–2011), *administered by Monash University,* 2008 POWMRI sub-contract amount $173,355

Sachdev P, Martin N, Ames D, Schofield P, Broe GA, Brodaty H, Trollor J, Wright M, Wen W, Halliday GM, Lee T, Gene-environment interactions in healthy brain ageing and age-related neurodegeneration, NHMRC/ARC Ageing Well Ageing Productively Program (2007–2011), $400,000 pa

Schofield PR, Blair I, The biological role of the cadherin gene FAT in bipolar disorder susceptibility, NHMRC Project Grant, (2006–2008), 2008 amount $120,780

Schofield PR, Cavanaugh J, Forrest S, Hopper J, Genetic Repositories Australia, NHMRC Enabling Grant–Special Facilities (2006–2010), 2008 amount $400,000

Schofield PR, Donald J, Mitchell P, Cloning and characterisation of a bipolar disorder susceptibility gene on chromosome 15q, NHMRC Project grant (2008–2009), 2008 amount $157,050

Schofield PR, Lewis T, Barry P, Clements J, Mechanisms of signal transduction and receptor activation in ligand gated ion channel receptors, NHMRC Project Grant, (2007–2009), 2008 amount $180,293

Schofield PR, Turner S, Shannon Weickert C, Kwok J, Halliday G, et al, QIAGEN Autopure LS AP-0098 Automated large volume nucleic acid purification system, NHMRC Equipment grant, 2008 amount $114,000

Sherrington C, Cumming R, Lord S, Close J, Dean C, Vogler C, Minimising disability and falls in older people through a post-hospital individualized exercise program (2007–2009), *administered by the University of Sydney,* 2008 amount $200,200, POWMRI sub-contract amount $109,161

Smith S, Multisensory determinants of postural instability and falls in older adults; prevention and rehabilitation, NHMRC Industry Career Development Award – Level 1 (2008–2011), 2008 amount $92,500

Taylor J, Senior Research Fellowship A (2007–2011), 2008 amount $109,750

Taylor J, Butler J, Corticospinal transmission in human subjects, NHMRC Project Grant (2007–2009), 2008 amount $121,746

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- **Other 3%**

Australian Research Council

Bilston LE, Brown J, Hatfield J, Optimising protection for motor vehicle rear seat occupants, ARC Linkage Projects (2008–2011), 2008 amount $52,366

Breakspear M, Morley J, Harris J, Sammut C, Goodhill G, Paxinos G, Lovell N, Knock S, Lagopoulos J, Malhi G, Macefield V, Optimizing autonomous system control with brain-like hierarchical control systems, Thinking Systems Grant (2006–2010), 2008 amount $679,000 POWMRI subcontract amount $165,162.36

Broe GA, ARC research network in ageing well, Research Network Grant (2004–2008), 2008 amount $10,000

Herbert R, Gandevia SC, Bilston LE, Passive mechanical properties of human muscles, ARC Discovery project (2007–2009), *administered by the University of Sydney,* 2008 POWMRI subcontract amount $64,488

Hodges J, Long-term memory systems and the human brain, ARC Federation Fellowship (2007/08–2011/12), 2008 amount $541,938

Mareels I, Egan G, McDonnell K, Rae C, Kotagiri R, Data management technologies for the magnetic resonance imaging e-research grid, ARC Linkage Project Grant (2006–2009), 2008 amount $58,000

Schofield PR, Gordon E, Identification of genetic polymorphisms of synaptically expressed genes that contribute to variation in normal brain function, ARC Discovery Project (2007–2009), 2008 amount $91,758

Williams LM, Schofield PR, Clark C, Kemp AH, Gatt JM, Gene-brain pathways in emotional brain stability and instability, ARC Linkage Project (2008–2011), 2008 amount $125,000, *administered by the University of Sydney*

Kilpatrick T, Mastaglia F, Halliday GM, Cowie TF, Rubio JP, Horne MK, Development of the PD GeneChip: a research and diagnostic tool for Parkinson's disease, ARC Linkage Project (2007–2009), *administered by the University of Queensland*

NSW Health Dept/NSW Office for Science & Medical Research

Hodges J, Long-term memory systems and the human brain, Office for Science and Medical Research–NSW Life Sciences Award (2007/08–2011/12), 2008 amount $100,000

Lord S Close J, Tiedemann A, Sherrington C, Development and validation of a fall risk screening tool for use in the emergency departments, NSW Health Department, 2008 amount $29,790

Lord S Close J, Tiedemann A, Sherrington C, Development and validation of a fall risk screening tool for use by ambulance officers, NSW Health Department, 2008 amount $29,790

Lord S Close J, Tiedemann A, Sherrington C, Development and validation of a fall risk screening tool for use by Aged Care and Rehabilitation Services, NSW Health Department, 2008 amount $14,864

McLachlan E, Brock J, Kiernan M, Macefield V, Altered nerve and muscle excitability after spinal cord injury–challenges for functional recovery, NSW Office for Science and Medical Research Program Grant (2006–2010), 2008 amount $375,000

Middleton J, Davis G, Gandevia S, Craig A, Nickolls P, et al, Enhancing functional recovery and independence after spinal cord injury, NSW Office for Science and Medical Research Spinal Cord Injury & Other Neurological Conditions Program Grant (2005–2008), *administered by the University of Sydney,* 2008 POWMRI sub-contract amount $60,502.59

Other Funding Bodies

Brock J, McLachlan E, Purves-Tyson T, Diabetes induced changes in neurovascular function in arteries supplying skin, UNSW Goldstar Award, 2008 amount $40,000

Butler J, McKenzie D, Gandevia S, Henderson L, Reflex, voluntary and involuntary control of breathing in health and disease, UNSW Goldstar Award, 2008 amount $40,000

Colebatch J, Ocular VEMPs (OVEMPs) a new method of vestibular assessment, Garnett Passe and Rodney Williams Memorial Foundation (2008–2010), 2008 amount $74,589

Davis M, Kochunov P, Lancaster J, Paxinos G, Petrides M, Tardiff S, Toga A, A neuroimaging study of primate brain development and aging in the marmoset, National Institutes of Health, Dept of Health and Human Services Research Grant Subcontract with University of Texas Health Science Center at San Antonio, 2008 amount $35,939

Dobson-Stone C, Genetics of variation in normal and attention-deficit hyperactivity disorder brain function, UNSW Vice-Chancellor's Postdoctoral Research Fellowship (2007–2009), 2008 amount $73,060

Double K, Differential regulation of human hydroxylase isoforms and the development of Parkinson's disease, Parkinson's NSW, 2008 amount $20,000

Fairhall J, Stoodley M, Smee R, Enhancement of thrombosis in brain arteriovenous malformations after radiosurgery, Pfizer NeuroScience Research Grant, 2008 amount $50,000

Finch C, Lord SR, Close J, Pascoe D, Sturnieks D, Tiedemann A, Twomey D, Development of a workforce education program for exercise practitioners in falls prevention and exercise prescription for older people, Commonwealth Department of Health & Ageing, Falls and Injury Prevention Community Grants Program, 2008 amount $194,289, *administered by the University of Ballarat,* 2008 POWMRI sub-contract amount $37,300

Fitzpatrick R, Lord S, McNulty P, Gandevia S, Neurophysiology of human balance and posture, UNSW Goldstar Award, 2008 amount $40,000

Foley P, UNSW Strategic Research Fellowship, 2008 amount $80,000

Foley P, Encephalitis lethargica and epidemic influenza: forgotten, but not gone, National Institutes of Health – National Library of Medicine Project Grant (2008–2009), 2008 amount US$53,832

Fullerton J, Identification of variants causing altered expression of melatonin receptor in bipolar disorder, NARSAD 2007 Young Investigator Award (2007–2009) 2008 amount $30,000

Garner B, Chalfant C, Targeting the biosynthetic pathway to treat atherosclerosis, UNSW Goldstar Award, 2008 amount $40,000

Herbert R, Gandevia SC, Bilston LE, Hoang P, Changes in passive mechanical properties of muscle fascicles and tendons in people with advanced multiple sclerosis, Multiple Sclerosis Research Australia Incubator Grant, 2008 amount $15,000

Huang Y, Characterising the phenotypes of a novel causative dementia gene (PD9), Australian Academy of Science Scientific Visits to China, 2008 amount $2,000

Huang Y, Kwok J, Halliday G, Chen S, Characterising the phenotypes of a novel causative dementia gene, Alzheimer's Australia Research Dementia Research grant, 2008 amount $22,000

Kiernan M, McKenzie D, Boland R, Cheah B, 2 INSPIRATionAL (Inspiratory Training for Amyotrophic Lateral Sclerosis 2), Australian Rotary Health Research Fund Mary Jane Douglas Motor Neurone Disease Research Grant, 2008 amount $40,350

Kim W, A nucleofector electroporator for transfecting primary brain cells at the Prince of Wales Medical Research Institute, Rebecca L Cooper Medical Research Foundation, 2008 amount $20,000

Kwok J, Biochemical characterisation and clinical imaging of a novel gene involved in multiple neurodegenerative diseases, The Mason Foundation Medical & Scientific Research Grant, 2008 amount $50,000

Martin P, Attendance at the 'Mechanisms of Plasticity and Disease in Motoneurones Meeting', June 26-29 2008, Seattle, Washington, Ian Potter Foundation travel grant, 2008 amount $1,700

Martin P, Attendance at the 'Mechanisms of Plasticity and Disease in Motoneuroes Meeting', June 26-29 2008, Seattle, Washington, CASS Foundation Travel Grant – Post doctoral Early Career Researcher, 2008 amount $3,000

Schofield PR, Brooks W, An information support system for families with hereditary dementia – An Australia-wide program, JO & JR Wicking Trust (2007–2009), 2008 amount $50,000

Shannon Weickert C, Confocal microscope for neurogenesis and neurodegeneration studies in the brain and spinal cord, Clive & Vera Ramaciotti Foundations Equipment Gift, 2008 amount $30,000

Shannon Weickert C, Enhancing neurogenesis in adult primate brain, UNSW Goldstar Award, 2008 amount $40,000 *administered through UNSW School of Psychiatry*

Shepherd C, Targeting mediators of inflammation in Alzheimer's disease, Anonymous (2007–2009), 2008 amount $100,000

Shepherd C, Monocyte chemoattractant protein-1 as a potential modifier of Alzheimer's disease, UNSW Goldstar Award, 2008 amount $40,000

Shepherd C, Monocyte chemoattractant protein-1 in Alzheimer's disease, The Mason Foundation Medical & Scientific Research Grant – Alzheimer's disease, 2008 amount $49,744

Stoodley M, Bilston LE, Cerebellar tonsil movement and CSF flow in Chiari malformation and syringomyelia, Neurosurgical Society of Australasia Research Grant, 2008 amount $30,000

Turner S, Schofield P, Cavanagh J, Forrest S, Hopper J, Genetic Repositories Australia, Rebecca L Cooper Medical Research Foundation Research Grant, 2008 amount $20,000

Turner S, Schofield P, Genetic Repositories Australia, Baxter Charitable Foundation Equipment Grant, 2008 amount $40,000

Vucic S, The role of fatiguing exercise in the aetiology of motor neurone disease, Motor Neurone Disease Research Institute of Australia Research grant, 2008 amount $25,000

Wasner G, McLachlan E, Sympathetically maintained pain mechanics in spinal cord injured people, International Association for the Study of Pain Collaborative Research Grant, 2007/8 amount $15,000

Weickert T, Clinical trial of a selective oestrogen receptor modulator in schizophrenia, UNSW Faculty Research Grant, 2008 amount $30,000 administered through UNSW School of Psychiatry

Winhammar J, Clinical trial to assess the neuroprotective properties of flecainide in motor neurone disease, Motor Neurone Disease Research Institute Australia Bill Gole MND Postdoctoral Fellowship, 2008 amount $72,500

Scholarships

- Allen B, South Western Sydney Children's Hospital Postgraduate Research Scholarship (2007–2010), $24,947
- Brooks D, Michael & Elizabeth Gilbert Postgraduate Scholarship in Parkinson's Disease Research (to May 2008), $5,333
- Brown E, Royal Australasian College of Physicians ResMed Foundation Research Scholarship 2008, $20,000
- Butler A, Albert Chua Scholarship (2006–2008), $19,000
- Cheah B, Brain Sciences UNSW PhD Scholarship (2008–2010), $25,007
- Cheng D, Brain Foundation Parkinson's Tulip Foundation PhD Scholarship (2008–2010), $30,000
- Giesebrecht S, UNSW University International Postgraduate Award (2008–2010), $20,007
- Glaros E, DEST Australian Postgraduate Award (2007–2009), $20,007
- Han E, NHMRC Biomedical Postgraduate Scholarship (2008–2009), $22,257 plus MAWA Trust supplementary scholarship (2008–2009), $25,000
- Liang A, UNSW University International Postgraduate Award (2008–2010), $10,004
- Loy C, NHMRC Postgraduate Scholarship (2005–2008), $16,045
- McAuley E, NHMRC Dora Lush (Biomedical) Postgraduate Scholarship (2005–2008), $11,156
- Murray N, NHMRC Postgraduate (Medical) Research Scholarship (2006–2008), $16,045
- Park S, DEST Australian Postgraduate Award (2007–2009), $20,007
- Reyes S, Michael & Elizabeth Gilbert Postgraduate Scholarship in Parkinson's Disease Research (2008–2010), $21,000 plus Parkinson's NSW Postgraduate Award (2007–2009) $6,000
- Sinclair D, DEST Australian Postgraduate Award (2008–2010), $10,004
- Song C, GlaxoSmithKine Postgraduate Support Award (2007–2008), $10,000 plus Parkinson's NSW Research Student Award 2008, $6,000
- St George R, The Cowled Postgraduate Research Scholarship for Brain Research 2008, $20,000
- Zheng J, Brain Sciences UNSW PhD Scholarship (2008–2010), $25,000

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Wood AO, Hon Justice James
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Wrigley, Ms Cecily
Wyner, Ms Iris
Y
Yarrawonga Bridge Club
Yarrow, Ms Susan
Young, Mr Keiran
Young, Mr Stanley

THE INSTITUTE'S FOUNDATION

FUNDRAISING & COMMUNICATION

The Foundation is the Institute's newly-formed fundraising arm which will enhance the scientists' vital neuroscience research efforts through a new fundraising strategy and environment. The Foundation's mission is:

> ***To build a strong public profile resulting in ongoing endowments to fund the research for the prevention, treatment and cure of brain disease to benefit all Australians***

The Institute's scientific leadership is reflected in the many competitive grants that scientists receive; however, financial support through government, donations and bequests plays a key part in underpinning their research. This support allows research teams to further establish and identify significant opportunities as well as set up new laboratories, purchase equipment and attract outstanding researchers from Australia and overseas resulting in global recognition of their work.

The challenges of fundraising for the Foundation's team are great but the long-term rewards make the efforts worthwhile. It is important that the Institute continues to grow now and in the future. The Institute is sincerely grateful for the generosity of its donors. It is only through this financial support that researchers can hope to improve the health and well-being of so many people in the community.

Bequests – The Phyllis Luker Society

The Phyllis Luker Society was established in 2005 as the Institute's bequest society. It is named in honour of a long-time supporter, whose commitment to brain research led her to make significant donations over a number of years, culminating in her on-going support through a provision in her Will. The Society was set up to honour people who have made a bequest and the Institute thanks them for their on-going generosity and trust. To learn more about ways to include the Institute in your Will, please contact Bequest Manager, Leonie Harle, on 02 9399 1125.

Direct Mail Appeal Program

Appeal letters seeking financial support for research into Alzheimer's disease, Motor Neurone Disease and for a scholarship to support a talented PhD researcher, were mailed this year. The Program was successful, contributing significant donations to support research plus attributing to a significant increase of new supporters in the donor base. Sincere thanks to everyone who supported these appeal programs.

ASX-Reuters Charity Foundation

The Institute continued to receive financial support from the ASX-Reuters Charity Foundation which allows continuity in the employment of a Clinical Studies Volunteer Coordinator to assist with the recruitment for the following projects:

- **Schizophrenia Research Bank**
  Initiated by the Schizophrenia Research Institute, the Schizophrenia Research Bank holds brain-related data from 2,000 Australian volunteers with schizophrenia and 2,000 people without schizophrenia. This will be the largest schizophrenia research facility of its type in the world. The goal of the bank is to deposit brain related data to allow scientists to unlock the secrets of this devastating disease.
- **The Cognition and Ageing Research Program**
  Institute scientists are interested in studying the ageing brain, including neurodegenerative diseases such as Alzheimer's disease, frontotemporal dementia, Parkinson's disease and other conditions. The goal of the program is to understand how these diseases affect brain structure and function to improve methods of diagnosis and assist patients with dementia and their families.

Researchers sincerely thank the ASX-Reuters Charity Foundation for its continued financial assistance.

Institute Tours

Visitors on the Institute's tours expressed enthusiasm for the laboratory research work they witnessed. These tours provide an opportunity to meet senior scientists, experience first-hand the research being undertaken and to see how donations assist scientists in a tangible way. Visitors also met members of the Board to hear about the Institute's plans for the future.

Key Events

The Institute wishes to acknowledge the support of a group of volunteers who contributed to making the annual dinner a success. Sincere thanks are extended to Mardi Le Page, Sandra Constantine, Leanne Hayward, Alistair Keep, David Morgan Mike Da Silva, Robyn Kiddle and Pira Carroll.

Food for Thought Gala Dinner

Five Melbourne award-winning chefs took 266 guests on a culinary trip 'over the border' to showcase their signature dishes at the Annual Gala Dinner to raise funds for research into mental illness. An outstanding six-course degustation menu, accompanied by Victorian wines, was presented at this five star event. Sincere thanks to Simon Marnie, Matthew Carroll AM, Cairellie Showcraft, Rawson Graphics, URSA, Jam Jar Design, chefs Ben Shewry, Andrew McConnell, Geoff Lindsay, Matt Wilkinson, Robin Wickens and Jochen Hess plus sponsors and generous guests.

Bridge for Brain Research Challenge

This was the fifth year of the Challenge and it is stronger than ever. With support from the Australian Bridge Federation (ABF), 93 clubs participated with over 2,340 bridge players involved nationally. The event raised over $25,000 for Alzheimer's, Parkinson's and Dementia research at the Institute. Special thanks to Valerie Cummings, Ron Klinger, The Australian Bridge Federation, in particular John Delaney, Martin Willcox and Jane Rasmussen and major sponsors Captain Cook Cruises, Nokia, Penguin Group and The Bridge Shop.

Creative Madness Art Exhibition

Creative Madness, an annual art event, was held during October in conjunction with Mental Health Week to raise both funds and awareness about mental illness, especially bipolar disorder (manic depression). All 39 artists explored the theme 'madness' and interpreted it as widely as possible. Special thanks to Orson & Blake, European Catering, participating artists and generous guests.

Publications

The newsletter Brainworks and the Annual Report are key information tools updating and promoting all areas of research and fundraising undertaken at the Institute. These publications are central to communication and education programs both to the community and to donors.

Tax Deductibility of Donations

All donations over $2 are tax-deductible. The Institute is endorsed as a deductible gift recipient (DGR).

> ***You have the power to make a significant difference. Donate to the Foundation, funding the Prince of Wales Medical Research Institute.***

More than ever before, Australians are facing the anguish of caring for family members living with diseases that affect their mind and their mobility. Solutions will only be found through medical research. By financially supporting the Institute's Foundation, you will provide researchers with a vital resource to move closer to diagnostic tools, treatments that alleviate symptoms and discoveries that will lead to cures of brain diseases. There are a number of ways you can make a donation or a bequest to the Foundation.

Corporate Partnerships

There are many benefits in building a corporate partnership which enables you to meet your customer, staff, shareholder and community responsibilities. Your company could make a tax-deductible donation to sponsor a young researcher, an event or a publication. You may wish to discuss how your employees can participate in a Workplace Giving program. To discuss these and other options, please call 02 9399 1125.

- **A Bequest**
  For more information on how to include a bequest to the Prince of Wales Medical Research Institute in your Will, please call Leonie Harle, Bequest Manager on 02 9399 1125.
- **Regular or Single donation**
  A regular donation every month, or even every year, is immensely valuable as it enables research teams to plan ahead with confidence. Every donation is sincerely appreciated.
- **Donate by phone**
  please call Cathy Rienmueller, Donations Manager, on 02 9399 1125.
- **Donate Online**
  www.powmri.edu.au.
- **Donate by mail**
  Please send your cheque to Donations Department, Prince of Wales Medical Research Institute, PO Box 82, St Pauls NSW 2031. *(All cheques should be made payable to the Prince of Wales Medical Research Institute)*
- **Hold an Event**
  If you would like to organise an event with the proceeds going to the Foundation, please call Suzy Randjelovic, Event Manager, on 02 9399 1075.

The Institute appreciates all donations and greatly values donors. To discuss any of the above, please do not hesitate to contact Professor Peter Schofield on 02 9399 1003.

MAKE A DONATION TODAY

Call **02 9399 1125** or donate online at **www.powmri.edu.au**

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