

## BRAIN AND MIND DISORDERS: IMPACT OF THE NEUROSCIENCES

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Terms of Reference for the Working Group are provided in Appendix 1.

## CONTENTS

EXECUTIVE SUMMARY AND RECOMMENDATIONS	3
1. INTRODUCTION	9
1.1 What are brain and mind disorders?	9
1.2 Neuroscience's contribution to understanding brain and mind function	10
1.3 Purpose of the paper	11
1.4 Formal submissions	11
2. HEALTH IMPACT OF BRAIN AND MIND DISORDERS	11
2.1 Overall health burden	11
2.2 Brain and mind disorders of youth	13
2.3 Brain and mind diseases of the elderly	19
3. THE GLOBAL NEUROSCIENCE REVOLUTION: AUSTRALIA'S CONTRIBUTION	24
3.1 The neuroscience promise	24
3.2 How is Australia going to capture maximum benefits from the neuroscience revolution?	26
4. THE PATH FORWARD	29
4.1 Fragmented approaches impede the national research effort	29
4.2 Some initiatives to overcome fragmentation	29
4.3 The Brain and Mind Research Alliance	32
4.4 Implementing a national approach to brain and mind disorders	33
4.5 An Action Agenda for the Brain and Mind Research Alliance	35
5. CONCLUSIONS & RECOMMENDATIONS	37
APPENDICES	
Appendix 1: Terms of Reference	38
Appendix 2: Estimated Health and Business Costs Associated with Alzheimer's disease	39
Appendix 3: Professional Societies, Organisations and Bodies Involved in Neuroscience	41
Appendix 4: Overview of the Australian Neuroscience Industry Sector	44
Appendix 5: Additional Details on Strategies for the Brain and Mind Research Alliance	54
Appendix 6: Summary of Submissions Received	67
REFERENCE MATERIAL	68

## EXECUTIVE SUMMARY AND RECOMMENDATIONS

### The Largest Health Burden

Brain and mind disorders pose the largest health, economic and social capital burden to Australia of any disease group. This arises because these disorders are chronic and debilitating.

The nature of brain and mind disorders changes across the human lifespan. The young have a higher incidence of psychiatric disorders, including depression, anxiety, schizophrenia and substance abuse. In contrast, the elderly suffer particularly from neurodegenerative conditions such as dementia or stroke.

Early adult life is faced with more chronically disabling psychiatric disorders than is widely realised. This results in much personal suffering and the need for costly care, but also long term unemployment and erosion of the tax base.

In fact, psychiatric disorders in our youth are increasing, reflecting a wider range of social, family, drug and alcohol problems.

More widely appreciated is that the elderly suffer neurodegenerative disorders, and that these are increasing because of an ageing population – the “baby boomers”.

We have seen national successes in reducing the incidence of broad disease classes, such as cardiovascular disease.

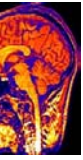
Without success in reducing brain and mind disorders, Australia faces both a blowout in direct health and aged care costs and indirect welfare and social security payments over the next 40 years in addition to a reduced revenue base.

The outcome for Government is a major effect on both the revenue base, which will get far worse and expenditure outlays, which will increase. This case is eloquently made in the *Intergenerational Report*, and in other health related reports.

### The Savings

Curing brain and mind disorders would provide potentially immense budgetary savings. Modest examples include:

- a 25% reduction in the incidence of one uncommon disease, schizophrenia, is estimated to save the Government about \$0.5 billion per annum
- curing Alzheimer’s disease would save the Government about \$1 billion per annum and the nation over \$6 billion.
- Positive externalities from a more healthy population would be very high, such as contributions to the workforce and establishment of small businesses.



## The Cure

There is light at the end of the tunnel, as one example may illustrate. Alzheimer's disease may be preventable and curable within ten years. This is based on global research to which Australia has made very major contributions. There is now a worldwide race to take this research to an effective treatment of the disease.

Incremental improvements in therapies that provide limited symptomatic relief are not the answer. We need basic understanding of the disorders, to prevent or cure them. Basic research provides the pipeline of cures.

The prospects of effective interventions to contain or arrest neurodegeneration, restore function, or even to prevent disease from occurring, are realistic goals in the areas of morbidity such as stroke, dementia, multiple sclerosis and peripheral neuropathies. At a later stage, radically novel therapeutic or preventive interventions are likely to become available in psychiatric disorders. Powerful technologies, such as functional neuroimaging of living brain in action, have a great potential of improving the quality of personalised clinical care.

The *National Health and Medical Research Council* has mental health as a priority area for research funding. This funding has grown but stabilized at \$31 million per annum. Is this commensurate with the problem? It currently costs Australia \$6.6 billion per annum for the 162,000 people affected by dementia while schizophrenia, with 37,000 sufferers, costs the nation \$1.85 billion.

The Australian neuroscience research effort appears underfunded. Individually, there is considerable research talent, which unfortunately is widely dispersed in small pockets across the nation.

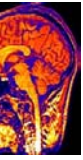
We need a holistic approach, better basic research support, and a mechanism to achieve this.

We need to provide the optimal pathway to understanding and curing brain and mind disorders because they largely depend on interactions between the environment and our genes. We therefore need to understand the role of both "nature AND nurture" to improve brain and mind disorders.

Creativity in brain and mind research is being stimulated by researchers themselves dismantling barriers to cooperation. However, Government programs need to more vigorously lead the way forward by themselves cooperating more fully.

Cooperation is beginning to extend across the basic neurosciences, the clinical disciplines of neurology and psychiatry, and the population-based health approaches, such as epidemiology.

Their borders are giving way to a holistic brain and mind endeavour that uses powerful research technologies for research data gathering, scientific modeling, and science communication to the public.



## Science and Society of the 21st Century

Unprecedented scientific advances over the last decade are leading to the widespread view that we are on the verge of a neuroscience revolution that will dominate scientific effort and societal change in this century.

These advances include:

- sequencing of the human genome - the greatest single advance in human knowledge, with over half of all genes coding for the central nervous system
- neuroinformatics – the analysis of neuroscience using information science
- non-invasive brain imaging technologies that visualize brain function in real time
- regeneration of nerve cells
- access to family and population databanks
- stem cell therapies for nervous disorders
- genetic therapies for inherited and acquired diseases

Many dozens of laboratories around the world are now competing in efforts to identify and characterise at cellular and molecular level the neural pathways involved in higher nervous functions, ranging from language to the experience of personal identity. We will uncover the detailed bases of memory, perception, intelligence, our moods and emotions, and how all of this changes over our lifespan. This knowledge will provide a much deeper understanding of how these processes go awry in brain and mind disorders.

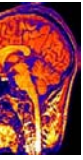
An important objective, which necessitates the collaboration between developmental neuroscientists and behavioural researchers, is the study of controllable influences on critical phases of neurodevelopment, aiming to maximise the positive educational and environmental impacts on the brains of children.

Clearly, such knowledge will raise tremendous ethical, legal and social issues and debate in a society that will need to be highly informed and educated about science.

The advances that may be achieved by the neuroscience revolution have encouraged the UK's *Medical Research Council* to propose "Biobank", a huge data repository on the genetics and lifestyle of the British population. This proposal has raised concerns about privacy issues.

Similarly, on the other side of the Atlantic, concerns have been raised that non-invasive brain imaging might be perceived as "spying on the cortex" and invading people's privacy.

In Australia, these new technologies may change society's approaches to life insurance risk, criminal law, education, and even the kind of person we want to be. We must be proactive



in managing this challenge in order for the ethical debate to keep pace with scientific advances and so avoid issues that have arisen in other areas.

Nobel Laureate neuroscientist, Eric Kandel, recently wrote that following the completion of the human genome project “...*progress, not only in neuroscience, but in neurology and psychiatry, will proceed at an unprecedented pace. So rich will this harvest be that it is not too rash to state that it will completely transform both clinical disciplines and put them on the sound scientific foundation that has so long been one of their principal goals*”.

## National Research Priorities

*Promoting and maintaining health* is a federal research priority.

Given that brain and mind disorders have the largest impact of all disease groups in Australia, and the great promise and scientific opportunities that neuroscience and related clinical disciplines hold for reducing Australia’s burden, neuroscience needs to be a high priority in the national research effort.

Such a priority should strategically position Australia as a full participant in the leading, most promising edges of the global neuroscience effort. We must link very strongly internationally, in areas such as those offered by the *Human Frontier Science Program*.

Neuroscience involves a multi-disciplinary approach for long-term effective outcomes, and this fits well with the objectives of our national research priorities. A fragmented and weakly coordinated approach to neuroscience research and research funding in Australia imposes a major barrier.

In large part:

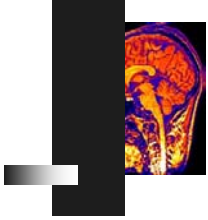
- basic research tends to still be organized along traditional clinical disciplines, mostly funded by discipline-related agencies
- partnerships between researchers and stakeholders, including the industry sector, tend to be *ad hoc*
- ethical implications of science are usually considered *post hoc*

What is most needed is a cross-disciplinary national research effort that is coordinated, cooperative, focused on the outcome, and well linked to patients, carers and the marketplace.

We must connect neuroscience, frontier technologies, and industry capabilities. To all of this it is essential that we link to overseas nodes of excellence.

The setting of research priorities by the Government is an important step in refocussing the Australian research effort towards building critical mass in areas related to our aspirations and our needs.

Research priorities will have limited impact if they rely only on the existing mechanisms for funding advice and coordination. The *Alliance* concept proposed below is a model that



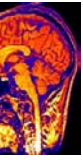
could be applied in other areas of the national research priorities. The *Australian Research Alliance for Children and Youth* (ARACY) is an existing example.

### **Brain and Mind Research Alliance**

We propose the establishment of a *Brain and Mind Research Alliance* to achieve this. This would aim to achieve critical mass by means such as:

- a holistic approach by forming networks across the neurosciences, social sciences, frontier technologies, and industry
- connectivity with nodes of international research excellence
- a national repository of research and clinical data
- enhance philanthropic and other funding of basic neuroscience research
- linkages between funding agencies
- partnerships between researchers and stakeholders
- advice on neuroscience priorities
- monitor new treatments and preventive approaches to brain and mind disorders
- promote public awareness on bioethics, social stigma, health care practices
- promote adoption of ‘brain and mind’ research as a vital component of the *National Research Priorities*

The *Alliance* would help position Australia’s scientific capacity to participate in and capture global advances related to brain and mind disorders.



## RECOMMENDATIONS

There are two recommendations:

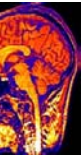
### **Recommendation 1: Basic research networking**

Government programs should encourage the development of an enhanced basic neuroscience research effort in Australia. This should be characterized by internationally recognized centres of research excellence and networking of smaller research groups for the purposes of assisting the development of multi-disciplinary teams linked to carers and consumers, working towards the amelioration of brain and mind disorders.

### **Recommendation 2: Forming an *Alliance***

A *Brain and Mind Research Alliance* should be established in order to foster the coherence, focus and integration of the neuroscience research centres and to ensure their effective linkage with the international neuroscience effort. The *Alliance* would recommend procedures for identifying and implementing national neuroscience priorities as well as advising on the formation of a national neuroethics advisory body. The aim of the *Alliance* would be to position Australia's scientific capacity to participate in, and capture, global advances to reduce the burden of brain and mind disorders.

To this end a broadly based *Neuroscience Consultative Task Force* should be formed for three months with the role of developing the *Brain and Mind Research Alliance*.



## 1. INTRODUCTION

### 1.1 What are brain and mind disorders?

The human nervous system is the most complex organ we know. It determines our most uniquely human function, namely, consciousness. Its activity underlies all aspects of our behaviour from basic requirements such as breathing to supporting our most private thoughts and feelings. Brain and mind disorders can result directly from intrinsic dysfunction of the brain or from complex interactions between the brain and the social and physical environment. Brain and mind disorders include a wide range of common neurological and psychiatric illnesses. They afflict a very significant portion of the population, right across the life span, and are prevalent worldwide - in both developed and developing countries.

Brain and mind disorders result in premature losses of life and dramatic reductions in our capacity to function. We are well familiar with the devastating impact of Alzheimer's disease and other forms of dementia in our aged populations, but it is perhaps less well-known that the highest rate of brain and mind disorders occurs in the 18-35 year olds. These include conditions, which are often not thought to be associated with brain dysfunction and include depression and anxiety, psychoses and substance abuse. Such common disorders underpin our very high rates of suicide in youth and early adult life.

The integrated concept of brain and mind disorders is a 21<sup>st</sup> century idea, replacing the traditional boundaries between psychiatry and neurology. In the late 19<sup>th</sup> century many of the common degenerative disorders such as dementia, Parkinson's disease, stroke and epilepsy were first linked to specific pathologies within the brain. However, these disorders not only affect basic functions such as speech and movement but also result in profound changes in thinking, memory, emotions, sense of self and other 'mind-related' concepts. In combination with other nervous system disorders, such as multiple sclerosis, chronic pain and muscular dystrophy, up to 75% of the community at some stage in their lifetimes are likely to experience these conditions. Most of these disorders are now recognized by the general population as brain-related or 'neurological' illnesses rather than purely psychological or socially determined conditions.

Those brain and mind disorders that until recently could not be linked directly to specific brain dysfunction with 19<sup>th</sup> century pathology techniques have since been dealt with largely by psychiatry and psychology. These include depression, anxiety, schizophrenia, substance abuse and childhood developmental disorders such as autism, attention deficit hyperactivity disorder and dyslexia. As no direct brain pathology could be demonstrated in the 19<sup>th</sup> and early 20<sup>th</sup> centuries, greater emphasis was placed on the social and environmental risk factors to such conditions. Major recent technical advances now permit us to characterize the genetic, biochemical and brain changes that underpin these conditions. So, while these disorders are associated with profound changes in mood, perception, cognition and behaviour, such changes typically result from underlying brain dysfunction interacting with the environment.

In the future, therefore, we will no longer arbitrarily separate ‘neurological’ disorders from ‘psychiatric’ conditions. The newer concept of brain and mind disorders recognises that all these conditions involve abnormalities in brain function that result from complex interactions of genetics, past experience and current social and physical environments. Our capacity to prevent or treat such conditions will depend on not only our capacity to manipulate key environments but also on a deeper understanding of brain function based on advances in neuroscience.

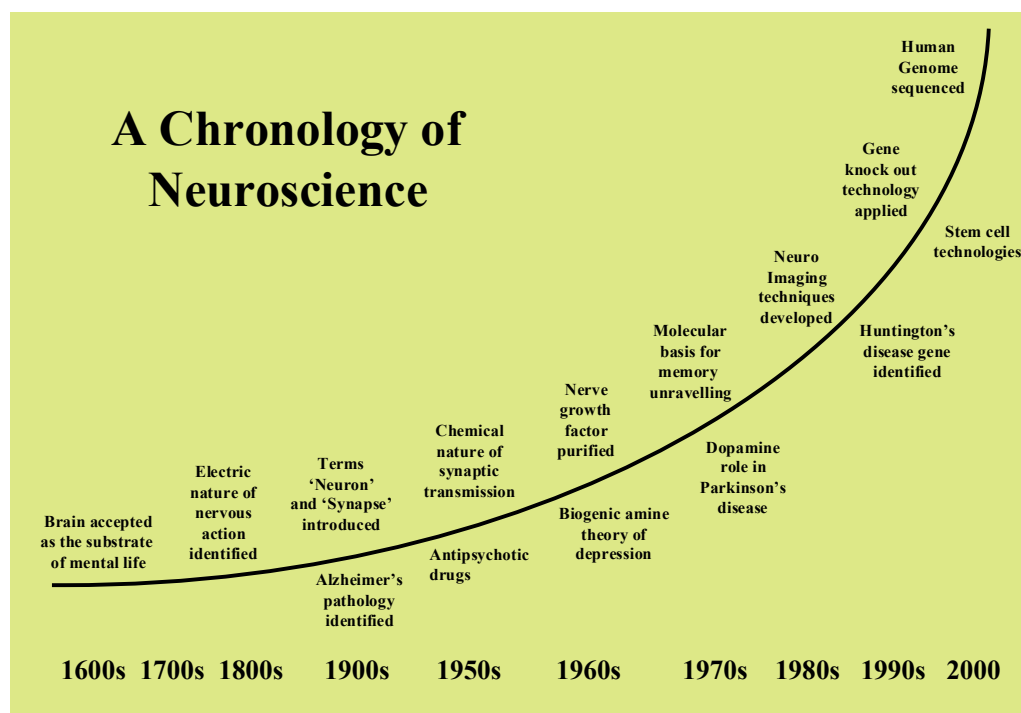
## 1.2 Neuroscience’s contribution to understanding brain and mind function

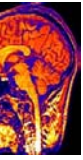
Neuroscience is an interdisciplinary and large field that links the biological and psychological sciences through its central focus on the biology of the brain. The scope of neuroscience is broad, ranging from genes to cognition, from molecules to mind.

It collectively reflects the diversity of disciplines that are required to determine the structure and function of the various regions of the brain, the mechanisms of neurotransmission and the molecular and cellular processes underlying the pathology of brain and mind disorders. These disciplines span cell and molecular biology, genetics, biochemistry, pathology, physiology, psychiatry and psychology, and they build on platform and frontier technologies such as genomics, proteomics, informatics, stem cell sciences and non-invasive imaging.

Historically, some of the key developments in neuroscience and their links to important diseases are illustrated in the following diagram (1).

*Figure 1: The historical contribution of neuroscience to the understanding of brain and mind disorders*





There is now a widespread view that we are on the verge of a neuroscience revolution that will open up unprecedented opportunities for increasing the knowledge base about brain and mind function and dysfunction. This revolution arises from dramatic advances in technology, particularly the results of sequencing the human genome.

Nobel Laureate neuroscientist, Eric Kandel, recently wrote (2) that following the completion of the genome project “...*progress, not only in neuroscience, but in neurology and psychiatry, will proceed at an unprecedented pace. So rich will this harvest be that it is not too rash to state that it will completely transform both clinical disciplines and put them on the sound scientific foundation that has so long been one of their principal goals*”.

These opportunities give hope of major advances in disease control over the next ten years.

### **1.3 Purpose of the paper**

This PMSEIC paper delineates the health impact of brain and mind disorders in modern society, and the contribution the neurosciences are making to reduce that health burden.

It makes the case that we are on the verge of a revolution in the treatment of many brain and mind disorders, due in significant part to the unprecedented pace at which neuroscience is expected to progress over the next decade.

In order for Australia to remain at the forefront of this field, we will need a strong, integrated and well-funded national neuroscience research capacity linked with a vibrant biotechnology industry sector, as well as with/to carers and consumers.

This paper maps out the pathway to achieving that vision.

### **1.4 Formal submissions**

Submissions were sought from over 150 individuals, organisations and companies involved in neuroscience. A list of formal responses is given in Appendix 6.

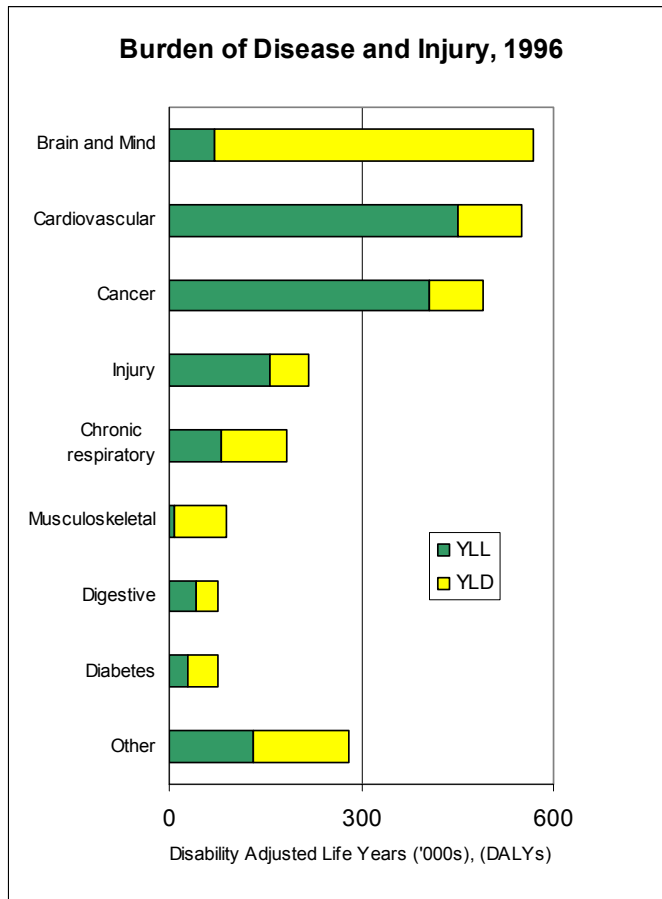
## **2. HEALTH IMPACT OF BRAIN AND MIND DISORDERS**

### **2.1 Overall health burden**

Almost everybody knows somebody who has a condition that affects the brain and mind, such as depression, stroke, Parkinson’s disease, epilepsy, or schizophrenia. All of us are interested in maintaining our memory, intellect and insight and maintaining our ability to participate actively in our society. All of us want our children to grow up, live and work within environments that are safe, efficient and supportive of the health of brain and mind.

Brain and mind disorders affect as many as 1.5 billion people worldwide, and the number is expected to increase as life expectancy increases. According to WHO and World Bank estimates (3), no less than 25% of the total burden of disease in the established market economies is at present attributable to brain and mind disorders.

*Figure 2: The Contribution of Brain (Nervous system) and Mind (Mental Illness) Disorders to the Total Burden of Disease and Injury in Australia*



The chart shows *Disability Adjusted Life Years (DALYs)* for each disease category. DALYs are a combination of *years of life lost (YLL)* through early death, and *years of life disabled (YLD)* through health impairment. Taken from data in *The Burden of Disease and Injury in Australia*, Australian Institute of Health and Welfare, November 1999.

Brain and Mind disorders are responsible for more total life years lost than either cardiovascular diseases, or cancer. Brain and Mind disorders largely result in disability, and long term costs in health care, unlike cardiovascular and cancer disorders.

Since most disorders affecting the brain and the mind result in long-term disability and many have an early age at onset, measures of prevalence and mortality vastly underestimate the burden of disease and the losses in terms of human capital they cause.

Figure 2 shows that brain and mind disorders impose the greatest burden on Australian health of any disease group, accounting for over 22% of the aggregate losses, well ahead of cancer (11.3%) or heart disease (9.9%).

Even more strikingly, the brain and mind disorders comprise 50% of the burden when disability alone is considered (YLD, Figure 2) because of their tendency to be long term or even lifelong.

Brain and mind disorders collectively take a major slice of the health care budget. The treatment and rehabilitation of individuals affected by brain and mind disorders already accounts for well over 30% of the total health care budget in developed countries. In Australia, this amounts to health system cost (Commonwealth, States and private hospitals) in excess of \$4 billion (4).

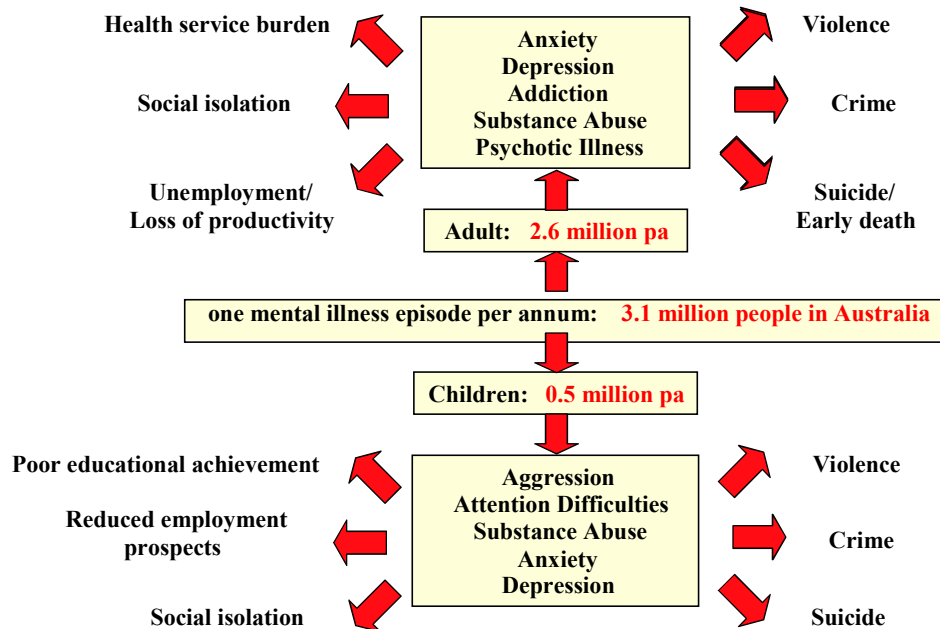
## 2.2 Brain and mind disorders of youth

Different brain and mind disorders show specific differences in their age distributions, reflecting quite distinct ages of onset. Conditions such as depression or anxiety, schizophrenia, and alcohol or substance abuse have their onset between ages 15 and 34 years of age. By contrast after the age of 75 the greatest disability is due to dementia and other neurodegenerative disorders.

In addition to the health burden, the social, educational, employment and productivity costs of these problems are frightening. To illustrate this with just a few examples:

- 40% of people lodging a medical certificate at Centrelink in 2002 claimed a brain and mind condition as their primary illness.
- Over 100,000 Australian teenagers experience a depressive illness each year, with perhaps four times that number experiencing significant depressive symptoms.
- Over 50% of young people attending a general practitioner have a significant psychological problem and 6% have made serious plans to take their own life.

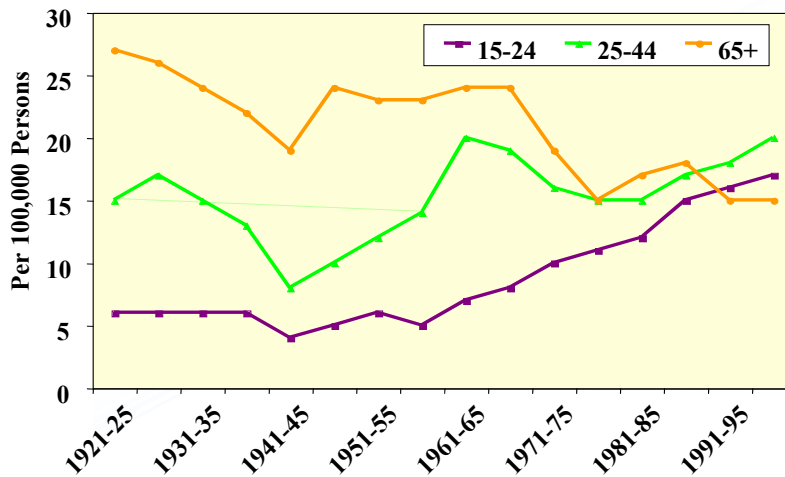
The demands of care, treatment and rehabilitation strain entire families, seriously diminishing their productivity and quality of life. Because of their early age of onset, and often chronic or relapsing nature, the social and personal impact of disability from the brain and mind disorders of early to mid adult life is immense. They carry with them a number of well-recognised sequelae as illustrated in the following flow-chart.



It is even more alarming to realize that the prevalence of many of these problems of youth, particularly severe drug problems and attempted suicide, have increased steadily over the last three decades. Even very recent indicators include an increase in the proportion of all disability support services due to psychiatric disability from 11.3% in 1997 to 15.1% in 2001, and a youth suicide rate in Australia that will soon exceed deaths by motor vehicle

accidents (Figure 3). Suicide rates in the 25-44 year age group are now steadily increasing, following on from earlier rises in youth suicide in persons born in the 1960s and 70s.

*Figure 3: Suicide rates in Australia, 1921 to 1998*



Although the overall suicide rate is unchanged, the rates have decreased for older people and increase in the young, particularly in 15-24 year old males.

Source: ABS statistics

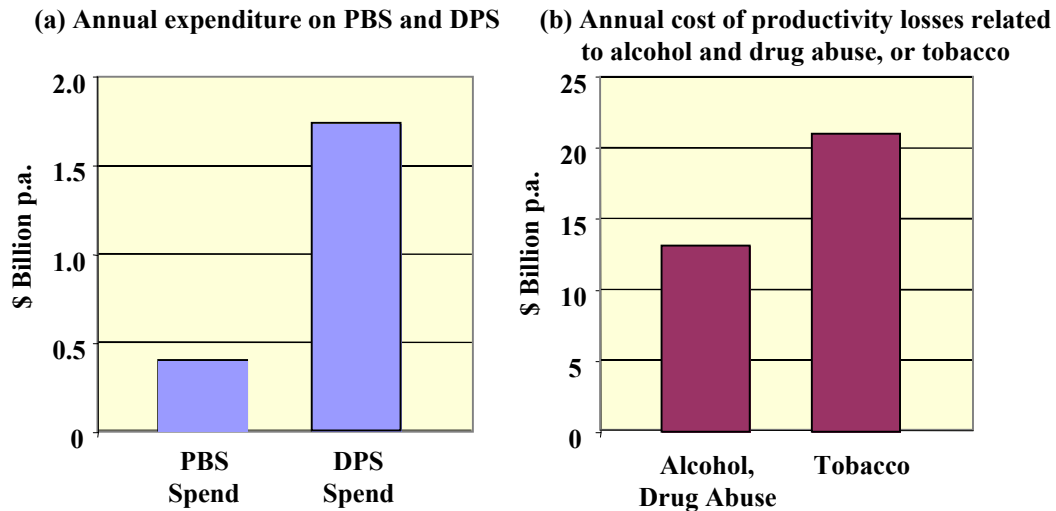
Australian indigenous peoples are experiencing the extremes of mental illness problems, with alcoholism, homicide and violence 11 times higher than for the total Australian population. Neurological disease associated with diabetes accounts for 10% of all deaths in the Aboriginal population and risk factors for developmental brain disorders are 10 times higher than for the total Australian population.

*What would be the economic impact of preventing the major brain and mind disorders of youth?*

This can be illustrated firstly by the annual Government expenditure related to mental health disorders in the pharmaceutical benefits scheme (PBS) or the disability pension scheme (DPS). These together accounted for \$2.2 billion (0.3% GDP) in Australian Government expenditure in 2001/02 (Figure 4a). As an alternative measure, we can consider the cost of lost productivity in terms of lost earnings and household productivity. This amounted to a staggering \$34 billion per annum in Australia in 1998/99 (Figure 4b). Presumably the productivity losses of all mental health diseases combined would be several fold higher.

*Even a 10% reduction in these costs would result in direct Government savings of \$0.2 billion, and a saving in productivity costs to the Nation of at least several billion dollars annually.*

*Figure 4: Annual cost of mental disorders in terms of Government spend on the Pharmaceutical Benefits Scheme (PBS) and Disability Pension Service (DPS), or the costs due to loss of productivity in the community*



*How are we going to achieve significant improvement in the brain and mind disorders of young people?*

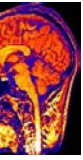
Part of the solution has been clearly articulated by the Australian Research Alliance for Children and Youth (ARACY), an organisation established following an earlier PMSEIC presentation on the needs of early childhood development.

ARACY is establishing a National Partnership between Government, industry, service providers and researchers for the enhancement of early human development. This Partnership is focused on preventing the rising prevalence of problems related to adverse environmental experiences during the developmental years through a collaborative research agenda.

ARACY is able to point to the very positive outcomes that can be achieved for children through psychosocial stimulation, nutritional supplementation, good health care, and parental training. However, it also recognizes that the current gaps in our understanding of brain function during development and of the biology of disease progression pose serious limitations to progress in this agenda.

A nurturing environment and improved health care can go so far - but new breakthroughs in neuroscience will also be essential.

Research from the Australian Twin Registry indicates that approximately 30% of the causation of anxiety and depression is accounted for by genetic rather than environmental factors. Therefore reductions in these disorders and in the associated suicide rates will require further basic research to understand the ways in which genetic, brain development and social and other environmental factors interact.



## **Towards Understanding and Preventing Schizophrenia**

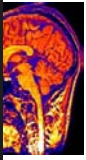
Schizophrenia is characterised by disturbances of the mind, personality and behaviour with perceptual abnormalities such as hearing voices, and bizarre delusional ideas. The lifetime risk of the disorder is about 1% and onset is usually in the late teens or early twenties. The burden associated with schizophrenia is high. It is among the top 10 causes of burden of disease in young Australian men and women aged 15-24 and in the prime of life. The Australian National Survey of Low Prevalence Disorders, headed by Professor Assen Jablensky, found that, in any one month, some 58,000 Australian adults with schizophrenia or another psychotic illness will be in contact with mental health services. This study revealed the extent of the ongoing social and functional disabilities that affect these patients and their quality of life. At any point in time, 72% are unemployed; almost 50% are impaired in their capacity to carry out normal, routine activities; social isolation is prevalent; and one-third live alone, many in marginal accommodation. While most will be taking medication for their illness, two-thirds report side effects severe enough to interfere with daily functioning.

As early as the beginning of the twentieth century, scientists believed that schizophrenia was associated with a disturbance of the brain, but did not have the technology to identify the mechanisms involved. As a consequence, up until the 1970s, research into schizophrenia focused on the psychological and social consequences of the illness. The introduction of the first effective drug treatment, chlorpromazine, in the 1960s, revolutionised the treatment of schizophrenia, and allowed the psychosocial reintegration of patients back into their communities. In 1976, a group of scientists in Edinburgh identified brain abnormalities in schizophrenia for the first time, starting a neuroscience revolution in research into this disorder.

Over the last 15 years, the dominant hypothesis has been that fetal brain development is critical in schizophrenia. This has led to the belief that the changes in the brain in schizophrenia are fixed at this early stage and do not progress. In 2003, Australian researchers headed by Associate Professor Christos Pantelis challenged this notion with the findings of high-resolution brain scans in young people who had not yet developed schizophrenia, and compared them with scans taken after the onset of the illness. This research suggests that those individuals who subsequently go on to develop schizophrenia already have brain abnormalities in the key brain regions, and that the loss of brain grey matter increases as the illness develops. This work was the first to demonstrate that it may be possible to predict who will develop schizophrenia, as well as showing that the brain is actively changing as the illness develops. Meanwhile, Professor Patrick McGorry and his team have been able to identify young Australians at risk of developing schizophrenia and demonstrated that early treatment in these individuals may prevent the illness from developing.

These Australian researchers, working together with the neuroscience community, are well placed to understand the molecular and genetic basis of these findings and to use these findings to develop new treatments to prevent or at least to delay the onset of the illness.

The average annual cost to the Australian government of psychosis is \$30,000 per person, while the community carries an additional cost of at least \$46,000 per person. The economic impact of reducing the incidence of schizophrenia by 25% can be estimated as a saving of \$0.5 billion per annum. More profound, however, is the potential personal impact of disease reduction and the amelioration of disease progression in individuals at risk for schizophrenia, their families and close community networks.



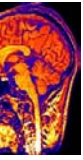
### **Depression: Opportunities for Prevention and Earlier Intervention**

Severe depression will affect one in five persons in their lifetime. Over 800,000 adults and 100,000 young Australians experience this illness every year. At least six million work days are lost each year and another 12 million days of reduced productivity are attributed to depression. Worldwide depression is predicted to be the second leading cause of all death and disability by the Year 2020. Depression in early adult life is commonly preceded by anxiety in early teenage years. It often leads to alcohol, tobacco and cannabis abuse, educational failure and unemployment. Depression disrupts physical health by a range of immune and nervous system mechanisms and is a risk factor for heart disease of the same order as smoking, high blood pressure and raised cholesterol. As depression is the most costly to society of all the brain and mind disorders it is the subject of the most intense international research and clinical service development. Internationally, the focus of research is on genetic risk factors, changes in brain development, development of new antidepressant compounds and reduction of depression in association with physical illness and brain degeneration in later-life.

Australian researchers, primary care developments and public health innovations such as *'beyondblue: the national depression initiative'* are at the forefront of key preventative and early treatment strategies. Professor Nick Martin and his team at the Queensland Institute of Medical Research have utilized the Australian Twin Registry, to determine the genetic and environmental determinants of anxiety, depression and alcohol abuse in young persons in the community. Professors Philip Mitchell and Peter Schofield from the University of New South Wales and Garvan Institute have characterised possible genetic determinants of bipolar disorder (manic-depressive illness) in Australian families. Clinical research by Hickie and colleagues has characterised key genetic, neuropsychological and structural brain changes in patients with late-life depression. Increases in provision of new antidepressant drugs have been associated with recent decreases in suicide in some groups of older persons and middle-aged women. Preventative trials of improved parenting of primary school children, early intervention in pregnancy to prevent post-natal depression and schools-based teaching of enhanced coping skills to teenage children, all funded by beyondblue, are now underway. All such trials would be greatly enhanced by more extensive knowledge of genetic risk factors and specific brain changes in response to both psychological and biological strategies.

To date, Australia's capacity to lead international developments has been constrained by lack of research capacity. A recent commonwealth-funded review highlighted the discrepancy between the size of the international need and the degree of national investment in depression-related research. Given the potential international impact of this field, the current failure to capitalize on Australian strengths may well lead not only to lost opportunities but considerable and ongoing increased health costs.

A particularly relevant study was conducted by Professor Gavin Andrews and co-workers from the University of NSW (4). They calculated that we currently avert only one seventh of the burden of mental disorders and that evidence-based medicine implemented at the present level of coverage would avert one fifth of the burden at no greater cost. With some modest increase in budget and a focus on the most cost effective treatments perhaps one third of the burden of mental disorders could be averted. *However, a surprising finding was that more than a half of the burden of mental disorders cannot be averted by current knowledge, even given unlimited funds.*



In view of these compelling findings, we conclude that additional investment in basic research aimed at understanding the causes of the disorder will be an essential prerequisite to the development of future treatment programs and prevention strategies for brain and mind disorders of young people.

Neuroscience has already made great strides in the understanding of brain and mind disorders. An example was the research of the Australian psychiatrist, John Cade, who in 1949 discovered lithium to be effective in treating and preventing symptoms of bipolar disorder (also called manic depressive illness). Lithium is still a major treatment for this disorder. It has been estimated that lithium treatment saves the United States \$9 billion US annually in health care costs (5).

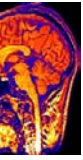
Large multidisciplinary studies of the major psychiatric disorders have been developing over recent years with the goal of defining the causation of the major psychiatric disorders. These are providing the foundation for eventual identification of all genes that act as genetic risk factors, and from that, the development of a host of new therapeutic drugs. New preventative strategies will depend not only on what we know about the social environment (e.g. parenting and schooling experiences) but also on blocking the detrimental effects of key genetic factors.

It is also now clear that while the principal connections in the brain are genetically determined, they are not fixed in stone. 'Abnormal environments' during critical periods of development can over-ride the genetic program and lead to 'abnormal connections'. These have profound repercussions for the normal or abnormal behaviour of the individual.

Of particular relevance to the brain and mind disorders of youth, neuroscience is now able to identify the critical periods in development when specific brain functions are determined. For example the brain is undergoing its final stage of development during the late teenage and early adult years, this is a crucial period in which connections within the frontal lobes are modified. The frontal and temporal regions of the brain are responsible for complex tasks such as reasoning and planning, emotional regulation and key interpersonal and social behaviours. This crucial developmental period corresponds with the period of onset of common disorders such as depression and anxiety, schizophrenia and alcohol and substance abuse.

The most intriguing hypotheses as to the causes of these disorders build on our growing understanding of this final stage of brain development. As it is now possible to view and measure changes in these key areas of the brain during these phases of development, it is apparent that there are associations between these brain and mind disorders and disruption of frontal lobe development. Moreover, the powerful combination of imaging technology with molecular biology has led to the tentative identification of specific genes that are affected in this region of the brain. This knowledge will in future underpin the development of strategies to improve early development and, hopefully, prevent these disabling disorders. It will also inform education strategies to help ensure our healthy children can reach their full developmental potential.

Another surprising finding is that contrary to general belief, the mature nervous system has not lost the capacity to form new neurons (brain cells) or to make connections between them ("synapses"). Under appropriate environmental or pharmacological stimulation new



synaptic connections can form in a very short period of time - less than 30 min. Such rapid plasticity of synaptic connections and the ability to form new neurons in the mature nervous system indicates the potentiality for recovery from conditions such as stroke. There are also implications for the capacity to learn as well as to increase mobility, opening the possibility of enhancing normal development and learning, as well as reversing neural decline.

With such rapid progress evident over the last 10 years, we can look forward to an even greater explosion of neuroscience discoveries over the next 25 years. Provided we capture the benefits of that opportunity, Australia will be able to make significant inroads into the prevention of those brain and mind disorders that so disrupt the lives of young people.

### 2.3 Brain and mind disorders of the elderly

Although some neurological disorders such as epilepsy, multiple sclerosis, motor neurone disease and chronic pain have a broad age distribution, some common diseases such as stroke, Alzheimer's disease and other forms of dementia are typically diseases of the elderly.

Alzheimer's disease is the most common form of dementia, with about 10 million sufferers in the western world and 160,000 in Australia. This is increasing by 10% per year as a result of the ageing population - one in 25 persons over sixty and one in five over eighty now suffer from dementia. Current treatments are of limited effectiveness, cause side effects and do not halt the progressive downhill course of the disease.

Stroke and cerebrovascular disorders are associated with 6% of the total burden of disease in the developed countries. Stroke is the third most common cause of death in Australia, with 100 cases per day or 37,000 per year. Of new stroke victims, one third will die and another third will be permanently disabled. This imposes a very high health burden, with direct and indirect costs amounting to \$1-2 billion per year in Australia alone.

Parkinson's disease is a condition of neurological degeneration for which some causative gene changes have recently been identified, but a detailed understanding of the cellular changes that underlie the disease are still unclear.

As with mental problems, the economic burden of these specific neurological disorders is substantial and includes over \$1 billion per annum in health system costs (Commonwealth, States and private hospitals). In addition, they are responsible for a significant proportion of aged care costs. It is estimated that over 50% of residential aged care patients suffer from Alzheimer's disease.

Although neurological disorders are most prevalent in retired persons, there is still a large impact on business productivity and costs, particularly when caregiver time commitments are taken into account. Just for Alzheimer's disease alone, a recent US study calculated current total costs to American business at US\$61 billion a year in caregiver time, productivity loss and medical expenses (8). This dollar amount is equivalent to the net profits of the top 10 Fortune 500 companies - according to the study. On a comparative

population basis, this means that Australian business would be losing approximately \$4 billion per annum due to Alzheimer's alone.

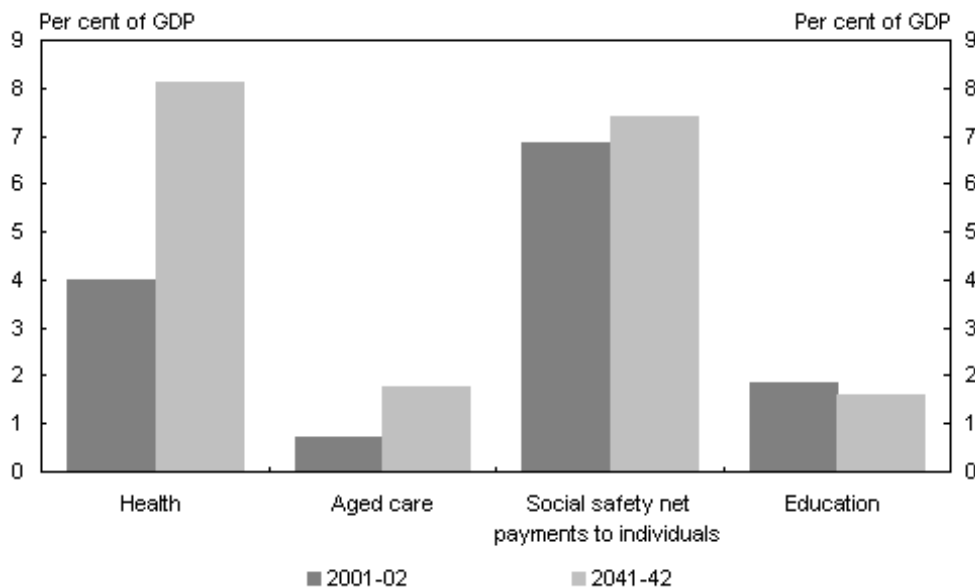
Perhaps the most alarming aspect of these disorders is the projected rise in prevalence and health burden to unacceptable levels over the next generation.

According to the above US study (8):

*“The \$61 billion cost is just the tip of the iceberg. These calculations are based on 4 million people - the number estimated to have Alzheimer's disease now. Within the decade, baby boomers will enter their retirement years, and the number with Alzheimer's will begin to explode - to as many as 14 million by the middle of the century. The costs - to families, to government, and to business - will be unsustainable.”*

In Australia, sharp rises in the total costs of health and aged care are likely to be responsible for most of the increase in Commonwealth expenditure over the next 40 years (Figure 5). Total health costs will increase from 3.96% of GDP to 8.13% in 2042, while aged care will increase from 0.72% to 1.77% GDP over the same period. The combined costs of health and residential aged care will then represent a massive 9.58% of GDP. In 2001/02 dollar terms, this equates to a rise from \$32 billion in 2001/02 to \$167 billion pa by 2041/02.

*Figure 5: Predicted increases in Commonwealth spending over the next 40 years (from chart 19, Intergenerational Report, Commonwealth of Australia, 2002)*



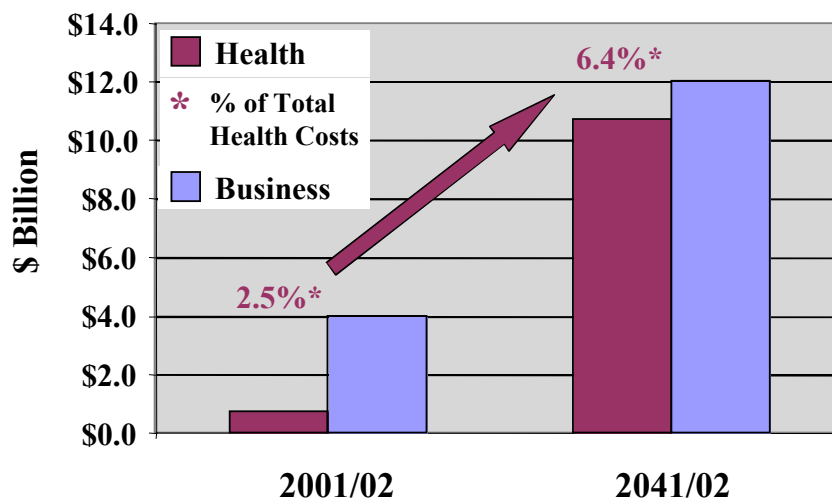
A disproportionately high component of these costs will be due to brain and mind disorders. As a group they are predicted to comprise a progressively higher percentage of the burden of disease, so that by the year 2020 they will comprise 27%, up from 25% at present. By 2020, cerebrovascular disease will rank as the second leading cause of death, accounting for 11.3% of deaths worldwide.

Mind and brain disorders, notably dementia, will also be responsible for a substantial proportion of the increased aged care costs by 2042. From the current 162,000 people with dementia, it is projected that Australia will have 460,000 sufferers by 2042. While our total population will increase by only 40%, our population with dementia will increase by three and a half times (8) due to the ageing population demographics.

Costs arising from Alzheimer's disease constituted 2.5% of these total Commonwealth health and aged care costs in 2001/02 (\$0.8 billion). Trends analysis suggests that these costs will escalate over the next 40-year to reach 6.4% of the total health and aged care costs by 2041/02 (\$10.7 billion) (Figure 6, Appendix 2).

Productivity losses are projected to increase even more sharply than Commonwealth costs. With a three fold or more increase in Alzheimer's disease, the costs to Australian business in lost productivity from this disease alone can be predicted to rise from the current \$4 billion to at least \$12 billion by 2042, if no improved Alzheimer's treatments are developed (Figure 6, Appendix 2).

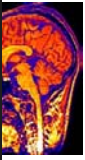
*Figure 6: Predicted increases in the economic burden in Australia from Alzheimer's disease over the next 40 years (see Appendix 2 for detailed calculations)*



Clearly these costs - to families, to government, and to business - will become unsustainable and must be a Government priority for action.

*How are we going to prevent the projected explosion in health and business costs due to mind and brain disorders?*

The case for additional basic neuroscience research in the brain and mind disorders of the elderly is compelling. For most of the chronic neurodegenerative disorders, very little is known about their basic causes, and we are at present powerless to alter their progressive downhill course.



Nevertheless, recent neuroscience advances are showing promise in the search for new therapies. For example:

- We now understand the causes of multiple sclerosis and the way it causes disability in younger people. First generation treatments have now been in place in Australia for three or four years and are starting to reduce long term disability, with the likelihood that second and third generation medications will be available in the next few years which may well eliminate this problem.
- Much is now understood about the mechanisms of cell loss in neurodegenerative disease including Parkinson's disease, Alzheimer's disease and motor neuron disease and advances and insights through study of rare familial conditions is opening new therapeutic targets.

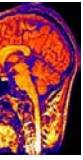
Examples of where deeper understanding will likely lead to much better treatments of brain disorders are Alzheimer's disease, epilepsy, schizophrenia and depression. In each case understanding basic mechanisms of the disorders will lead to rational design of new treatments with better outcomes. In these examples Australian researchers are leading the way.

#### **Towards Understanding the Cause of Alzheimer's disease**

Five years ago there were no treatments for this relentlessly progressing neurodegenerative condition. Based on the results of 1970s science, cholinesterase inhibitors were developed and are now the only approved Alzheimer's disease therapeutics. Glutamate receptor blockers are starting to be released on the market, but both types of drug only able to delay progression of symptoms.

However, recent research discoveries regarding the basic causes of the disorder suggest that effective treatments and preventions will be achievable, perhaps within a decade - and Australian researchers are playing a key role.

In 1984, Australian scientist, Prof Colin Masters, and collaborators elucidated the structure of an abnormal protein called beta-amyloid, deposited in the brain of patients with Alzheimer's disease and now widely accepted as causing the extensive nerve damage that leads to devastating memory loss. There is now a world-wide race amongst researchers to devise methods to block the formation of the toxic beta-amyloid or to promote its dissolution from the brain. It is very likely that one or other of these approaches will succeed. When they do succeed, the prospect of using them to treat, and indeed prevent, Alzheimer's disease, will become possible.



### **Epilepsy: Understanding the genetic basis**

Three percent of the population may develop epilepsy at some during their lives and there are more than a dozen forms of epilepsy, some of which can be lethal. Current treatments do not adequately control the disease and can have significant undesirable side effects.

Australian research, led by Prof Samuel Berkovic leads the world in the identification of abnormal genes that cause epilepsy. They have identified a large family pedigree affected by a particular form of epilepsy. This enabled identification of the first defined gene mutation in epilepsy.

They have gone on to define many further mutations, in each case involving changes to ion channels that regulate excitability of nerve cells. These discoveries now set the scene for developing new drug treatments for epilepsy, based on a precise knowledge of its causes.

In conjunction with pharmaceutical companies, the Australian biotechnology company, Bionomics, is using these epilepsy-associated genes as a basis for the discovery of more effective treatments. The world market for anti-epileptic drugs is estimated at around US\$3 billion per year and is projected to grow rapidly over the next decade.

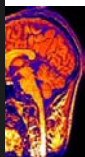
Development of treatments that allow patients to resume a productive life and are cost-effective will have a very positive impact because most burden from brain and mind disorders results from chronic debilitation rather than premature death.

The associated economic savings would be immense. For example, US studies have predicted that (Society for Neuroscience, USA):

- a treatment which delayed the onset of Alzheimer's disease by five years would halve the disease burden from that condition with an enormous reduction of costs in looking after our ageing population, cutting health expenditure by \$50 billion in the US alone.
- a five-year delay in the onset of stroke would save \$15 billion annually in the US. Extrapolated to Australia, this would equate to a saving of AUD \$1.5 billion pa.
- a five-year delay in the onset of Parkinson's disease would save \$3 billion in health care costs in the US (\$0.3 billion in Australia).

As further illustration of the benefits that effective cures for brain and mind disorders could generate, we refer back the trends analysis of Alzheimer's disease, which showed health costs of this disease rising to \$10.7 billion by 2042, exacerbated by a trebling in business costs to \$12 billion the savings (Figure 6, Appendix 2).

*It follows that by just minimizing the incidence of this one neurological disease, Australia could eliminate over 6% of the total health plus residential care costs over the next 40 years - amounting to a saving of over \$10 billion pa. In addition, there would be savings to business in terms of caregiver time, productivity loss and medical expenses of approximately \$12 billion p.a.*



In summary, the data on disease severity and trends analysis for both brain and mind disorders provide compelling evidence that:

- (a) brain and mind disorders pose the highest health, economic and social capital attrition burden to Australia of any disease group, reflecting an ageing population prone to neurological disorders (such as dementia and stroke) as well as the consequences of the prevalence of psychiatric disorders (such as depression and addiction) in our young people
- (b) without new, cost-effective strategies to prevent, reduce or contain the chronic and debilitating consequences of these disorders, Australia risks both a blowout in health costs as well as a decreased revenue base over the next 40 years
- (c) a reduction in the health and economic burden of these disorders will not be achieved by improvements in health care delivery alone. Rather, these disorders will require novel means of prevention and cost-effective treatment that can only arise from intensified scientific research to understand their biological basis.

### 3. THE GLOBAL NEUROSCIENCE REVOLUTION: AUSTRALIA'S CONTRIBUTION

#### 3.1 The neuroscience promise

Neuroscience has entered a very exciting decade because of two major developments:

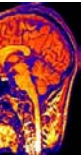
1. The compelling evidence that mental disorders, not just neurological disorders, involve abnormalities in the brain itself and are both influenced by genetics, past experience and the environment - the traditional division between mind and brain is now known to be artificial; and
2. The explosion of neuro- and biotechnologies over the last ten years.

These neuro- and bio-technological breakthroughs have included:

- the sequencing of the human genome. This is the greatest single advance and is dramatically facilitating a deeper understanding of brain structure and function
- new imaging technologies that non-invasively observe brain function in real time
- the emergence of cellular and molecular neuroscience, especially knowledge of the processes of formation of synapses (specialised connections) between nerve cells and of chemical transmission at these synapses
- the emergence of genomics, proteomics and bioinformatics
- stem cell sciences and gene therapy
- ability to create animal models of disease through gene manipulation, and
- rational drug design.

We can illustrate the power of these new technologies with a few examples.

The completion of sequencing of the human genome has been the most significant boost to neuroscience in the last 50 years. More than half of the genes in the human genome are expressed exclusively or preferentially in the brain and are key to understanding its development and function.



Using functional magnetic resonance imaging (fMRI), neuroscientists are now able to view and measure changes in key areas of the brain non-invasively and in real time. This has revealed, for example that the onset of schizophrenia may be associated with disruption within key frontal lobe structures.

Stem cell technology now holds the promise of being able to grow neurons (brain cells) so that dead or diseased parts of the brain can be replaced with healthy, functioning nervous tissue. This is of particular relevance to the many brain conditions of aging, particularly Alzheimer's disease, Parkinson's disease, hearing loss, etc. in which brain cells die.

New DNA microarray technologies can be used to determine which of thousands of genes are inactivated or activated in disease. In a study of schizophrenic patients' brains as an example, scientists were able to show by DNA array technologies that the disrupted frontal lobe structures possessed inactive genes for particular proteins necessary for normal neuron activity.

These developments open enormous opportunities for the international neuroscience effort and its impact on disease treatment. This has been clearly articulated by the respected Lasker Foundation, which together with the American Medical Association, published in 2001 "Opportunities for Medical Research in the 21<sup>st</sup> Century" (6). This publication made minimal estimates of medical progress in the prevention, treatment or eradication of disease over the next 25 years.

Of their 12 major predictions, 5 related directly to the prevention or control of brain and mind disorders, with two others relating to imaging technology and drug development advances that will have a major impact in the field. An associated article by Cowen and Kandel (2) made the case that advances in neuroscience-related research will be the primary determinant of this progress.

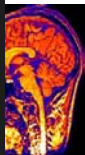
***Lasker Foundation (6):***

***Minimal estimates of medical progress over the next 25 years: neuroscience related***

- Alzheimer's disease is a strong candidate for disease prevention.
- Many chronic diseases, including Parkinson's will be brought under control.
- Both neurology and psychiatry will proceed at an unprecedented rate, resulting by 2020 in more personalized therapies for disorders such as depression and schizophrenia.
- Techniques for the replacement of defective genes will provide a way to treat spinal cord injury and stroke in ways that will be absolutely curative.
- By 2025, engineered tissues - to replace blood vessels, restore vision, ... may effectively eliminate the long waiting lists for specific organ transplantation.
- Non-invasive surgery may be the norm in 2025 through advances in bioengineering and imaging technologies.
- Drug development and success will be accelerated...for complex diseases.

***.and the role of neuroscience in that progress: Cowen and Kandel (2)***

- Developments related to molecular biology are likely to account for most new advances in both neurology and psychiatry in the next quarter century.



- When the human genome is fully sequenced and annotated (by 2004), progress in neuroscience, neurology and psychiatry will proceed at an unprecedented rate.
- So rich will this harvest be that it will transform the clinical disciplines of neurology and psychiatry and put them on a sound scientific foundation.
- Within 20 years, we should, for the first time, be able to provide a mechanistic basis even for the polygenic psychiatric disorders such as schizophrenia and manic depressive illness.
- Concurrently, proteomic and genomic identification of the protein products of these genes will provide new targets for drug development.

### 3.2 How is Australia going to capture maximum benefits from the neuroscience revolution?

It could be argued that as a small population with only 2% of the global GDP, the Australian effort should focus on translating and adopting the results of overseas R&D rather than inventing it ourselves.

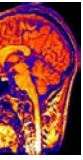
However, this approach would be disastrous for Australia because our ability to capture quickly the benefits of overseas developments is contingent on maintaining a vigorous scientific effort ourselves.

Living standards are increasingly dependent on a country's knowledge-based industries. But even more importantly, if Australia is to ensure early access to overseas developments, we need to be prominent players in the international effort. It is the widespread view of global business leaders that unless Australia has a vigorous scientific community of its own, that can make a contribution and fully understand the contribution of others, we will not be in a position even to exploit international developments unless we wait until they have been implemented by others (9).

On the other hand, when a country has research capabilities that are considered pillars of international strength, and a clearly identified route to market and end-uses of those research strengths, pursued with the same vigour as the research effort, then that country has the best chance of adopting new technologies or deciding which ones to import from the rest of the world.

On this basis, neuroscience would have to be considered a high priority area for Australia's strategic investment. As a small country with a strong neuroscience capability, Australia can be far more agile than most countries in identifying and implementing innovative solutions.

As indicators of Australia's world-class neuroscience capability, this paper has already mentioned the discovery of lithium (John Cade) the pioneering work in Alzheimer's pathology (Colin Masters), and the identification of novel epilepsy genes (Samuel Berkovic).



Additional examples of groundbreaking discoveries by Australian scientists include:

#### **Examples of Australia's Contribution to Advances in Neuroscience**

- Pioneering work in the 1950s and 1960s by Sir John Eccles' group on chemical transmission between nerve cells was awarded the Nobel Prize;
- In the 1960s, David Curtis and Jeffrey Watkins discovered the principal excitatory and inhibitory transmitters in the brain;
- Peter Bishop received the Australia Prize for his discovery of the neurons in the brain that allow us to see the world in three dimensions;
- Graeme Clark developed the bionic ear;
- Alan Finkel developed a range of innovative acquisition and analysis products for cellular neuroscience;
- Bennett and Burnstock discovered new transmitters in the peripheral nervous system;
- Perry Bartlett and co-workers were the first to isolate neural stem cells from the adult brain;
- Jack Pettigrew has played a leading role in comparative studies on brain evolution;
- Max Coltheart has pioneered research on psychological aspects of language and reading;
- John Shine was the first to clone a human gene;
- The Australian Twin Registry is considered a unique resource for genetic analyses.

Our pillars of international research capability in neuroscience span (see Appendix 3 and 4 for more details):

- over twenty research institutes or centres with a primary neuroscience focus and several major research consortia, including beyondblue and Neurosciences Victoria
- a Major National Research Facility in Neuroscience (National Neuroscience Facility)
- internationally competitive neuroscience research efforts in at least ten universities
- six umbrella professional organisations for neuroscience and mental health research.

Australia also has centers of research excellence in Frontier technologies such as:

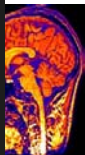
- MNRFs in proteomics (APAF); genomics (AGRF) and phenomics
- a Centre of Excellence in stem cell sciences.

While industry development has been modest (as with all medical research in Australia), a growing market application of Australian neuroscience research is indicated by:

- at least 10 ASX-listed Australian companies with a primary interest in Neuroscience and combined capitalization of \$2 billion;
- over 15 additional unlisted Australian companies with core focus on neuroscience, of which half were formed since 2000;
- significant investment in Australian neuroscience research by global pharmaceutical companies, e.g. \$25 million by Schering AG to Neurosciences Victoria and Eli Lilly has established a large clinical neuroscience research group in Australia.

*What are the priorities for research into control of brain and mind disorders?*

The advances that have already been achieved in experimental neuroscience will begin to impact on patient outcomes over the next decade. Many of the improvements in treatment will be incremental, with some improvement in the natural history of various conditions,



whereas others will involve major breakthroughs, which prevent, arrest or eliminate a condition.

Clearly the latter group should be given higher priority over the incremental ones - if science had concentrated on incremental research in polio rather than a vaccine, we would have had a better iron lung, but not a cure.

The other category of treatments that should be high priority for chronic debilitating diseases such as brain and mind disorders are those that allow patients to resume a productive life and are cost-effective.

On the other hand, expensive treatments of marginal effect must be given a low priority. The full cost of developing a new drug is currently of the order of US\$500 million. If these new drugs only serve to give limited improvement in disease symptoms, and require long-term application, the effect on Australia's health costs could be unsustainable.

The Government has already expressed concern over the high costs of the Pharmaceutical Benefits Scheme (PBS), which is a major component of Australia's overall health costs. PBS costs can be expected to increase markedly over the next 20-40 years as new expensive drugs become available and the concept of personalised medicine becomes a reality.

The issue is particularly relevant in the neuroscience field because many of the new drugs that will be developed over the next decade will be targeted at brain and mind disorders. PBS expenditure on mental health related problems in 2000/01 was \$409 million and antidepressant drugs are now one of the fastest growing areas of PBS expenditure.

Given the importance of controlling the costs of health and aged care, as well as the economic impact on business and the tax base, the Working Group recommends that a high priority should be given to research that leads to the development of preventative approaches to brain and mind disorders, as well as cost-effective treatments that allow patients to resume a productive life.

We therefore make the following recommendation:

### **Recommendation 1: Basic research networking**

Government programs should encourage the development of an enhanced basic neuroscience research effort in Australia. This should be characterised by internationally recognised centres of research excellence and networking of smaller research groups for the purposes of assisting the development of multi-disciplinary teams linked to carers and consumers, working towards the amelioration of brain and mind disorders.

## 4. THE PATH FORWARD

### 4.1 Fragmented approaches impede the national research effort

Australia has all of the pieces of the jigsaw needed to capitalize on the neuroscience revolution - a world-class basic and clinical neuroscience research base, excellence across the range of frontier technologies and a growing neuro-biotechnology industry.

Innovative Australian organisations, networks and associations (summarized in Appendix 2) that can contribute to the neuroscience revolution include:

- over twenty research institutes or centres with a primary neuroscience focus
- internationally competitive research efforts in at least ten Australian universities
- major research consortia such as beyondblue and Neurosciences Victoria
- a Major National Research Facility in neuroscience
- six umbrella professional organisations covering neuroscience and mental health researchers.

There is no one successful model of cooperation and networking. Indeed it is important that Australia retains a diversity of research effort - from the individual innovator to institutes and Centres of Excellence focused on neuroscience. However, there remains a serious impediment to the way in which all of these individuals and groups contribute to the challenge of brain and mind disorders - a fragmented approach to research and research funding.

In large part this arises because:

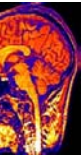
- basic research is organised by discipline and funded through “vertical” mechanisms impeding interdisciplinary interfaces
- basic research is not yet seamlessly linked to the industry sector
- partnerships between research and community stakeholders such as patients, carers and their families tend to be *ad hoc*
- the ethics of science is usually considered *post hoc*.

What is most needed is a cross-disciplinary research effort that is coordinated, cooperative focused on the outcome, and well linked to consumers and carers and to the marketplace.

### 4.2 Some initiatives to overcome fragmentation

Many of the past therapeutic advances have been made accidentally, rather than by deliberate design, and often these treatments are not fully effective. The unfolding opportunities in neuroscience offers a more strategic approach.

This will require an innovative research effort that crosses the traditional boundaries between mental and nervous system disorders, and capitalises on the frontier technologies that have exploded over the last decade.



The kinds of outcomes that can be achieved with this approach include the following:

- The cross-disciplinary approach of functional brain imaging and magnetic resonance spectroscopy in conjunction with genetic markers will soon be a very powerful tool for the early preclinical diagnosis of risk factors and precursors of brain disorders.
- Through advances in genetics and molecular biology, personalised treatment of neurological disease based on genetic profiling using microarray gene expression studies will become a reality in the near future.

An elegant example of the power of combining genetics, biochemistry, cognitive sciences and epidemiology is provided by a recent study into the biological causes of anti-social behavior (see box below).

### **The power of multi-disciplinary approaches to neuroscience**

A recent study on the role of genes in the cycle of violence in maltreated children (12) used epidemiological studies of a large cohort of NZ children, followed from birth, to ask why some maltreated children grow up to develop antisocial behavior while others do not.

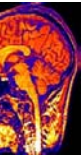
Childhood maltreatment, both abuse as well as erratic, coercive and punitive parenting is a universal risk factor for the development of antisocial behaviour, conduct disorder and of becoming violent offenders. The monoamine oxidase A enzyme is involved in the normal breakdown of several common neurotransmitters and rare genetic deficiencies result in aggression in humans and mice. In the population as a whole there are natural variants of the enzyme that result in higher or lower enzyme activity. While severely maltreated boys were more likely to exhibit anti-social behaviour, this was more likely in those boys who had low enzyme activity. This group was twice as likely to show conduct disorder and three times as likely to be convicted of a violent crime by age 26. This is the cutting edge of genetic and environmental research.

The results need to be replicated in other studies, and researchers including Australian groups who have developed similar birth cohorts are pursuing these studies vigorously. However, consider how neuroscience discoveries such as this can be utilised. Identification of at risk or maltreated children could be directly aided through cognitive therapies as well as by possible therapeutic strategies to reduce the risk of adverse social outcomes.

The recent establishment of Federal research priorities is an excellent first step - and the brain and mind disorders fit very well within the nominated priority area of "Promoting and maintaining good health" ([www.dest.gov.au/priorities](http://www.dest.gov.au/priorities)).

However, the implementation of research priorities will be difficult if the issue of vertical research funding is not addressed.

The Working Group proposes the establishment of a Brain and Mind Research Alliance that can bring together all of these stakeholders into a cooperative and problem-based effort to integrate neuroscience research across the full spectrum from benchtop discovery to clinical application.



## **Recommendation 2: Forming an *Alliance***

A *Brain and Mind Research Alliance* should be established in order to foster the coherence, focus and integration of the neuroscience research centres and to ensure their effective linkage with the international neuroscience effort. The *Alliance* would recommend procedures for identifying and implementing national neuroscience priorities as well as advising on the formation of a national neuroethics advisory body. The aim of the *Alliance* would be to position Australia's scientific capacity to participate in, and capture, global advances to reduce the burden of brain and mind disorders.

To this end a broadly based *Neuroscience Consultative Task Force* should be formed for three months with the role of developing the *Brain and Mind Research Alliance*.

An example of a successful initiative in network funding was the NHRMC Network for Brain Research into Mental Disorders (1994-2001) which involved over 50 chief and associate investigators from over 20 different organisations. The Network was successful in establishing many new linkages and in demonstrating that fostering partnerships between neuroscientists and psychiatrists can be immensely productive.

Another notable collaboration, Neurosciences Victoria (NSV), representing a consortium of Victorian research organisations, recently secured a 3-year renewable contract with the German pharmaceutical company, Schering AG. Schering is investing up to \$5m per annum up-front in a series of specific projects commissioned by NSV and sub-contracted to the institutions. NSV effectively acts as a "one-stop-shop" by which Schering can contract research through one single contract at multiple institutes.

NSV was successful in obtaining Major National Research Facility funding from the Commonwealth Government for a National Neuroscience Facility that is managed by the consortium Neurosciences Australia (NSA).

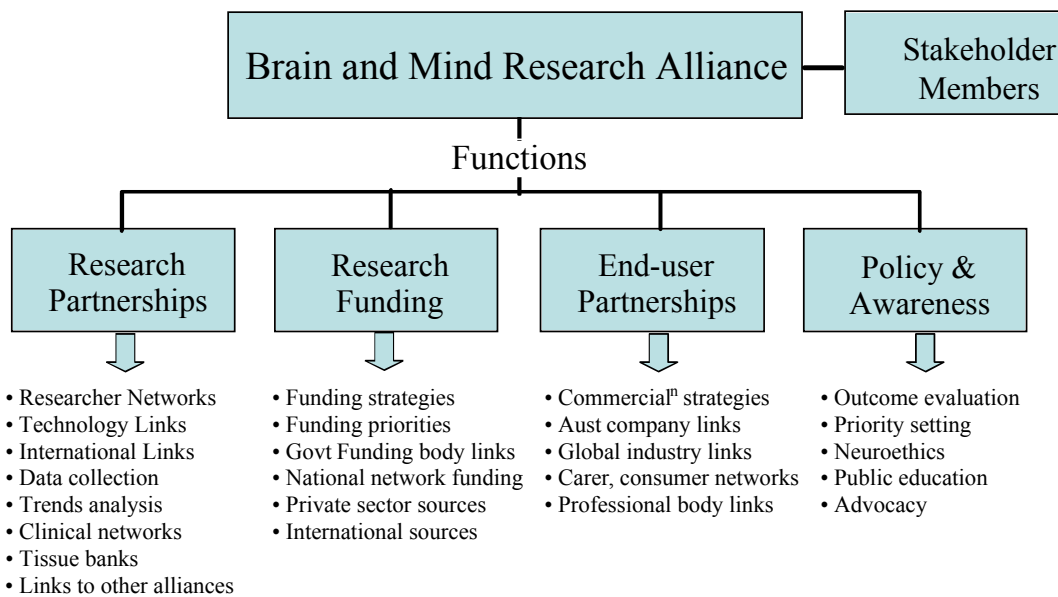
If the Brain and Mind Research Alliance gives priority to early intervention, and particularly prevention, of chronic and debilitating diseases, conquering one or more of the major diseases could be achieved within the next 25 years.

### The Working Group's Vision for the next 25 years

1. **An integrated neuroscience partnership through the Brain and Mind Research Alliance will yield significant advances in the prevention and early treatment of priority mental and neurological problems of Australia over the next 25 years;**
2. **At least one of the major brain and mind disorders will be solved; and**
3. **Australia will have a well-developed export base for Australian neurobiotechnologies that will ensure Australia's position in the international market for ideas and technologies.**

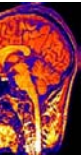
#### 4.3 The Brain and Mind Research Alliance

A summary of the types of activities that could be promoted by the Alliance are shown below, and discussed in more detail under *Specific Initiatives*.



For some of these functions the Alliance could have direct responsibility - for example the convening of consensus workshops to identify research priorities, the development of policy advice to Government and public education initiatives. However, in many cases its role will primarily to facilitate implementation via another entity - for example:

- neuroethics would probably be best managed under the NHMRC
- carer and consumer networks might be best achieved through the establishment of a Neurological Health Council equivalent to the Mental Health Council
- in National Network Funding, the Alliance could serve as a catalyst to bring funding bodies together for joint initiatives.



Regardless of the ultimate roles of the Alliance, the Working Group considers that it should be established as a formal entity with a high profile board.

The first step towards establishing the Alliance will be to canvass stakeholders on their views of the concept and the role and structure of a potential Alliance.

It is therefore recommended that Government immediately establish a Consultative Task Force to undertake review and report back to Government. This Task Force would be established on a time-limited basis for the period required to establish the Alliance.

A short-term Consultative Task Force should be established comprising scientists, Government, service providers, representatives of the biotechnology industry and representatives of consumer and carer organizations. Through a process of broad consultation the Task Force would determine the most appropriate composition, structure and terms of reference of the Brain and Mind Research Alliance.

The effectiveness of the research alliance approach is already evident through the early successes of the Australian Research Alliance for Children and Youth (ARACY). In its short existence, the ARACY has established a high-profile board, attracted significant private sector funding, and established a clearinghouse for identification of interventions that are effective in enhancing developmental health.

#### 4.4 Implementing a national approach to brain and mind disorders

The implementation of the Brain and Mind Research Alliance will require a concerted effort from all relevant stakeholders including researchers from all relevant disciplines, research funding agencies, Government, industry, clinicians, carers, patients and their families.

The cooperative effort will need to undertake the following:

*a. Foster basic research and its translation to consumers, carers and industry*

Effective translation of research will also depend on a well-informed and supportive public. This will require public awareness initiatives to overcome the social stigma attached to mental disorders and ensure acceptance of effective care and treatment practices.

Australia must build on its strong reputation for research excellence in neuroscience by ensuring that it is well funded and promoted. We must also maximize the opportunity to capture the commercial benefits of that research and build a thriving neuroscience-based biotechnology industry.

*b. Take advantage of neuroscience strength that already exist in Australia, as well as build new networks and research collaborations*

Support must continue and build upon the established centres of research excellence and cooperation (see Appendix 3 for details), but it must also stimulate new networks between researchers in the various neuroscience-related disciplines plus the frontier technologies and industry.

*c. Provide national network funding as the 'glue' to encourage innovative collaborative ventures*

The process for research funding allocation has also contributed to R&D fragmentation in Australia. For example, NHMRC, ARC and CSIRO all fund research that is highly relevant to neuroscience, but there are few effective mechanisms to promote partnerships between the agencies or to stimulate the new research networks described under (b). There are examples of successful network funding programs that can be followed - such as the NHMRC Network for Brain Research into Mental Disorders, the European Union FP6 funding mechanism and the US Consensus Workshops (Appendix 5).

*d. Enhance international research and industry links*

Even given the prominence of the contributions of Australian neuroscientists to the understanding of brain function we can still only expect to produce a fraction of the world's effort in this area. To ensure that we are at the forefront of global developments, Australian researchers must form and maintain very strong international research collaborations, both with neuroscience peers and with the biotechnology and pharmaceutical companies that will ultimately bring the new therapies to market.

Part of the network funding under (c) should be allocated to ensure Australian neuroscience research participation in major international projects (see Appendix 5).

*e. Contribute to policy setting in terms of research priority setting, health outcome evaluation and ethical issues*

The effective translation of neuroscience research into health benefits will require a cross-disciplinary forum in which research priorities can be widely debated and agreed, the cost-benefit of new treatments can be evaluated objectively and ethical issues can be addressed in a proactive manner:

- It will not be possible to fund every area of neuroscience endeavour to an internationally competitive level. Hence, research prioritisation for major initiatives will be required.
- Given the high cost of developing a new drug, a forum is needed where the novel therapies can be evaluated and prioritised in terms of cost-effectiveness.
- The rapid pace at which neuroscience is now moving poses the serious risk that ethical consideration will be left behind. The public concern over stem cell technologies and genetically modified foods provide vivid examples of the barrier this poses to the adoption of new technologies.

- f. *Build infrastructure such as databases, tissue banks and networks of volunteers, twins and families with genetic disease linkages*

Neuroscience research has traditionally been carried out in relative isolation of the patient support groups or the patients themselves. This has limited the opportunity to create the national registers of persons with specific illnesses and their families that provide an essential resource to clinical and genetic neuroscience research. Research in isolation of patient input can also make it difficult to ensure that research projects respect their needs, priorities and ethical considerations.

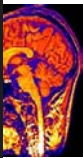
While Australia already has some excellent infrastructure, such as a world-class twin registry, the research community has not had the infrastructure to take full advantage of this resource. Tissue banks and databases have been initiated - for example the Brain Bank under NHMRC Network funding - but efforts have generally been fragmented.

#### 4.5 An Action Agenda for the Brain and Mind Research Alliance

The Working Group considers the following initiatives would be appropriate for implementation of the Alliance's Action Agenda (see Appendix 5 for further information):

##### A. Research partnerships

1. Identify ways to enhance cross-disciplinary national R&D linkages that bring together research excellence in the various neuroscience disciplines together with related and frontier technologies such as genomics, proteomics and neuroimaging.
2. Promote connectivity with international centres of research excellence so that Australia is well-positioned to access the best developments, regardless of where they occur.
3. Promote the establishment of a national research data and clinical resource infrastructure including twin, family and volunteer registries, tissue banks, epidemiological and diagnostic reference centres, with a view to streamlining access for researchers, encouraging data sharing, and allowing effective pooling of unique resources for population modeling of brain and mind diseases, and forecasting of trends and costs.
4. Recommend strategies to develop critical mass in neuroscience at key geographical loci. It will be necessary for the country to have several world-class neuroscience institutes to ensure international competitiveness. Possible models including development of neuroscience centres within large universities which bring together researchers from different departments and across different disciplines, and the development of large national research institutes with a neuroscience focus. Ideally these large research foci will be networked with similar activities in other states and with smaller research laboratories within their own home states to maximise research effectiveness.



## **B. Research funding**

5. Develop strategies to enhance funding of neuroscience research in Australia, with particular emphasis on provision of national network funding as the ‘glue’ to encourage multi-disciplinary, collaborative research efforts.
6. Reduce the fragmentation approach to research funding by encouraging linkages between funding agencies.

## **C. Partnerships with consumers and carers**

7. Identify impediments to technology transfer of Australian neuroscience to industry or other end-users and develop strategies to address these impediments.
8. Facilitate new and effective partnerships between researchers, carers and consumers.
9. Promote connectivity with representative bodies such as the Mental Health Council of Australia, patient care support groups and the professional societies well as other national initiatives such as the Early Human Development Alliance.

## **D. Policy and Awareness**

10. In collaboration with the relevant government and non-profit research and funding agencies, together with other stakeholders, identify gaps in the existing research effort and encourage debate on priorities for future research focus.
11. Monitor and evaluate the cost-effectiveness of novel interventions for the treatment and prevention of brain and mind disorders.
12. Promote public awareness and education in brain and mind disorders as a means to inform the public on the nature and importance of these conditions and their management, to reduce the social stigma associated with many of these conditions, and to optimise health care practices.
13. Promote adoption of ‘brain and mind’ research as a vital component of broader National Research Priority implementation plans

The Brain and Mind Research Alliance should provide policy and program advice and help facilitate initiatives in each of the key areas: national research linkages and infrastructure, international research linkages, research funding, partnerships with consumers and carers, policy and awareness.

Some key early actions within a year of the Alliance’s establishment and an indicative timetable of initiatives are given in Appendix 5

## 5. CONCLUSIONS AND RECOMMENDATIONS

The conclusions from this analysis are clear-cut. Brain and mind disorders pose the highest health, economic and social capital burden to Australia of any disease group. This arises from an aging population prone to neurological disorders as well as the consequences of psychiatric disorders, particularly depression and addiction, in our young people.

A reduction in the health and economic burden of these disorders will not be achieved by improvements in health care delivery alone. Rather, it will require a deeper understanding of the way the environment and genetic makeup interact to determine brain function.

This can be achieved through an integrated and innovative research effort that capitalises on the neuroscience revolution to deliver real health benefits to Australia. The Brain and Mind Research Alliance will provide the means to achieve this by bringing together all relevant stakeholders into a cooperative effort that integrates neuroscience research across the full spectrum from benchtop discovery to clinical application.

## APPENDIX 1

### Terms of Reference

*Refer to the following sections of the paper:*

- |   |                               |
|---|-------------------------------|
| 1. Describe the major brain and mind disorders, their associated burden if disease, costs and trends in the Australian population   | <i>Section 1.1, 2.1-2.3</i>   |
| 2. Describe the contribution of neurosciences, both in Australia and overseas, over the recent past to the understanding and amelioration of brain-and-mind disorders.  | <i>Section 1.1, 2.4</i>       |
| 3. What are the likely developments in neurosciences, both in Australia and overseas, that will impact over the next 25 years on the burden and amelioration of these disorders?  | <i>Section 2.4, 3.1</i>       |
| 4. What are the optimal organisational structures to promote the national neuroscience effort?  | <i>Section 3.2, 4.1, 4.4</i>  |
| 5. What are the likely public health equity and bioethical public health issues.  | <i>Section 4.2 - 4.4</i>      |
| 6. Outline the care needed to avoid such conditions and the issues affecting public health and health delivery policy in better management of neuropsychiatric disorders, especially in the early childhood phase.  | <i>Section 4.2 - 4.4</i>      |
| 7. In the light of these developments, what are the effective short, medium, or long term strategies to deal with brain and mind disorders of major public health significance, such as:  | <i>Section 3.2, 4.1 - 4.4</i> |
| <ul style="list-style-type: none"> <li>➤ Mood disorders - depression and bipolar disorder</li> <li>➤ Psychotic disorders – schizophrenia, drug-induced psychoses</li> <li>➤ Addiction – illicit drugs, alcohol and nicotine</li> <li>➤ Anxiety / post traumatic stress disorder / obsessive compulsive disorder</li> <li>➤ Chronic neurodegenerative disorders - Alzheimer’s disease, Parkinson’s disease, Motor Neurone Disease</li> <li>➤ Stroke</li> <li>➤ Neurotrauma</li> <li>➤ Childhood developmental disorders – e.g. autism, ADHD, dyslexia</li> <li>➤ Others such as hereditary disorders, multiple sclerosis and epilepsy</li> </ul> |                               |

## APPENDIX 2

## Estimated Health and Business Costs Associated with Alzheimer's disease

(Australian figures, \$ 2001/02)

Source	2001/02	2041/42	
GDP, \$ billion	\$710 b	\$1747 b	(1)
<u>Total Commonwealth Health and Aged spending:</u> <u>Intergenerational Report</u>			
Total Health costs, % GDP	3.96%	8.13%	(1)
Total Residential Care costs, % GDP	<u>0.58%</u>	<u>1.45%</u>	(1)
<b>Total Health + Residential Care, % GDP</b>	<b>4.54%</b>	<b>9.58%</b>	
<b>Total Health + Residential Care, \$ billion pa</b>	<b>\$32.2 b</b>	<b>\$167.4 b</b>	
<u>Alzheimer's disease (AD):</u> <u>Health Costs, including Residential Care Costs</u>			
<b>Annual cost, \$ billion pa</b>	<b>\$0.8 b</b> (2,3,4)	<b>\$10.7 b</b>	
<b>Annual cost, % <u>Total Health + Residential Care Cost</u></b>	<b>2.5%</b> (2,3,4)	<b>6.4%</b>	
<u>Alzheimer's cost to business</u>			
Annual cost, \$b	\$4 b	\$12 b	(4)

**If Alzheimer's disease was cured, eliminating all cases by 2042:****Cost savings in 2042:**

Health + Residential costs, \$ pa	\$10.7 b (6.4% of total health plus care costs)
Savings in business costs in 2042m \$ pa	\$12.0 b

These figures show that the costs of health care (including residential aged care) will more than double over the next 40 year to a massive 9.58% of GDP (Intergenerational Report). In dollar terms, this equates to a rise from \$32 billion in 2001/02 to \$167 billion pa by 2041/02.

Alzheimer's disease constitutes 2.5% of these total health costs in 2001/02 (\$0.8 billion), but can be expected to rise to 6.4% of the total by 2041/02 (\$10.7 billion).

*That is, just curing this one neurological disease could eliminate over 6% of the total health plus residential care costs over the next 40 years - amounting to a \$ saving of over \$10 billion pa. In addition, there would be savings to business in terms of care giver time, productivity loss and medical expenses of approximately \$12 billion p.a.*

### **Sources and Explanatory Notes**

- (1) Intergenerational Report, part III
- (2) Mathers C, Vos T, Stevenson C. The burden of disease and injury in Australia. Australian Institute of Health and Welfare: Canberra, 1999
  - estimates health costs due to AD as \$0.714 billion in 1993/94. Since the Intergenerational Report (1) estimates that the percentage of aged people has increased by about 12% over the last decade, health costs due to AD in 2001/02 are probably also 12% higher, so we have assumed 2001/02 costs of \$0.8 billion.
- (3) Research priorities in mental health: Jorm A, Griffiths K, Christensen, H, Medway J. Commissioned for the Commonwealth Department of Health and Ageing, Nov 2001:
  - the total health costs of mental health are estimated at \$3 b pa, of which AD constitutes about 25%. For simplicity, we have assumed a similar percentage in 2042 (although this is likely to be an underestimate).
- (4) Alzheimer's disease: The costs to U.S. Businesses in 2002, Prepared for the Alzheimer's Association by Ross Koppel, Dept Sociology, University of Pennsylvania, USA:
  - predicts the number of Alzheimer's patients to treble by 2042, so it is assumed the costs of health care will also treble as a proportion of the total.
  - Koppel also estimates a cost to American business at US\$61 billion a year in caregiver time, productivity loss and medical expenses. Extrapolating to Australia (7% of US population), this equates to approx \$4 b pa. If the number of Alzheimer's patients trebles by 2042, this will increase to \$12 b pa.

## APPENDIX 3

### Professional Societies, Organisations and Bodies Involved in Neuroscience

#### 1) Professional bodies and Research Consortia

##### *Australian Neuroscience Society*

- Widely representative multidisciplinary body representing basic neuroscience researchers.
- Over 600 members Australia wide.
- Founded in 1971, it holds annual scientific meetings, awards and prizes.
- Is the Australian affiliate of the Brain Research Organisation

<http://www.ans.org.au>

##### *Australian Association of Neurologists*

- Professional association for medical specialists in neurology.
- Determines standards for education and training and evaluation of neurologists, organises annual scientific meetings, thrice yearly newsletter and responds to enquiries regarding neurological practice, research and public education.

<http://www.medeserv.com.au/aan/index.cfm>

##### *Australian Psychological Society*

- The largest professional society for psychologists in Australia, representing around 13,000 members

<http://www.psychsociety.com.au>

##### *Australian Society for Psychiatric Research*

- Professional organisation for persons interested in psychiatric research
- Membership over 200

<http://www.anu.edu.au/aspr>

##### *Beyond Blue*

- A depression initiative begun in Victoria but which has developed a national spread and expertise

<http://www.beyondblue.org.au>

##### *Mental Health Council of Australia*

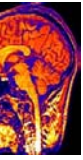
- An umbrella organisation designed to represent all stakeholders in mental health

<http://www.mhca.com.au>

##### *Neurosciences Victoria*

- A consortium of universities, research institutes and teaching hospitals working together to enhance scientific and technological capabilities in neuroscience and to facilitate commercialisation opportunities

<http://www.neurosciencesvic.com.au>



### *National Neuroscience Facility*

- A newly created National, not-for-profit company located in Victoria with a node in NSW, has been established to manage the Major National Research Facility in Neuroscience Facility funded by the Commonwealth Government's Major National Research Facility Backing Australia's Ability initiative

<http://www.neurosciencesvic.com.au>

### *Society for Neuroscience*

- The Society for Neuroscience in the USA began in 1968 with about 600 members – now has more than 25,000 members. It is the defacto international neuroscience organisation. Many Australian neuroscientists are members.

<http://www.sfn.org>

### *International Brain Research Organisation (IBRO)*

- A major international organisation dedicated to advancement of brain research. Comprises sixty-five different national and regional neuroscience societies and academic bodies devoted to neuroscience.

<http://www.ibro.org>

## **(2) Institutions and research organisations involved in neuroscience**

Anzac Institute, Concord, NSW

Austin and Repatriation Medical Centre, Heidelberg, Victoria

Bionic Ear Institute, East Melbourne, Victoria

Black Dog Institute, Randwick, NSW

Brain and Mind Research Institute, Sydney, NSW

Brain and Institute, Brisbane, Qld

Brain Research Institute, Heidelberg, Victoria

Brain Sciences Institute, Hawthorn, Victoria

Centre for Clinical Research in Neuropsychiatry, Claremont, WA

Children's Medical Research Institute, Westmead, NSW

Epilepsy Research Institute, Austin & Repatriation Medical Centre, Heidelberg, Victoria

Garvan Institute for Medical Research, Darlinghurst, NSW

Howard Florey Institute of Experimental Physiology and Medicine, Parkville, Victoria

Hunter Medical Research Institute, Newcastle, NSW

John Curtin School of Medical Research, Australian National University, Canberra, ACT

Melbourne Neuropsychiatry Centre, Parkville, Victoria

Mental Health Research Institute of Victoria, Parkville, Victoria

Millenium Institute, Sydney, NSW

Murdoch Children's Research Institute, Parkville, Victoria

National Ageing Research Institute, Parkville, Victoria

National Stroke Research Institute, Heidelberg, Victoria

Neuroscience Institute of Schizophrenia and Allied Disorders (NISAD), NSW

ORYGEN Research Centre, Parkville, Victoria

Pain Management Research Institute, Sydney, NSW

Prince of Wales Medical Research Institute, Randwick, NSW

Queensland Centre for Schizophrenia Research, Wacol, Qld

Research School of Biological Sciences, Canberra, ACT

SUN (Sydney University Neuroscience) Consortium, NSW

Vision Touch & Hearing Research Centre, Brisbane Queensland

Walter & Eliza Hall Institute of Medical Research, Parkville, Victoria

### (3) Universities with Major Neuroscience Activities

ACT            Australian National University

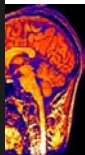
SA             Flinders University  
University of Adelaide

Victoria      Monash University  
University of Melbourne

NSW          Macquarie University  
University of NSW  
University of Sydney  
University of Newcastle

Queensland   Griffith University  
University of Queensland

WA            University of Western Australia



## APPENDIX 4

### Overview of the Australian Neuroscience Industry Sector

The market for neuroscience-related therapies or devices is enormous. For example, the worldwide Central Nervous System based market is currently estimated at \$US23.1 billion. Within 2 years, neuro-pharmaceuticals could be the greatest single drug class globally.

Australia is already playing a significant role in this market, with at least 10 ASX-listed Australian companies (combined capitalization of \$2 billion), plus over 15 additional unlisted Australian companies with core focus on neuroscience (see table below). Cochlear is a notable example. From its beginnings in Sydney 20 years ago, Cochlear has grown to a \$2 billion company with over 700 employees worldwide, and regional offices in many countries (See later in this section for additional details). There are also a number of multi-national pharmaceutical companies with significant operations in Australia in the neuroscience field (see table below). For example, Bristol-Myers Squibb and Eli Lilly and Company each has in Australia over 500 employees with sales around A\$300 million.

There are very positive links between the Australian neuroscience research sector and industry. Most of the Australian neuroscience companies evolved from public sector research or have drawn heavily on that sector for their core technologies. Cochlear is a clear example of this. Another is Prana Biotechnology Ltd, which was established to commercialise Australian research into new therapies for Alzheimer's disease.

The global pharmaceutical industry views Australian neuroscience highly for its research discovery and clinical trials capabilities, as evidenced by the following submissions:

**Bristol-Myers Squibb:** *“The value of intellectual input into global product plans from Australian scientific and academic leaders is well recognised by the broader Medicines Industry.”*

**Eli Lilly & Company:** *“Australia has world-class researchers and facilities in many areas of biomedical science, but especially so on neuro-psychiatric research” and “Australia has led the world in developing approaches to identify and intervene in early psychosis”*

This has led to extensive collaborations with Australian researchers. For example, Bristol-Myers Squibb, whose main neuroscience focus is in migraine and depression, has recently chosen Australia as one of 14 international hubs for clinical research and development, and has doubled its investment in Australian R&D to A\$17 million in the last 2 years. Eli Lilly, which has a pipeline of products in depression, schizophrenia, Alzheimer's and Parkinson's diseases, has established the largest clinical research group in the industry in Australia. A large number of Phase III and post-marketing trials are conducted in Australia because of the high quality research personnel and competitive costs.

As another notable collaboration, Neurosciences Victoria (NSV), representing a consortium of Victorian organisations, recently secured a 3-year renewable contract with the German pharmaceutical company, Schering AG. Schering is investing up to \$5m pa up-front in a

series of specific projects commissioned by NSV and sub-contracted to the institutions. NSV effectively acts as a "one-stop-shop" by which Schering can contract research through one single contract at multiple institutes. These include translational research as well as innovative discovery research and IP sharing arrangements.

There is also significant collaboration between pharmaceutical companies and the Australian biotechnology industry. As an example, the Australian SME, Brain Research Company has a lucrative contract with Eli Lilly in the area of functional brain analysis.

### Australian companies

#### (a) ASX-listed companies

<i>Company</i>	<i>Location</i>	<i>Market Capitalisation</i>	<i>Neuroscience focus</i>
AGT Ltd	Vic	\$12m	Depression/Anxiety
AMRAD Corporation Ltd	Vic	\$54m	Pain
Antisense Therapeutics Ltd	Vic	\$15m	Multiple Sclerosis
Axon Instruments Inc	USA	\$77m	Neuroscience equipment manufacture
Bionomics Ltd	SA	\$10m	Epilepsy and other neurosciences
Biotron Ltd	ACT	\$18m	CNS/epilepsy/anaesthetics
Brain Resources Company Ltd	NSW	\$15m	Brain analysis centres
Bresagen Ltd	SA	\$16m	Neurodegen./Parkinsons (stem cells)
Circadian Ltd	Vic	\$46m	Alzheimer's/Analgesics/MS/memory
Cochlear Ltd	NSW	\$1743m	Ear/Hearing disorders
Compumedics Ltd	NSW	\$39m	Sleep disorders equipment
Prana Biotechnology Ltd	Vic	\$52m	CJD, neurodegenerative disorders

#### (b) Unlisted Australian companies

<i>Company</i>	<i>Location</i>	<i>Year of Incorporation</i>	<i>Neuroscience focus</i>
Alzhyme Pty Ltd	WA	2002	Alzheimer's therapeutics
Calibre Biotechnology Pty Ltd	Vic	2002	Parkinson's therapeutics
Cogstate Ltd Pty Ltd	Vic	1999	Cognitive assessment services
Cyclotek (Aust) Pty Ltd	Vic	n/a	Imaging technologies for brain tumours
Dynamic Hearing Pty Ltd	NSW	2002	Hearing disorders
ES Cell International Pte Ltd	Vic	2000	Parkinsons (Stem Cells)
Neopraxis Pty Ltd	NSW	2001	Limb Stimulation
NeuroTech Research Pty Ltd	Qld	n/a	Software on neurodegenerative disorders
ObjectiVision Pty Ltd	NSW	1997	Visual field test using evoked potentials
Polychip Pharmaceuticals Pty Ltd	Vic	n/a	Alzheimer's therapeutics
Praxis Pharmaceuticals Pty Ltd	ACT	n/a	Multiple sclerosis therapeutics
Psygene Pty Ltd	NSW	1988	Genetics of mental illness
QRxPharma Pty Ltd	Qld	2002	Pain control
Syngene Ltd	Vic	n/a	Brain delivery of therapeutic molecules
Tinnitech Ltd	WA	2001	Rehabilitation methods for tinnitus
Xenome Ltd	Qld	2000	Neurotoxins/pain

*n/a: not available*

## International Pharmaceutical Companies with an Australian Division

Company	Market
Pfizer	Depression Alzheimer's disease Epilepsy Schizophrenia
Eli Lilly and Company	Depression Schizophrenia Parkinson's disease
Schering AG	Alzheimer's disease Parkinson's disease Multiple Sclerosis
Novartis	Epilepsy Alzheimer's disease Parkinson's disease
Bristol-Myers Squibb	Migraine Depression
Glaxo-Smith Kline	Migraine Epilepsy
Novartis	Epilepsy

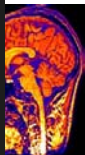
### Profiles of the Australian Companies

#### **AGT Ltd (formally Autogen) (Vic) [www.autogenlimited.com.au](http://www.autogenlimited.com.au)**

AGT specialises in using gene discovery approaches to identify novel therapeutic and diagnostic targets, with major technology platforms in genomics and proteomics. Its research programs include a diabetes and obesity program and a new program in depression and anxiety. AGT also offer services to pharmaceutical, biotechnology and genomics companies wishing to access its technologies and resources.

#### **Alzhyme Pty Ltd (WA) [not available](#)**

This is an early stage company for the validation of lead molecules directed at the cause of Alzheimer's disease, specifically to block the toxicity of beta amyloid, a key factor linked to the cause of Alzheimer's disease. It is proposed to test and validate the functional characteristics of these molecules in pre-clinical studies.



**AMRAD Corporation Ltd (Vic)** <http://www.amrad.com.au>

Amrad is a research and development company which has interests in allergy/inflammation, CNS diseases and infectious diseases. Part of Amrad's strategy is to develop therapeutic compounds to at least the end of Phase II, but look for co-development partners or licencees. Amrad's key products are therapeutic compounds for the treatment of diseases that have an unmet need. Amrad currently seeks a co-development partner or a licensee for several of these compounds. These include a conotoxin for the treatment of chronic pain. Amrad's R&D strength includes the area of neurologicals.

**Antisense Therapeutics Pty Ltd (Vic)** [www.antisense.com.au](http://www.antisense.com.au)

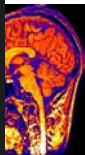
Antisense Therapeutics aims to create antisense drugs for diseases where there are large and/or poorly met markets, including the devastating neurological disease, multiple sclerosis, a chronic autoimmune disease in which the body damages its own nerve cells. The lead neuroscience-related product, ATL1102 is an antisense oligonucleotide targeting VLA4, an immune cell molecule. Blocking of VLA4 is expected to lead to a reduction of new lesions in Multiple Sclerosis patients.

**Axon Instruments (USA)** [www.axon.com](http://www.axon.com)

Axon Instruments, Inc. was founded in 1983 in Australia to design, manufacture and market instrumentation and software for cellular neurosciences and biophysical research. It is now based in California, but listed on the ASX. The company is recognized as the world leader in low-noise signal amplification instruments and related data acquisition and analysis products for cellular neuroscience. The main product lines are in the area of Cellular Neurosciences: cellular electrophysiology and Cell-Based Screening high-resolution fluorescence imaging and electrophysiology (patch and voltage clamp). In 1997, Axon Instruments entered the clinical market with the release of a movement disorder monitor used in the assessment of tremor, reaction time and rigidity in patients with Parkinson's disease and similar movement disorders. This was followed in 1998 with the introduction of microelectrode guidance systems used to accurately identify targets during neurosurgery.

**Bionomics Ltd (SA)** [www.bionomics.com.au](http://www.bionomics.com.au)

Bionomics Limited is a publicly-listed SA biotechnology company. It combines a strong genomics-based research focus on the discovery of genes associated with serious medical conditions with validation and development efforts leading to new drugs, gene therapies and diagnostic applications. The Company concentrates its research and development activities in the areas of breast cancer, epilepsy and angiogenesis. In addition to an extensive patent portfolio on novel epilepsy genes, Bionomics has established a number of drug targets for this condition as well as a specific mouse model that is being applied to evaluate therapeutic candidates.

**Biotron (ACT) [www.biotron.com.au](http://www.biotron.com.au)**

Biotron Limited was incorporated in February 1999 to fund, manage and commercialise a number of existing biomedical projects arising from the John Curtin School of Medical Research (JCSMR), a leading research institute within the Australian National University (ANU). Biotron is engaged in both diagnostic and therapeutic research. While its primary focus is in cancer diagnostic tests and antiviral agents, one of its projects is developing compounds which act on gamma-aminobutyric acid (GABA) receptors in the central nervous system for the suppression of epileptic seizures, and to provide tranquillisers and a new general anaesthetic.

**Brain Resources Company Ltd (NSW) [www.brainresource.com](http://www.brainresource.com)**

The Brain Resources Company is in the business of measuring and analyzing functional brain activity and relating this information to underlying disorders. It leads the field in the development of functional brain analysis in the clinical trial process for pharmaceuticals and has franchised clinics around the world. Its technology is under assessment by several major pharmaceutical companies including Eli Lilly, Bayer and Pfizer.

**BresaGen Ltd (SA) [www.bresagen.com.au](http://www.bresagen.com.au)**

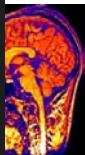
Bresagen undertakes R&D into cell therapy, and is developing therapeutic proteins to treat cancers and asthma. It also produces and markets human and animal growth hormones and offers contract bio-pharmaceutical manufacturing. Bresagen has a major focus on stem cell technologies aimed at finding a cure for debilitating human diseases including neurological and bone marrow disorders. Parkinson's disease is one of the major diseases targeted by the Cell Therapy Program.

**Calibre Biotechnology Pty Ltd (VIC) [Not available](#)**

Calibre is an early stage company that designs and develops growth factor mimetics and inhibitors. Growth factors are endogenous molecules that regulate the growth of cells. They offer potential for the treatment of a variety of diseases including neurological disorders such as Parkinson's disease. However, being large protein molecules, they are generally not suitable for use as drugs. The Calibre approach allows for the creation of small molecules that can be tailored to either mimic or inhibit the action of a given growth factor.

**Circadian Ltd (VIC) [www.circadian.com.au](http://www.circadian.com.au)**

Circadian Ltd is an interesting biotechnology company model. It listed on the ASX in 1985 and provides management and funding for the development and commercialisation of Australian biomedical research. It identifies high potential investment opportunities from within Australian research institutions, focussing on projects, which have the potential to address large markets or significant unmet medical needs. Promising opportunities can then be spun out into separate companies. Circadian also takes equity in other companies, including several in the neuroscience area - Syngene Ltd, Antisense Therapeutics Ltd and U.S. based Axon Instruments Inc. Circadian is also the largest shareholder in Amrad Ltd. In addition to the neuroscience developments in those other entities, Circadian has a number of university-based projects in the field, including development of a potential new



treatment for Alzheimer's disease and the identification of memory enhancing compounds based on specific brain receptors.

**Cochlear Ltd (Vic) [www.cochlear.com](http://www.cochlear.com)**

Cochlear has developed and markets cochlear implants to help those with severe to profound hearing loss or "nerve deafness". The Cochlear Implant is a technical medical device that electrically stimulates the hearing nerve in the cochlea (inner ear). The electrical sound information is sent through the auditory system to the brain for interpretation. Speech coding strategies control the digital processing of environmental and speech sounds, with different strategies emphasizing different pitch, loudness and timing cues.

Cochlear has achieved more world firsts in cochlear implant technology than any other company. Today Cochlear is working on more than 90 collaborative research projects in 60 countries around the world. Since the first commercial implant 20 years ago, Cochlear's award winning Nucleus product range has been implanted in nearly 40,000 people across the world. Over 60% of all cochlear implant recipients use Cochlear's devices. From its beginnings in Sydney over 20 years ago, Cochlear now employs over 700 people worldwide, with regional offices in the US, UK, Belgium, Switzerland, Germany, Japan and Hong Kong.

**Cogstate Ltd (Vic) [www.cogstate.com](http://www.cogstate.com)**

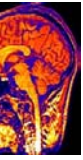
Cogstate was founded in 1999 to develop and market screening software for the assessment of cognitive health to improve early diagnosis of neurological and psychological disorders. It aims to be a global online provider of performance based cognitive assessment services for the medical and sporting industries. Examples of the application of this technology include the definitive and objective measure by sports doctors and trainers of an athlete's cognitive function after a concussive episode, or its application for serial screening of a patient's cognitive function during medical assessments. Cogstate has also licensed and is developing two series of molecules for the early treatment of Alzheimer's disease.

**Compumedics Ltd (NSW) [www.compumedics.com](http://www.compumedics.com)**

Compumedics, is a global technology leader in computer-based patient monitoring and diagnostic systems with a core focus on the Sleep Medicine and Neurology markets. The Company is also expanding into a number of related market sectors including cardiac diagnostics, fatigue monitoring, in-depth anesthesia monitoring and sleep disorders therapy. Compumedics leads the sleep diagnostic market in Australia, with a market share of approximately 70%, and a growing international business, especially in the USA, which is the world's largest medical device market. All products are developed, designed, manufactured and marketed from the company's Australian corporate headquarters in Melbourne, Australia.

**Cyclotek (Aust) Pty Ltd (Vic) not available**

Cyclotek uses radioisotope labeled tracers to detect brain tumours through digital imaging.



**Dynamic Hearing Pty Ltd (NSW) [www.dynamichearing.com.au](http://www.dynamichearing.com.au)**

Dynamic Hearing is a start-up company that aims to be a market leader in the development of software applications for the emerging digital hearing aid industry. The company's first product is ADRO™; advanced digital signal processing software, which produces improved speech perception for hearing aid users. Dynamic Hearing is a spin off from the CRC for Cochlear Implant and Hearing Aid Innovation.

**ES Cell International Pty Ltd (Singapore/Vic) [www.escellinternational.com](http://www.escellinternational.com)**

ES Cell International is a regenerative medicine company providing products and technologies derived from human embryonic stem cells. The corporate strategy is to convert its significant platform technology into products for the treatment of degenerative diseases. ESI is incorporated in Singapore but originates in part from Australian technology. The company retains a substantial Australian base, together with a research and production facility, housed within the Monash Institute of Reproduction and Development. ESI is concentrating its resources on the therapeutic areas of Diabetes and Parkinson's disease, with additional scientific undertakings in the areas of cardiology and haematology.

**Neopraxis Pty Ltd (NSW) [www.neopraxis.com.au](http://www.neopraxis.com.au)**

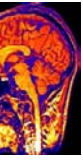
Neopraxis, a subsidiary of Cochlear Ltd, aims to improve quality of life for people with neurological damage through the use of "Functional Electrical Stimulation" to help restore functions lost as a result of neurological damage. The Company is conducting a study of the Praxis™ multifunctional FES system. This technology is intended to allow people with paraplegia to use their own muscles for upright mobility, bladder control and exercise.

**NeuroTech Research Pty Ltd (Qld) [www.neuromathix.com](http://www.neuromathix.com)**

NeuroTech Research is a biotech/IT company, designing software-based solutions to improve clinical medication of chronic diseases. The Company's activities involves the international cooperation of cutting-edge researchers in a number of diverse fields: from neurology to aerospace-based guidance and control, from pharmacology to nuclear magnetic resonance, from clinical care of patients suffering degenerative diseases to the programming of sophisticated software applications. The company is developing software to aid treatments against chronic neurodegenerative diseases.

**ObjectiVision Pty Ltd (NSW) [www.objectivision.com](http://www.objectivision.com)**

ObjectiVision is a medical technology company that designs, patents and markets high value vision related products that contribute to the prevention of blindness. It aims to produce innovative products that can be used simply and cost effectively in clinical practice to diagnose and manage a wide range of eye diseases. ObjectiVision's leading product, the AccuMap®, is an objective perimetry system for assessment of the human visual field with applications in glaucoma diagnosis and other eye diseases. The multi-award winning AccuMap computerised glaucoma detection unit may also be capable of identifying other conditions such as cerebral tumour and multiple sclerosis.



**Polychip Pharmaceuticals Pty Ltd (Vic) [www.circadian.com.au](http://www.circadian.com.au)**

This wholly owned subsidiary of Circadian Technologies Ltd is developing novel approaches to the treatment of Alzheimer's disease using inhibitors of the p75 receptor to decrease the age-related death of cholinergic neurons.

**Prana Biotechnology Ltd [www.pranabio.com](http://www.pranabio.com)**

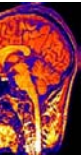
Prana Biotechnology is developing therapeutic drugs to treat the central disease pathways that cause age-related degeneration of the brain and the eye. The initial focus is on the treatment of Alzheimer's disease, while other potential applications include Cataracts, Tardive Dyskinesia (a major brain disorder that is caused by prolonged treatment with drugs used to treat schizophrenia), Creutzfeldt-Jakob Disease (CJD or Mad Cow Disease), Motor Neuron Disease and Parkinson's disease. The Company's technology emerged from collaborative efforts between US and Australian scientists, notably Professor Colin Masters at the University of Melbourne and the Mental Health Research Institute. In the 1980s Professors Masters and his colleagues identified the protein (beta-amyloid) that has since become the dominant focus world wide of Alzheimer's disease research. They went on to discover the way beta-amyloid was produced and how it interacts with metals, causing toxicity in Alzheimer's disease. This work paved the way for Prana to develop therapeutic drugs to treat the disease. The first of these (PBT-1) has successfully completed early clinical stage evaluation in Alzheimer's disease. Prana has now expanded the number of new chemical entities in its portfolio to over 200, and is building on the metal-protein interaction concept as being central to the toxicity seen in many of Prana's neurological disease targets.

**Praxis Pharmaceuticals Australia Pty Ltd (ACT) [www.praxis-pharmaceuticals.com](http://www.praxis-pharmaceuticals.com)**

Praxis is undertaking R&D on the development of a small carbohydrate-based molecule for the treatment of inflammatory disorders, particularly multiple sclerosis, which involves repeated episodes of inflammation of nervous tissue in any area of the central nervous system. Their front-running compound has shown good activity in preclinical studies, and prevents the inappropriate migration of certain types of immune cell, over activated in multiple sclerosis. The project involves a new approach to this disease and the objective is to develop the new range of compounds through to clinical studies in patients.

**PsyGene Pty Ltd (NSW) [www.garvan.org.au](http://www.garvan.org.au)**

PsyGene Pty Ltd is a pharmacogenomics company based upon investing in high-risk, but high potential research in the genetics of mental illness and dementia and translating this into new drug discovery and development opportunities through partnering with the international pharmaceutical industry. PsyGene was created to address a large market opportunity. Mental illness and Alzheimer's disease are major health problems accounting for more hospitalisation costs than any other disease category. Despite the scale of these problems, there is currently no rational basis for the development of new therapeutic drugs to treat bipolar affective disorder and Alzheimer's disease.



**QrxPharma Pty Ltd (Qld) [www.qrxpharma.com](http://www.qrxpharma.com)**

Although QRxPharma Pty Ltd was only established in November 2002, it is a developmental stage bio-pharmaceutical company committed to the commercialization of technology for the treatment of pain and control of bleeding. The Company's lead product is a high potency combination of two opioids for use in the treatment of acute and chronic moderate to severe pain. Compared with existing pain control products, it has the potential for lower side effects such as nausea, respiratory depression, sedation, constipation. Immediate Release, controlled release and injectable formulations are being developed. Preliminary clinical studies demonstrating benefits of the product have been successfully completed. Further studies to allow for product registration will commence in 2003.

**Syngene Limited (VIC) [www.circadian.com.au](http://www.circadian.com.au)**

Syngene is building a research portfolio in gene based diagnostics and therapeutics. In addition, Syngene has established a collaborative program with the Howard Florey Institute in Melbourne based on novel approaches to enhance the uptake of therapeutic compounds to various tissues, including the brain. This project is looking at both enhanced uptake and specific targeting of compounds.

**TinniTech Limited (WA) Not Available**

Tinnitech is an early stage company developing a rehabilitation technique and device for tinnitus sufferers that is consistent with contemporary understandings of the underlying pathology in the auditory system of which tinnitus is a symptom. The device will perform hearing tests, provide core treatment, and log patient performance.

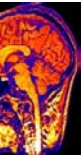
**Xenome Ltd (Qld) [www.xenome.com](http://www.xenome.com)**

Xenome is a public, non-listed biotechnology company for the discovery and development of novel therapeutics based on the components of venoms and toxins. The company has access to a large variety of unique venomous animals including coneshells, spiders, snakes, scorpions and centipedes. Xenome extends the natural diversity of venom peptides through the manufacture of peptide analogue libraries of drug lead molecules. Drugs under development include a small venom peptide active at a novel inhibitory site on the noradrenaline transporter, a key target in the treatment of CNS disorders such as depression and attention deficit syndrome, and a number of coneshell peptides targeted at pain modulation.

**Showcasing successful Australian Companies**

*(a) The Bionic Ear: From Discovery to a \$2 Billion Australian Company*

The development of the Australian Bionic Ear began in 1967 when Professor Graeme Clark commenced research at the University of Sydney to develop a cochlear implant - the "bionic" ear - to help those with severe to profound hearing loss or "nerve deafness". Funding for the research was obtained through charities. After a decade of development, Professor Clark succeeded in producing a unit that was successfully implanted in the first patient in 1978.



In the early 1980s, the Australian pacemaking firm Teletronics manufactured the device for clinical trial in the US. A new company, Cochlear Limited, and its holding company, Nucleus, were then formed to develop the Bionic Ear. In 1985 the Australian Bionic Ear was approved by the US FDA for use on people who became deaf after age 18 years, and became the first multiple-electrode device to be approved by the US FDA. In 1990 it became the first Bionic Ear to be approved for use in children - the first major advance in helping profoundly deaf children communicate since sign language for the deaf!

Cochlear has achieved more world firsts in cochlear implant technology than any other company. Its award winning Nucleus product range has been implanted in nearly 40,000 people across the world, and over 60% of all cochlear implant recipients use Cochlear's devices. From its beginnings in Sydney over 20 years ago, Cochlear is now an ASX-listed company with market capitalization of \$1.74 billion, over 700 employees worldwide, and regional offices in the US, UK, Belgium, Switzerland, Germany, Japan and Hong Kong.

*(b) Prana Biotechnology Ltd: Commercialising Leading-Edge Australian Research in Alzheimer's disease Therapies*

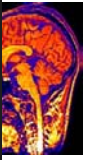
Current treatments for Alzheimer's disease are of very limited effectiveness, frequently cause side effects and do not halt the progressive downhill course of the disease. In the 1980s, collaborative research between US and Australian scientists, notably Professor Colin Masters at the University of Melbourne identified the protein (beta-amyloid) that has since become the dominant focus world-wide of Alzheimer's disease research. They went on to discover the way beta-amyloid was produced and how it interacts with metals, causing toxicity in Alzheimer's disease.

This work led to the establishment of Prana Biotechnology Ltd to develop therapeutic drugs for the disease. The first of these has successfully completed early clinical stage evaluation. Prana has now expanded the number of new chemical entities in its portfolio to over 200, and is building on the metal-protein interaction concept as being central to the toxicity seen other neurological disease targets.

Prana listed on the ASX in 2000 and has reached a capitalization of over \$50 million. It retains strong links to the Australian research sector, with Professor Masters on the board and chairman of the Scientific Advisory Board. If future clinical trials prove successful, this Australian research and commercial effort could achieve a world first in developing an effective therapy for Alzheimer's disease.

*(c) Brain Resource Company: a successful Australian SME*

Brain Resource Company (BRC) exemplifies a successful Australia SME with strong links to the global pharmaceutical industry. Having only incorporated in 2001, the company now has clinics in over 10 countries, and is listed on the ASX at a market capitalization of \$15 million. BRC has developed proprietary approaches to standardized testing and analysis of large amounts of brain function data and relating this information to underlying disorders. It leads the field in the development of functional brain analysis in the clinical trial process for pharmaceuticals and has franchised clinics around the world. Several major pharmaceutical companies including Bayer and Pfizer are now evaluating the technology and recently Eli Lilly Research Laboratories signed a contract of considerable dollar value for Brain Resource Company to conduct a large study of brain functioning in subjects receiving methylphenidate.



## APPENDIX 5

### Additional Details on Strategies for the Brain and Mind Research Alliance

#### 1. Key early actions for the Brain and Mind Research Alliance

- A. Meet with NHMRC, ARC and CSIRO and other relevant funding bodies to identify mechanisms to enhance cross-agency funding of neuroscience.
- B. Hold consensus workshops on youth related mental problems and brain disorders of the elderly to identify gaps in the national research effort and develop priorities for future research funding. The youth-related workshop should be held in conjunction with ARACY because of the commonality in outcome needs.
- C. Hold joint workshops with neuroscientists, consumers and carer organisations, such as Mental Health Council of Australia, for the purposes of building synergy with the Australian people in the neuroscientific effort being made on their behalf.
- D. Identify the international networks that Australian neuroscientists must belong to in order to ensure that we are always at the frontiers of knowledge in the neurosciences for the purposes of utilising the most cost effective best practice for the alleviation of brain and mind disabilities.
- E. As a first step to establishing a mechanism for pro-active identification, debate and policy setting on ethical, legal and social issues that will arise from neuroscience research, convene a national conference to review key issues related to ethics. This will include the practice of brain science; brain science and being human; brain science and social policy; and brain science and public discourse.

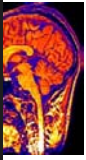
*An indicative timetable of initiatives could be:*

*2003*

1. Establish Consultative Task Force and initiate widespread stakeholder consultation
2. Meet with NHMRC, ARC and CSIRO and other relevant funding bodies to identify mechanisms to enhance cross-agency funding of neuroscience.
3. Establish the Brain and Mind Research Alliance with a high profile board.

*2004*

4. Hold consensus workshops on youth related mental problems and brain disorders of the elderly to identify gaps in the national research effort and develop priorities for future research funding.



5. Recommend strategies to enhance funding of neuroscience research in Australia, with particular emphasis on provision of National Network Funding as the 'glue' to encourage multi-disciplinary, collaborative research efforts.
6. In conjunction with the appropriate funding bodies, recommend the means and funding for Australia to participate in major international projects such as those of the Human Frontiers Science Program and the European Union 6<sup>th</sup> Framework Program.

2005

7. In conjunction with the appropriate funding bodies, advise on a program of national network funding to provide additional sources of funding to innovative research networks focused on either frontier technologies, or cross-disciplinary approaches to brain and mind disorders.
8. Convene a national conference to review key issues related to ethics.

## **2. Key roles for the Brain and Mind Research Alliance**

### **A. Research partnerships**

#### *1. Programs to support international research linkages*

While researchers generally have some funds for international travel, they do not have the funding required to participate in major international projects. The Alliance could play a valuable role here in facilitating the establishment of a fund through which Australian neuroscientists could participate in these projects.

Examples of international programs include:

#### a. Human Frontiers Science Program (HFSP)

This program has been in place for the last 12 years. Member countries of the HFSP include the USA, the UK, Japan and a number of members of the European Union. Thirty-one Australian neuroscientists have received HFSP Fellowships (worth US\$2.6 million) and thirty-two Australian neuroscientists have received HFSP Grants (worth US\$5.2 million). Although this success rate testifies to the strength of Australian neuroscience on an international scale, the funds had to be obtained through a member country of the HFSP. That is, Australians could not take the lead in initiating applications to the HFSP, thus considerably restricting the growth of international collaborations. It would at present cost Australia about US\$600,000 per year to become a full member of HFSP. Note that this is about the amount Australian neuroscientists have won per year through the HFSP without being a member country. Support for Australia to enter the HFSP would then greatly accelerate our international collaborations through the program, with no net cost to Australia. This is the most important potential source of collaborative support with the USA.

b. The European Union's Framework Program for Research and Technological Development

The European Framework Fund is intended to support Australian participation in European Union (EU) Framework Research and Technology Development Program projects. Assistance is available to support travel to Europe in order to negotiate participation in Framework Research projects with a European Program partner. Australians may seek or be invited to participate in a consortium as a full partner or a sub-contractor. Australians applying for travel support should be able to demonstrate that their EU partner has received funding approval for their project. In the 5<sup>th</sup> Framework Agreement a total of 38 projects were participated in with European countries. The sum total that went to these countries was 162 million Euros.

In 2002, thirty-five Australian researchers and research administrators attended the launch of the European Union's 6<sup>th</sup> Framework Program for research. Although Australian's cannot initiate 6<sup>th</sup> Framework Program alone, we should be more pro-active in this area. This can be done by funding travel by senior neuroscientists to Europe in order to sow the seeds for programs with European colleagues who may then put them forward to the European Framework Fund. More importantly, however, is the need to ensure that relevant Australian funding is available from agencies such as NHMRC, ARC, DEST, etc to support the Australia-based research activities of Australian participants in 6<sup>th</sup> Framework Programs.

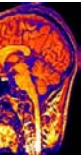
c. Other sources of support for Australian International Collaborations

There are a number of other smaller schemes than 1 and 2 above that are supported by Grant Assistance Schemes through the Australian Government. These can be found through the Science Portal at (<http://www.science.gov.au>). These schemes have an important limitation, however. They do not provide support for senior researchers to work in the USA so as to forge and maintain collaborative links.

## B. Research funding

### 1. *Linkages between Funding bodies*

National Health and Medical Research Council (NHMRC), Australian Research Council (ARC) and Commonwealth Scientific Industrial Research Organisation (CSIRO) have traditionally funded scientific research in separate "silos" with minimal interactions. This process has allowed the agencies to focus on their particular interests and was appropriate when the interchange between disciplines was typically less than today. However, scientific research, especially in its active growing areas, is increasingly multidisciplinary. Neuroscience is an excellent example of this, encompassing biology, medicine, psychology and cognitive sciences, biochemistry, molecular biology, physiology, mathematics and computer sciences.



This fragmented approach to research funding is inappropriate for neuroscience because it:

- Fails to recognise its multidisciplinary nature.
- Impedes cross collaboration between disciplines.  
The agencies not only largely lack mechanisms for cross-disciplinary funding, but in many cases their policies (stated or unstated) actually prevent it.
- Does not take advantage of the fact that many of the most fertile and productive areas of science are at the boundaries between disciplines.
- Is not suited to the new approach of funding by research priorities

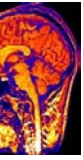
Paradoxically, NHMRC, ARC and CSIRO all fund research that is highly relevant to neuroscience, but there are few effective mechanisms to promote partnerships between the agencies. Moreover, there are issues with eligibility restrictions in some programs. A notable gap is the ineligibility (or non-support) of neuroscientists based in Medical Research Institutes and Hospitals under the Federation Fellowship program. This limits the capacity and effectiveness of the national neuroscience workforce.

The NHMRC has a focus on health and basic biomedical science. In 2003, 266 new and continuing grants were funded in mental health and neurosciences, representing \$30,857,368 expenditure or 15.2% of Project Grants, being the second largest area of funding.

The mission of the Australian Research Council is to advance Australia's capacity for quality research to the economic, environmental, social and cultural benefit of the community. To this end the Council supports Discovery research at the frontiers of knowledge and in our best and brightest researchers as well Linkage programs to encourage collaborative research, contributing to a strong knowledge economy, to create opportunities for co-operation across Commonwealth portfolios and to facilitate international linkages within universities and industry.

Under this framework ARC supports research in a wide range of areas but tends to exclude those with a clear health or biomedical focus that are regarded as the domain of the NHMRC. ARC supported research relevant to neuroscience includes psychology and cognitive science, physiology, brain development, genomics, proteomics, bioinformatics, computer science, to name a few. Two of the ARC Federation Fellowships are devoted to neuroscience: Professor Perry Bartlett of the University of Queensland on Cellular Plasticity of the brain and Professor Max Coltheart of the ARC Special Centre for Cognitive Neuropsychology.

One of the CSIRO's National Research Flagships is Preventative Health. As part of this there is a partnership focus aimed at developing national teamwork and collaboration as a primary ingredient for success in science, technology and innovation. All of the components of the Preventative Health Flagship partnerships program of CSIRO are relevant to neuroscience. These include nutrition, post-genomic diagnostics, psychology, data-mining and information technology. Furthermore, since disorders of brain and mind are the major causes of disability, attention to neuroscience is essential for the Program of CSIRO to achieve its aims.



In the wider context, many of the core technologies of CSIRO are highly relevant to neuroscience, as mentioned above. Those particularly relevant are genomics, proteomics, computer science and information technology, bioinformatics, organic and medicinal chemistry, molecular structural biology, protein engineering and bioassays.

In order to maximise Australia's ability in neuroscience, different Government Funding and Research Agencies need to form partnerships to fund major areas of neuroscience in a way that facilitates the skills of these different arenas.

The proposed Brain and Mind Research Alliance can play an important role in promoting neuroscience to the relevant funding bodies, identifying strategies to maximise funding to the field, and in facilitating funding partnerships. The Alliance should bring the ARC, NHMRC, CSIRO and other relevant Government Departments together to identify ways in which they can contribute to cross-disciplinary neuroscience research.

A key initiative will be for the funding agencies to agree to provide a proportion of their funding to the National Network Funding.

## 2. *Examples of mechanisms for network funding*

### a. The NHMRC Network for Brain Research into Mental Disorders

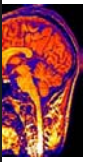
The National Health and Medical Research Council provided a Unit Grant from 1994-2001 to support a Network of Brain Research into Mental Illness. As an expert Committee of Review noted in recommending renewed funding from 1997

“the Network is a unique endeavour in Australia and has significant differences from other multicentre research groups, being funded not on criteria of scientific track record nor scientific hypotheses (which already existed in the area), but rather to enhance the specific area of medical research and to do so by ‘networking’ and by improving the quality and quantity of work comprising the sum of its separate components”. (Report of the Network Review Committee, chaired by A/Prof John Willoughby, November 1997)

The Network sought specifically to develop innovative collaborative research programs between Australian neuroscience and psychiatric researchers. The Network brought together a large and diverse group of researchers who shared the goal of enlarging the horizon of knowledge about the causes and nature of psychiatric disorders and who shared the assumption that the achievement of this goal will be reached via the study of brain biology.

#### Achievements:

- The Network involved over 50 chief and associate investigators from over 20 different organisations and supported work on three primary disease areas (schizophrenia, bipolar disorder and Alzheimer's disease) in five different areas of research (clinical assessment, genetics, neuroimaging, brain banking and animal models). Investigators came from all States of Australia.



- Through the Network there was national training and standardised use of selected diagnostic assessment instruments for psychiatric disorders – an important pre-requisite to national consistency in psychiatric research, where a biological test for disorders is lacking.
- Network collaborations facilitated two PET imaging centres in Sydney and Melbourne. Network members introduced into Australia neuroimaging techniques using 15O or 11C PET and standardized the techniques between PET sites in Sydney and Melbourne.
- The Network initiated research on inherited mutations in Alzheimer's disease that engaged clinical, neuro-imaging, neuropathology and genetic researchers who had not previously worked together.

The expert Committee of Review found that there had been significant increases in activity relevant to the aims of the Network.

- Publications in refereed journals increased by one-third.
- Grants held relevant to Network aims increased by 40%
- Projects on which members of different research groups within the Network were joint investigators increased three-fold during the life of the Network
- Meetings between different research groups were initiated and became regular, underpinning ongoing interdisciplinary projects.

In the five years between 1993 and 1997, there were some 141 publications by Network members, directly relevant to and supported in part by Network Activities (Unit Grant Renewal Report to NHMRC March 1997). In the two years 1998-99 there were 116 publications (Unit Grant Progress Report to NHMRC, 1999).

Importantly, amongst these publications there were an increasing proportion that involved authors from more than one research group – this more than doubled from 5 per year (1993-1997) to 14 per year (1998-99).

#### Limits and Lessons

Notwithstanding the considerable achievement of the Network, the relatively modest level of research support to facilitate the linkages it facilitated meant that the "glue" was spread very thinly (\$500,000 pa for 50 investigators and 15 areas of work). Much of the funding distributed in the Network was by the nature of seed-funding to encourage projects and collaborations that would otherwise have lacked resources.

The lessons learnt from the Network were that fostering partnerships between neuroscientists and psychiatrists can be immensely productive but that the most effective partnerships were focussed around specific research and disease questions. In this sense both the strength and weakness of the Network was its size and the range of the work it embraced.

#### Source

Prof David Copolov (Mental Health Research Institute of Victoria) and Prof Peter Schofield (Garvan Institute of Medical Research).

b. EU FP6 funding mechanism

National network funding could take the form of Integrated Projects (along the lines of the EU FP6 funding mechanism). This would involve researchers holding consensus workshops to identify the priority areas for support, followed by a call for expressions of interest in the selected areas. It is envisaged that these would be in relatively focused areas on either areas of disease and disability or on areas of technological integration. Examples of such work would be National Networks in Epilepsy, Dementia or Mood Disorders, etc. Such Networks would seek to integrate within a single research plan a series of studies aimed at delivering new knowledge and applied outcomes relative to the disorder under study. On the technological focus, expressions of interest could address National Networks focussing on areas such as Neuroimaging, Genetic Epidemiology or Neuroinformatics, etc.

c. US Consensus workshops

The US Government National Institutes of Health (NIH) undertakes national consensus meetings of stakeholders to decide the most urgent questions and areas in a particular field of medical science. Following this, a Request for Proposals (RFP) is released for targeted research proposals in the agreed priority areas.

In the Australian context, the selection, funding and review of successful projects and programs would involve partnerships of several major funding agencies and independent peer review. This would enable each agency to address its own objectives and in so doing support major, internationally competitive groups working on areas of agreed top national priority. Such a process is likely to delivery a much higher impact in terms of focus, success and outputs than the current piecemeal, fragmented process of research support.

### C. Partnerships with industry, consumers and carers

#### 1. *Accelerating industry uptake of R&D*

Notwithstanding the positive developments in neuroscience commercialisation outlined in Appendix 3, there is some way to go before Australian neuroscience could claim to have “market and end-use pursued with the same vigour as the research effort”.

The Brain and Mind Research Alliance can play an important role through initiatives to identify impediments to commercialisation and help network multinational companies, Australian companies and research organisations. It will be important to ensure that companies, as well as research institutions, are active participants in the Alliance.

The Alliance could also provide advice to Government on the effectiveness and importance of industry R&D support programs. These have been a vital source of R&D funding for cash-starved small companies and they have also catalysed industry uptake of public sector research as well as strategic links between Australian biotechnology companies and the pharmaceutical industry. For example:

Start grants: Most of the listed and some unlisted neuroscience companies in Appendix 2 have accessed the Start scheme for R&D projects. It is crucial that this scheme continues after the current allocation of funding ends in 2006.

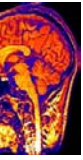
- BIF grants:** These Biotechnology Investment Fund (BIF) grants have kick-started most of the unlisted neuroscience companies shown in Appendix 3, and its continuation should be supported. There is no indication, however, that the scheme will be refunded after the initial tranche of \$40 million is expended later this year.
- Tax Concession:** The R&D tax concession is supported by the neuroscience industry, with the new tax-offset providing the added advantage of up-front cash rebate for small companies. The current limitation of the rebate to companies with less than 25% shareholding by tax-exempt entities is, however, a serious flaw in the program, since it excludes many of the neuroscience start-ups.
- PIIP:** The Pharmaceutical Industry Investment Program (PIIP) and its predecessor, Factor-F, has been an important factor in encouraging pharmaceutical companies to invest in Australian research. At least four of the current 5 beneficiaries - Pfizer, Glaxo-SmithKline, Bristol-Myers Squibb and Eli Lilly - have made a significant research investment in Australian neuroscience. For example, prior to PIIP, Pfizer had only two research collaborations in Australia, and now has over 45. There is scope, nevertheless, to improve the program for better targeting at value-adding linkages among major companies, small companies and Australian research institutions.

## 2. *Community Partnerships*

Increasingly, the burden of care for people with brain-related disorders falls on immediate family members. Those with the greatest investment in finding cures for the disabling mental and neurological disorders are those with the illnesses themselves, their families and their carers. Experience in Australia, and internationally, indicate that consumers, families and carers are strong supporters of basic and applied research. To date, consumer and carer groups in mental health and neurology have concentrated their efforts on advocacy for improved health services, fund-raising and mutual support. Experiences in other health areas (breast cancer for example - see box below) have indicated, however, the power of establishing Australia-wide networks to underpin nation-wide basic and clinical research.

### **Kathleen Cunningham Foundation for Hereditary Breast Cancer; an example of successful partnership with families**

This Australia-wide network of families whose members are commonly affected by breast cancer was developed to assist researchers make rapid progress in determining relevant genetic risk factors and develop effective treatments. Additionally, the research brief has been extended to investigate the relevance of psychosocial risk factors and quality of life issues. Given the number of families Australia-wide that participate voluntarily in all aspects of this research, it has become a major international resource (recognised recently by description in the international journal *Science*) and one that gives Australian researchers and their patients a considerable competitive advantage. It sets an excellent example for the way in which an Australian network of families with a specific illness can work effectively with a national network of Australian basic science and medical researchers to make rapid progress with finding the cause of a complex disease.



Many of the common mental and neurological disorders run in families. At this point in the history of medical research into mental and neurological disorders, we are unclear as to what aspects of many of the diseases we observe actually run in families and to what extent such familial clustering of cases is determined by specific genetic or environmental factors. For mental disorders, our current classification of illnesses is particularly unlikely to match easily with the genetic, brain, or biochemical measures that we have developed.

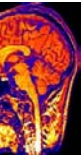
Our understanding of many of the mental and neurological disorders could be substantially improved now by research that focused specifically on large numbers of families that share particular illness or neurobiological characteristics. Twin registries have proven particularly useful in this regard (see box below). Such an approach has already proved successful in unravelling key genetic aspects of epilepsy. Specifically, the best way to identify families with these conditions is to work in close association with the national organisations that represent their interests. For those with mental disorders, that is the recently formed Mental Health Council of Australia. It represents over 30 national peak bodies representing the interests of consumers, carers, providers and non-government organisations in mental health. Additional disease-specific entities exist in both mental health (e.g. Schizophrenia Fellowship, bluevoices) and other neurological disorders (MS Society, Alzheimers Association).

### **The Australian Twin Registry**

The Australian Twin Registry is a major national resource for Australian medical research. Specifically, it has been recognised internationally for its contribution to our understanding of the relative contributions of genes, early childhood and later adult environments to common mental disorders such as depression, anxiety and alcohol and substance abuse. Recently, it has allowed us to develop more sophisticated understandings of childhood disorders such as ADHD and disorders of later life such as late-onset depression.

As the registry has collected information from many of the same twins for over a quarter of a century, its data now lies at the heart of national and international efforts to identify the genes underpinning common disorders of anxiety, depression and alcohol abuse. Increasingly, twins are not only supplying information about their health and behaviour but also participating in specific neurobiological tests (cognitive tasks, brain scanning, electrical brain maps) that may permit a far greater understanding in the types of brain-related disorders that are passed across generations and the extent to which common genes or shared environments contribute to the occurrence of specific disorders within specific families.

Through a process of active partnership and recruitment, it would be possible to create national registers of persons with specific illnesses, and their families, who would be willing to participate in key genetic, neurobiological and clinical studies. Correspondingly, it is then important to support a national network of researchers who are willing to respect the rights and contributions of these individuals and their families and then work with them to develop research projects that respect their needs, priorities and experiences. The research efforts need to be nationally coordinated to protect the rights and interests of the persons with illness and to prioritise those projects of greatest relevance to the participants.



Many of the clinical and pre-clinical studies essential to rapid drug development, as well as development and utilisation of other biotechnologies, requires access to those with disorders or those at high risk of developing disorders (such as immediate family members). Recruitment to such studies can be extremely difficult, especially given the increased risks associated with new drugs or investigative technologies. However, it is often in the interests of those most affected, or those at highest personal risk, to participate in the early phases of the development of new treatments or new prevention strategies.

National registers of willing volunteers for early stage drug or biotechnology developments would provide Australian researchers with considerable advantages over international competitors. In addition the capacity to track participants at later stages of enquiry is higher in Australia (due to more stable demographic patterns) than in many other countries. Australia also has the appropriate legal, ethical and privacy frameworks to balance the advantages of such voluntary registers with any possible negative or exploitative aspects.

#### **D. Policy and Awareness**

##### *1. Health outcome evaluation and priority setting*

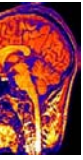
One of the barriers to achieving the Vision is the likely high cost of novel treatment technologies. The cost of developing a new drug and taking it to the patient is currently of the order of US\$500 Million. This will be exacerbated if, as predicted, many of the potential new treatments in brain medicine - such as gene therapy and stem cell approaches - are custom designed for each patient.

Many of the treatments that will emerge in brain medicine will result only in partial improvement rather than a cure of the condition. Industry will spend a great deal of money in developing these treatments and, especially in conditions where current treatments are inadequate, which is often the case in brain medicine, there will be some pressure to introduce these treatments into routine clinical practice with considerable cost to the community.

*It is important therefore to set in place adequate measures to evaluate health outcomes.*

Australia has very strong research expertise in clinical psychiatry and clinical neurology and a capacity to carry out detailed evaluations of potential new treatments. The Brain and Mind Research Alliance will provide the means to ensure that the scientific community assists government in ensuring optimal value for the health care dollar. Treatments that are extremely expensive and have only marginal efficacy should have a lower priority.

The Brain and Mind Research Alliance can also assist government authorities in educating the general public about the robustness of the processes in place to ensure optimum value for the health care dollar. Excellent clinical trial facilities in the neurosciences in both psychiatry and neurology are already in place in Australia with effective cooperative networks across the country. This ensures that Australian scientists are fully involved in the clinical trials process for many of the new compounds with data being obtained from our own country, which will assist in health outcome evaluation.



The area of health outcome evaluation in clinical neurosciences is still in its infancy. Some work needs to be done in establishing generally acceptable parameters for clinically useful patient benefits. The Brain and Mind Research Alliance should undertake to assist government in setting up robust processes. Mechanisms can be set in place, which will ensure that expensive marginal treatments do not find their way into this country but that the really useful treatments, which have a significant effect on brain illness, are available to Australians.

Another role for the Brain and Mind Research Alliance is to identify priorities for future development. It can achieve this by stimulating debate on priorities and identifying gaps in the current research effort.

## 2. *Pro-active consideration of ethical issues*

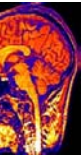
While the dramatic increases in neuroscientific knowledge are profoundly influencing and enriching our understanding of brain and behaviour, a number of complex ethical issues and concerns arise in relation to the conduct of research, the applications of research products, and the wider societal impact of neuroscience discoveries. Some of these issues are generic and homologous to those already examined by bioethics in the context of research involving human subjects – e.g. the duties and obligations of neuroscientists to safeguard privacy and confidentiality, or to ensure that any incidental findings of diagnostic significance would be appropriately conveyed to the participant or their doctor.

Other concerns, however, are novel and anticipate discoveries and developments likely to arise within the next quarter of a century. These range from ethics of the clinical applications of emerging revolutionary technologies to the interface between neuroscience and criminal law and the impact of neuroscientific knowledge on culture and society at large.

### *Clinical applications of neuroimaging research*

While not currently approved for clinical use, functional neuroimaging of the living brain in action has a great potential of improving the quality of personalised clinical care. Diagnostic procedures based on neuroimaging and on cellular and molecular neurobiology, including the capacity to identify disease precursors or risk markers in individual persons, will be the first to come on stage.

Ethical clinical application of functional MRI will require task and analysis standardisation and a systematic validation of functional MRI diagnostic paradigms against “gold standards”. The rational use of such tests may be difficult to regulate and control, and the distinction between probability-based prediction and preclinical diagnosis may be blurred. An example of the likely ethical and legal implications would be the case of an applicant for a life insurance being asked to submit to a structural brain scan to determine the presence of “silent” disease or risk marker.



### *Stem cell technologies*

Another fundamental issue concerns the clinical applications of stem cell technologies. The current controversy surrounding the future of stem cell research is impeding efforts to develop a regulatory policy similar to the one adopted for recombinant DNA research some 25 years ago. Greater and better communication is therefore necessary between researchers, industry, government and society at large. It has been suggested (Mackay, 2002) that “in a few years politicians might come to see stem cell research as an asset rather than a dangerous liability”.

### *Directed modification of cognitive and behavioural predispositions*

Neurobiologically mediated social engineering is another area of emerging ethical controversy. In the longer run, prospective neuro-genetic technologies may confer the capacity to enhance or augment desirable abilities and traits, as well as to “diminish” undesirable or risky behavioural propensities, such as violence or paedophilia. Such neurological biotechnologies will differ from others in that they ask us to explicitly consider the kind of person we want to be (Wolpe, 2002).

### *Equity of access and commercialisation of neuroscience research products*

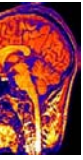
Radically novel therapeutic or preventive interventions are likely to become available in psychiatric disorders in future. Some, if not all, of these technologies will be exceedingly costly and their introduction will raise difficult questions about equity and regulation of access, public responsibility, and societal priorities. On a global scale, these issues will exacerbate further the disparities in access to health care between affluent and poorer nations.

### *Neuroscience in the courtroom*

Brain imaging studies and behavioural genetics data are adding a novel dimension to legal discourse and court practice. “Prognostic” neuroimaging of the propensity for violence is already the focus of imaging and genetic research. Studies of morphological or functional differences in the orbitofrontal cortex or the amygdala of persons who have committed violent offences or have been diagnosed with antisocial personality disorder are increasing in number (e.g. Raine et al., 1994).

Other studies are addressing the biological basis of a whole range of socially relevant issues, including racial attitudes (there are at least 3 published functional MRI studies on differential processing of racial aspects of human faces), the brain processing of moral and social knowledge, and studies on the capacity for empathy.

The dissemination of findings from such research is likely to result in an increase in criminal defence arguments based on irresponsibility due to a genetic predisposition or “predictive” neuroimaging studies. The defence may resort to brain imaging evidence to demonstrate that the accused is unable to stand trial because of some organic brain damage. The exact extent to which neuroscience in the courtroom will impact and change century-old legal concepts, beliefs and practices is difficult to predict, but the implications will be profound.



*The need for a pro-active approach to neuro-ethics*

The above examples indicate that there is an overriding need for a broad, critically informed dialogue involving neuroscientists, philosophers, theologians and, of course, the general public. Such dialogue should lead to an increasing, critical “neuro-literacy” and contribute to a societal sense of ownership and direction of the neuroscience revolution. As a first step, the Brain and Mind Research Alliance should convene in 2004 a national conference on this issue.

3. *Promote public awareness and education*

Surprisingly, Australians remain relatively unaware of the tremendous health, social and personal costs due to brain-related disorders. In two recent community surveys conducted by *beyondblue: the national depression initiative*, Australians recognised the importance of heart disease and substantially overestimated the relative importance of cancer and alcohol and other substances abuse.

By contrast, for young Australians, the significance of mental health, depression and suicide are largely missed. For older Australians, while the importance of dementia is recognised, mental health, depression, alcohol and substance abuse and suicide are all largely ignored. Important considerations in the underestimation of the health impacts of these disorders are the stigma associated with the mental disorders and the tendency to see mental disorders and suicide as largely social rather than health-related issues. As a consequence of national awareness campaigns, however, we are seeing some shift in these attitudes with now over 60% of people reporting that they or someone close to them has experienced a depressive illness (*beyondblue national survey, 2002*).

Improved public awareness and education regarding neuroscience and its application to brain and mind disorders therefore offers many potential benefits. These range from benefits to the sufferer and their family, to society at large and to the overall progress of neuroscience.

Education regarding the possible impact on neuroscience on brain and mind disorders and on current knowledge about brain and mind is likely to:

- Improve public awareness of access to treatment, prevention and support programs for sufferers.
- Reduce the stigma of brain and mind disorders thereby improving the likelihood of individuals and families seeking help.
- Enhance community support for neuroscience.  
This can take many forms such as encouraging private, philanthropic, corporate and public funding for research, as well as improving individual and family participation in research projects
- Engaging the wider community in the ongoing debate on directions of neuroscience and on the ethical issues that it raises.
- Inform students of exciting career prospects in neuroscience.

## APPENDIX 6

### Summary of Submissions Received

Submissions were sought from over 150 individuals, organisations and companies. The following formal responses were received:

CONTACT	ADDRESS
<b>RESEARCHERS</b>	
Anderson, Warwick	Medicine, Monash Uni
Andrews, Gavin	Psychiatry, UNSW
Badcock, David	Psychology, UWA
Barry, Peter	Medical Sciences, UNSW
Bartlett, Perry	UQ
Brain Centre	Monash Uni
Calford, Mike	Biomedical Sciences, Newcastle Uni
Catts, Stan	UNSW
Christie Mac	Medicine, Sydney Uni
Colheart, Max	Cognitive Science, Macquarie Uni
Copolov, David	Mental Health Res. Inst.
Furness, John	Melbourne Uni
Gage, Peter	JCSMR, ANU
Gandevia, S	UNSW
Grainger, David	Eli Lilly
Halliday, Glenda	Prince of Wales Med Res Inst.
Hart, William	NSV
Harvey, Alan	UWA
Hay, David	Psychology, Curtin Uni
Horne, Malcolm	Neurology Monash Medical C.
Kulkarni, Jayashri	Alfred Psychiatry Rese. Centre
Kyrios, M	Psychology, Melbourne Uni
Levy, Florence	Psychiatry, UNSW
Martin, Nick	QIMR
Martins, Ralph	UWA
McLachlan, Elspeth	UNSW
Mitchell, Phil	UNSW
O'Boyle, M	Melbourne Uni
Parker, Gordon	Black Dog Inst., UNSW
Pettigrew, Jack	VTHRC, UQ
Sah, Pankaj	Neuroscience, JCSMR, ANU
Stanley, Fiona	UWA
Tourette Association	
Wildenauer, Dieter	UWA
<b>COMPANIES</b>	
Bristol Myers Squibb	VIC
Eli Lilly	NSW
<b>SOCIETIES</b>	
Aust. Neuroscience Soc.	
Psychology Foundation of Australia	

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