Australian Academy of Science

RECOMMENDATIONS FROM THE

2013 THEO MURPHY HIGH FLYERS THINK TANK

Inspiring smarter brain research in Australia

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GPO Box 783, Canberra, ACT 2601

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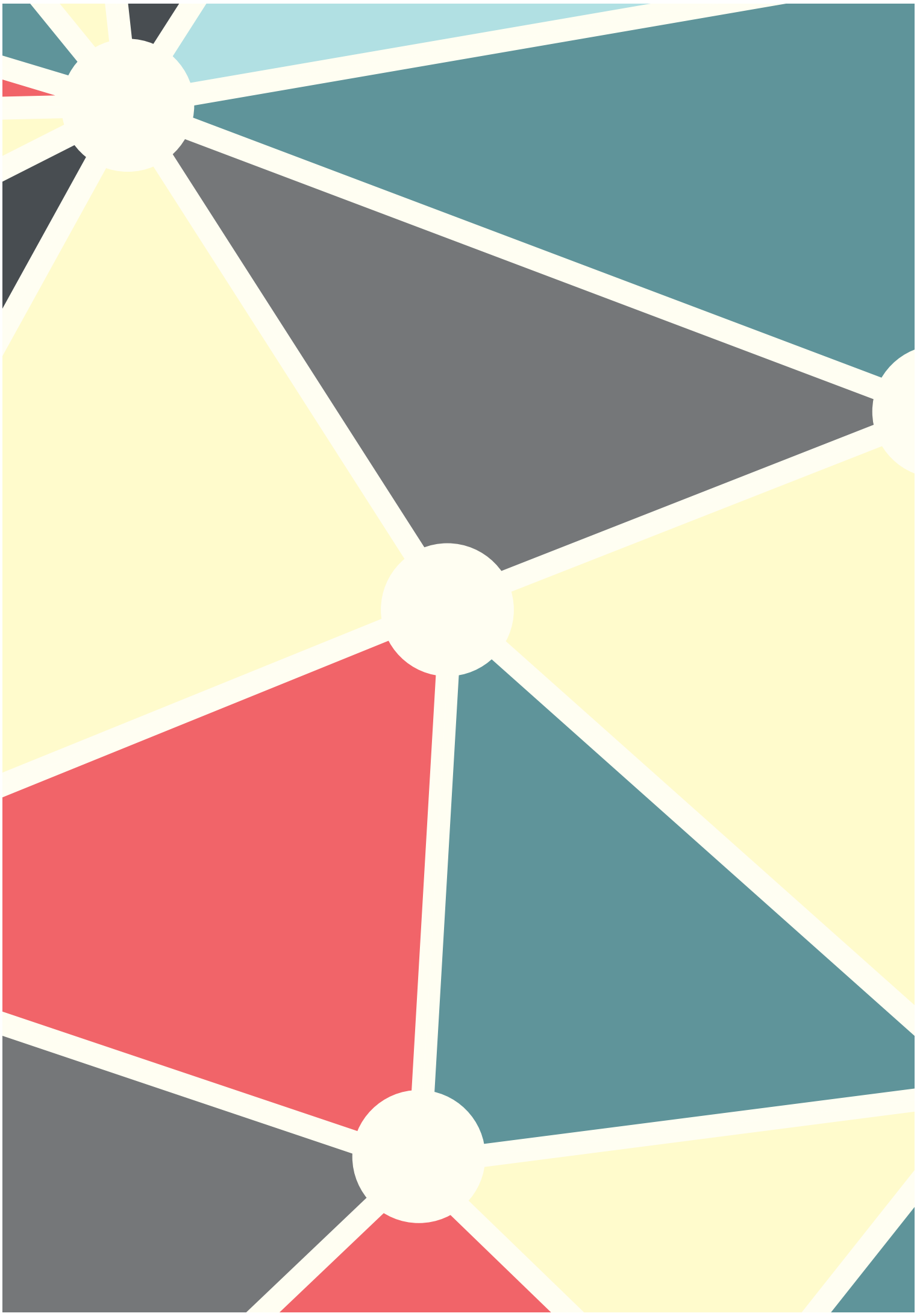


EXECUTIVE SUMMARY

Large, difficult, interdisciplinary projects are the ones that are most likely to make a major difference to society. They have the potential to affect many areas of human existence. During the past 50 years, the two most obvious examples are human flights into space and the human genome project. A research program that is constructed to answer a problem as large as these will be by definition expensive, collaborative and international in scope. But the rewards are great – the human genome project has revolutionised much of medicine, and created thousands of new skilled jobs. The US recently estimated that every dollar that was put into the human genome project generated more than one hundred dollars in outcomes.

Understanding the human brain is exactly this kind of project. One purpose of the 2013 Think Tank was to determine whether we in Australia have the scientists, the resources and the will to participate in the growing international commitment to major brain research projects over the coming decade. In April 2013 President Obama announced that the United States was launching the federal one billion dollar Brain Research through Advancing Innovative Neurotechnologies (BRAIN) initiative, an ambitious 10-year long research project designed to revolutionise our understanding of the human brain, which will be complemented by many, smaller American brain research projects. The European Union launched its 'Flagship' Human Brain Project through its Seventh Framework Programme, allocating more than one billion euros (€, approximately A$1.5 billion) to a 10-year initiative that aims to coordinate European efforts to simulate and understand functions of the human brain through the use of supercomputers (see Appendix A for more details on these two initiatives). There are slightly smaller, but equally ambitious, initiatives in China and Norway. In addition to the scientific excitement that these massive international research initiatives have generated, there is also the 'elephant in the room' question for us: is there a real risk that Australia will be left behind (as happened for the human genome project), while the rest of the world takes advantage of the commercial, medical, social and electronic advances that will be based on brain research?

What are the key areas that will facilitate and be represented in future research, and do we or can we have relevant strengths in these areas? Can we predict where the problems will lie, so we can focus on these places in our own research efforts? Can our researchers, who are traditionally 'silo-based' (working in groups isolated from each other and often competing), find ways to pool efforts and work in a mutually beneficial and collaborative research program in this area when they so rarely do so in other areas? Are we prepared as a nation to invest, when we see the massive investments from the United States and Europe, and with China waiting in the wings? These are the issues that were discussed by 60 of Australia's brightest young scientists at the Theo Murphy High Flyers Think Tank in Melbourne in July 2013.

The Think Tank had strong representation from researchers in basic neuroscience and in neurology, neuropathology, genetics and cognitive science, which to some extent reflects research areas that are traditionally strong in Australia. Fewer attendees had experience in translating basic science into outcomes, whether in technology, medicine, or public health and ethics. Think Tank participants joined one of four groups, each focusing on a particular aspect of brain research (their four reports follow this summary). The groups were asked to identify the major research problems that face neuroscience, discuss Australia's strengths and weaknesses in each, and offer suggestions on how we can make a realistic yet ambitious contribution to the international effort to understand the structure and function of the human brain.

Brain research is unusual in that it operates at several levels, from the molecular and cellular levels through to the study of consciousness, intelligence and executive function. The human genome project has identified all human genes, but the functions of many (especially those expressed only in the brain, perhaps half of the total number of genes) are still obscure. However, single neurons can now be analysed for gene expression patterns, and the connections made by groups of neurons can be studied using high definition structural and functional magnetic resonance imaging (MRI). The rate of advance in molecular genomics and imaging is such that we can anticipate that accurate data on the human brain's single cell structure, gene expression and alteration, and connectedness will be available to all within the coming decade.

All of the groups agreed that the study of the brain was becoming an international focus of great importance. All groups felt that Australia was very strong scientifically in many areas, by virtue of our healthcare system and our universities and medical research institutes, although teams are often separate from one other and do not integrate and collaborate. All concluded that Australia must identify some areas where we can make a

high-level, and hopefully unique, contribution if we want to remain a collaborative international player. Four areas were noted as particularly important:

1. The understanding of higher cognitive function and intelligence (and ultimately consciousness itself), and their relationships with the fine and gross structure of the brain, both in adults and in the complex processes that occur during development.
2. The need to develop computer software and hardware sufficiently powerful to model brain function. The creation of a 'bionic brain' might require new algorithms and paradigms because the complexities might involve working in several new dimensions, and perhaps with a number of more simple animal models. This will need to be done in concert with high-level technicians, bioinformaticians and computer scientists trained specifically to work on the brain.
3. The need to ensure that there is a seamless interface between clinical provision and research investigation, so that we can advance medical research with every patient, and so that all clinical tests and measurements (including imaging) are available to researchers. This interface will allow the translation of research endeavour into improved outcomes for patients and society.
4. A strengthening of our resources in ethics, public health, and health services research. Ethics committees should see their role as being facilitators of research. Health services research, and the concepts of ageing and end-of-life decisions, should be included in all key discussions on cost-effectiveness of treatments and on the level of resources allocated to elderly patients who might suffer from neurodegenerative diseases such as Alzheimer's.

In Australia, our most notable weaknesses compared with Europe or the United States are the extent to which our researchers are divided into many siloed teams that compete against each other for scarce resources rather than collaborate; and the absence of long-term funding that prevents scientists from undertaking the 'hard projects' and diminishes the confidence of early career researchers in building enduring scientific careers. In spite of our clinical strengths (in terms of well-trained doctors, nurses, paramedics, psychologists and rehabilitation therapists), we have a hospital system that often looks down on, or even refuses to facilitate, research. While we are strong in IT and programming, we do not have a fully competitive computer industry. However, we also have advantages. We have a very egalitarian healthcare system; most people in Australia with a serious neurological disorder will have ready access to tertiary care at a high standard, including contemporary diagnostic imaging and gene tests. We have an excellent university system, based for the most part on domestic students, with great strengths in neuroscience, particularly clinical neurology and neuropathology, developmental biology and imaging. Finally, we have a population and politicians who believe in and support medical research, and are willing to participate in research if given the opportunity.

THE BENEFITS

An Australian brain research program with domestic and international collaborations would have far-reaching benefits for both current and future generations.

1. This large proposed initiative aims to understand the relationship between the molecular and cellular events that occur in the brain and higher processes such as thinking and reasoning. There will be immediate positive outcomes in medicine, where clinicians will be able to understand more about mental illness, ageing (Alzheimer's and Parkinson's diseases in particular) and intellectual handicap.
2. The findings of this research program will also tell us much about normal brain function. One area of high importance will be the study of changes induced in the brain by different environments; there is already a US study determining whether social and environmental factors can induce epigenetic changes in children.
3. Investment in brain research will benefit the education sector (schools and universities) via new educational principles and teaching materials that will increase student achievement.
4. There will almost certainly be significant industrial and defence outcomes, such as new services born from improved connectivity and treatments for post-traumatic stress disorder. Genuine innovation will be born from understanding the way the brain assimilates and interprets subtle signals and differentiates them from noise. The development of new products such as diagnostic tools, pharmaceuticals and other therapeutics and software or mobile computing applications will also be accelerated.
5. Australian innovation and productivity growth will depend in large part upon the availability of competitive skills and creative intellectual capital. Participation in a global brain program will most benefit the service sector, which in Australia comprises over 65% of our GDP.

6. We will be better able to retain excellent scientists and doctors in Australia, and attract a new intake of highly skilled researchers to work here, based on the excellence of our research. Without a competitive research environment, the best of our own doctors and scientists will leave for other countries where there are more and better opportunities.
7. We will be able to integrate our excellence in computing, neuroscience, pathology, translational medicine, psychology and ethics, a unity that will bring benefits to other fields. We will be able to operate (more easily than most countries) in an efficient yet ethical research environment.

RECOMMENDATIONS

Those who attended the meeting are strongly of the opinion that Australia needs to make a strategic investment in brain research now, to enable us as a nation to share the benefits of this booming global endeavour. Strategic investment will not only afford the preservation of excellence of our current biomedical research strengths, but allow us to share the health, defence and commercial benefits that will result from the US$5 billion global venture over the next decade.

Wherever possible, Australia's contribution should be in an area where we have advantages because of the strength of our existing research, or from other national structures such as our health system. We recognise that we represent groups with a vested interest in increasing the national investment in brain research, and therefore we propose that the Australian national brain initiative ('AusBrain') be coordinated by a national consortium committee that includes federal and state governments, patient support groups, information technology, the Defence Science and Technology Organisation, NICTA, the Australian Nuclear Science and Technology Organisation and CSIRO, the health and hospital systems and industry, as well as representatives of the universities and medical research institutes.

Because of the 10-year perspective for major programs of research into the brain, the discussions did not only focus on the obvious, immediate clinical targets such as Alzheimer's disease. Over the longer time scale appropriate for this research, it is likely that areas of concern such as post-traumatic stress disorder, autism, and the interaction between genes and environment in mental illness will begin to be elucidated. The real benefits from a major commitment to brain research will be most likely to come in these areas that are presently very poorly understood. Commercial and entrepreneurial opportunities that arise might be in fields that hardly exist at present, such as epigenetics and brain/machine interfacing.

Many practical ideas were put forward. Some were simple and inexpensive ideas, such as facilitating a series of workshops that allow people from various discipline backgrounds to meet, exchange ideas and begin collaborations. The need to train scientists with experience in two disciplines (neuroscience and bioinformatics, for instance) is also a recurrent theme, as is the need to involve patient support groups in determining the research agenda. Equally important is the need to increase the number of clinicians who have experience with basic research to PhD level, and to embed a research culture in clinical training, both for doctors and for allied health professionals such as nurses and psychologists. There is a powerful argument for a national ethics framework, as at present research ethics committees are locally based and often lack a national and international perspective. Several individuals noted that it is important to free scientific research from ethics reviews that inhibit rather than facilitate important research programs, based on fears that have little substance.

'Big ideas' were also put forward and received substantial focus and attention. One group urged a commitment to create a 'bionic brain', while two others suggested large, properly funded teams with 10-year support to work on difficult, interdisciplinary projects. One such project would involve the careful study of simple animal models (such as the bee, fly or worm brain) as proof-of-concept model systems for the much larger human brain projects. The sorts of sums required for such research are large enough to make a difference and to be a fruitful contribution to global efforts (particularly if they are allocated on merit, but

with an eye to ambitious, visionary research, and are committed for 10 years to a group including early career researchers). We note that the Cooperative Research Centre (CRC) structure is ideal for some aspects of ambitious brain research, as it is by nature transdisciplinary and includes a commitment to both commercial and clinical translation into practice.

Even a total allocation of the order of $250 million over 10 years – perhaps $25 million a year – would be less than 1% of the Commonwealth Government's total commitment to research at present. We see this sum as additional to the welcome commitment that has already been made by the Government to fund dementia research with $200 million over five years. Dementia research is a small component of brain research, and will be subject to different drivers from much of what is outlined below. The meeting felt that it would be important that the new commitment (which would be known as an RFA, or 'request for applications', in the United States) was overarching between several federal and state government departments, and would be seen with pride as 'whole of governments'.

Other recurrent themes were the need to be able to move seamlessly from lab to clinic to community (using, for instance, eHealth as a tool), and the involvement of the community in discussions on the ethics of neuro-research. It was noted that diseases associated with ageing (such as stroke and Parkinson's and Alzheimer's disease) would have a major impact in terms of numbers and funding on the community, but in some cases informative models for study may be found in neurological disorders that occur in children, including rare neurogenetics diseases. The most important point that came from the meeting was the need to ensure that new initiatives bring together people from many distinct disciplines, including neuroscience, computing and clinical research, and are firmly established within an ethical framework that is welcomed by the Australian community.

In the group summaries that follow, there is also an appropriate focus on some of the broader issues facing Australian science: the need to facilitate and value, rather than ignore or prevent international links, the need to ensure that the very best early career researchers are given security of funding, the need to promote collaboration and open access to patient material and raw data, and the value that would accrue from establishing three or four CRCs specifically in these fields.

We will attempt to flesh out this proposal, but we also believe it is for others to have an input as well (including the patient support groups, the Defence Science and Technology Organisation, CSIRO, NICTA [our Information Communications Technology Research Centre of Excellence], the Australian Nuclear Science and Technology Organisation, Australian Research Council (ARC) and National Health and Medical Research Council (NHMRC), the hospital system and the state and federal governments). There must be discussions to ensure that translational research proposals really meet the needs of patients and hospitals, and can integrate with our nascent Australian biotechnology, IT and pharmaceutical industries. This will be one role that requires coordination by an **Implementation Committee**, to progress these recommendations and involve state and federal government officials as well as representatives from the community and the science sector.

We believe that the single most important point is the most general one: if we fail to become involved, at the highest level intellectually and clinically, in the 'brain project', we will opt out of a world research program at the most exciting time in this seminal field. The consequences will include losing some of our best and brightest researchers, and the opportunity to implement aspects of knowledge of the brain that are of great importance for our community, our economy and our citizens with brain disorders.

GROUP A
COGNITION, INTELLIGENCE AND EXECUTIVE FUNCTION

Chairs Professor Max Coltheart, Professor Sarah Dunlop

Rapporteurs Associate Professor Alex Fornito, Dr Deanne Thompson

INTRODUCTION

A unique aspect of the human brain is our ability to think. Higher order functions such as cognition, intelligence and executive function are the keys to this process. These functions are derailed by diseases of the brain, including prevalent and high-burden disorders such as Alzheimer's and Parkinson's diseases, schizophrenia, major depression, stroke and autism, to name a few. These illnesses take an enormous toll on sufferers, carers and the community as a whole, costing Australian society billions of dollars each year. Dementia and schizophrenia, for example, have been estimated to cost Australia more than $6.6 billion and $1.8 billion a year, respectively[1]. Unfortunately, understanding the neural basis of cognition and its disorders has proven extremely difficult because the brain is itself an extraordinarily complex organ. Any attempt to unravel this complexity must be predicated on a detailed understanding of brain function, from molecules to mind.

The multi-scale organisation of the brain poses a major challenge for any attempt at formulating an integrated model. Within the neuron, genes are transcribed to assemble proteins that regulate and drive cellular function. At this level, complex interactions occur between metabolites, proteins and the environment to affect protein function. Neurons connect to other neurons to form highly organised and functionally integrated ensembles which, in turn, link to neuronal populations elsewhere in the brain. This connectivity provides the necessary substrate for precisely coordinated and synchronised dynamics in support of complex behaviour. The interactions unfolding within this connectivity web form the basis for all our thoughts, feelings and behaviour.

Different scales of resolution within the brain are typically researched by different sub-specialties of neuroscience: micro-scale intracellular and intercellular processes are studied by geneticists, cell and molecular biologists; meso-scale structure and dynamics of individual neurons or small neuronal populations are studied by physiologists and anatomists; and macro-scale properties of large-scale brain networks and their resulting phenotypic manifestations are the subject of psychology, social and clinical sciences. Physicists, engineers and mathematicians have the expertise to uncover the principles that link these disparate findings, while information technologists enable data and knowledge to be shared. Thus, these disciplines provide conceptual glue to integrate fields of enquiry that are often separate. Unfortunately, the brain has not traditionally been a subject of investigation for these scientists. As a result, great insight has been gained within each domain independently, but we have little understanding of how to link findings across different analytic scales.

This gap has practical implications. All pharmacological treatments operate at the micro-scale by modulating the levels of specific chemicals in the body. The symptoms of many brain disorders are however, typically only observable at the macro-scale. Thus, to select an optimum treatment, a clinician must infer the micro-scale causes of observable macro-scale behaviour. Accurate inference in such circumstances requires an understanding of how the observed symptoms relate to the behaviour of large-scale neural systems (macro-scale), of the underlying functional or anatomical disturbances (meso-scale), and of the originating molecular processes (micro-scale). In other words, effective clinical decision making critically depends on one's ability to seamlessly move across scales, from mind to molecule and back again.

The current gap in knowledge is akin to the much discussed lack of a unifying theory in physics that integrates the science of the small (i.e. quantum mechanics) with that of the large (i.e. relativity). Physicists have initiated large-scale endeavours, such as the Large Hadron Collider at the European Organization for Nuclear Research (CERN), to begin to address these gaps. A similar initiative is now required for neuroscience, one that attempts to discern the principles governing the relations between microscopic changes in cellular properties and observable behaviour in large-scale organisms. Just as revolutions in our understanding of electromagnetism and thermodynamics in the 19th century laid the foundations for unprecedented technological innovation in the 20th century, uncovering the principles of multi-scale organisation in the human

1 Read, L, Mendelsohn, F et al. (2003) *Brain and mind disorders: impact of the neurosciences*. Australian Government, Canberra.

brain will revolutionise the diagnosis and treatment of brain disorders in years to come.

How can resources best be allocated to support such an aim? We propose the ***Australian initiative for healthy brains***.

RECOMMENDATIONS

THE INITIATIVE

This initiative will establish five distinct transdisciplinary research centres across the country, devoted specifically to understanding how different resolution scales in the brain are integrated. Particular themes can be determined through an open, peer-reviewed competitive process. We use the term 'transdisciplinary' rather than the more frequently used term 'interdisciplinary' to emphasise that these research centres will need to translate methods, models, and understandings across disciplines and scales of analysis, rather than simply continuing to conduct research within the boundaries of any one discipline. Each centre will focus on a distinct theme which could include (but is not limited to) topics such as development, degeneration, and developing whole-brain computational models. The theme will not be determined *a priori*. Rather, it will be open to competitive applications from transdisciplinary teams of researchers and only the best proposals will be funded. This competitive process will stimulate creativity and innovation, promote collaboration between high calibre researchers and ensure that resources are allocated to the best projects. Furthermore, there will be a two-year lead-in time to encourage the development of proposals of the highest quality.

There are three critical requirements for each proposal. First, each centre must comprise a team with at least one researcher working at each of the specified levels of analysis – micro-scale, meso-scale and macro-scale – and must have both a modelling core, which engages researchers working with the physical and mathematical scientists to develop models that link the different analysis scales, and information technology and bioinformatics expertise to ensure overarching data sharing within and between centres, as well as with the general public. Second, funds can only be used to support projects specifically integrating measurements or models across different spatial or temporal scales in the brain. Finally, all data acquired in each centre must be made publicly available in a user-friendly and accessible format to further enhance international collaboration and the pace of discovery.

FUNDING MODEL

Each centre will be funded with $5 million a year over 10 years. Funding will be distributed across salaries, new transdisciplinary projects and public databasing. There will be no restrictions on applying for other grants for the duration of the initiative, allowing scientists to maintain other related or disparate research projects alongside the initiative.

CAREER DEVELOPMENT AND TRAINING

A proportion of funding will be allocated for fellowships providing vital personnel with career stability for the duration of the initiative. Mentoring and training for transdisciplinary research at all career levels (including professorial) will be built into the model. As part of the proposal, applicants will need to demonstrate that they will provide training opportunities such as internships to high-achieving undergraduate, masters and PhD students in order to attract and retain the brightest young researchers in Australia. National and international exchange programs will be encouraged in order to foster learning through collaboration. Furthermore, there will be an emphasis on flexible career training that includes industry engagement and external training programs for various health and education sectors, to ensure translation.

GOVERNANCE

Critical to ensuring the success of the initiative will be communication within and across centres. Thus, regular meetings across centres will be established via web or teleconferencing in addition to twice-yearly symposiums within each centre and an annual symposium across centres. Centre directors will also meet regularly. There will be regular scientific review both internally and via an international advisory board. There will also be a three-year external review of funding for accountability.

OUTCOMES

The *Australian initiative for healthy brains* will ensure Australia's international prominence in brain science and innovative technology, alongside other current large international initiatives. The initiative will result in direct health, economic and social benefits including new treatments and behavioural interventions, shaping policy, improved public resources and commercial benefits, efficiency gains through enhanced productivity, improved quality of life and social inclusion. Furthermore, curing and preventing brain and mind disorders is estimated to save the

nation billions of dollars, and therefore funding directed toward such research will ultimately pay for itself[2]. A priority of the initiative will be to ensure data and knowledge sharing in the form of open scientific databases, community engagement, web-based knowledge (new media), and engagement with advocacy groups. This initiative will encourage transdisciplinary co-authorship and grants, and the development of new biomedical and information technologies, leading to high impact transdisciplinary science which is largely lacking in current Australian brain research.

2 Read, L, Mendelsohn, F et al. (2003) *Brain and mind disorders: impact of the neurosciences*. Australian Government, Canberra.

GROUP B
NEUROGENETICS: INHERITED DISEASES AND DEVELOPMENTAL BIOLOGY

Chairs Professor Kathryn North, Professor Trevor Kilpatrick

Rapporteurs Dr Guy Barry, Dr Rony Duncan

INTRODUCTION

Our group focused on the fields of neurogenetics and neurodevelopment, with a particular focus on the challenges associated with analysis of complex human diseases that have a major impact on development, growth and maintenance of the human brain.

The field of neurogenetics has contributed significant advancements to our understanding of the human brain. We now have a far greater understanding of the complexity of genetic diseases traditionally thought to be caused simply by a small number of genes. Genetic approaches which have in the past been highly successful in identifying genes for rare disorders inherited in Mendelian fashion (following predictable inheritance patterns through families) have proven unreliable in most cases of brain disease. This has caused researchers to rethink traditional approaches for discovering the genetic basis of disease. It has led to an era of extremely large collaborative studies that aim to use hundreds of thousands of cases and controls to detect the many hundreds of genes that have a small effect on increasing disease risk. Neurogeneticists have also struggled with issues of heterogeneity; individuals who receive identical diagnoses often share very little, both in terms of symptoms and genetic profile. This has been a major impediment to successful gene discovery both in Australia and internationally, and has opened up a new era of research – the quest to identify clinical sub-types or 'endophenotypes' that might represent a more pure form of disease where the genetic contributors are more tractable.

Australia has an opportunity to make a significant contribution to this field internationally through data linkage across clinical and research settings. In designing and managing the infrastructure needed for data sharing across the country, we would break down traditional diagnostic categories for many complex traits using clinical sub-types or endophenotypes. This would occur through obtaining sample sizes that are powerful enough statistically to successfully uncover underlying disease-causing genes and pathways, and rigorously test hypotheses. Many of these smaller cohorts already exist within Australia but are statistically weak individually. Due to our depth and breadth of clinical expertise, Australia has the potential to explore neurogenetics using endophenotypes, which would be difficult, if not impossible, in countries with a less well supported health system.

Understanding how the brain develops to create a normal healthy adult brain is critically important. Only then can we understand the consequences of abnormal neurodevelopment and determine prevention and intervention strategies to treat brain disorders such as autism, epilepsy, mental retardation, multiple sclerosis, motor neurone disease, schizophrenia and bipolar disorder, which typically result in lifelong disability and dependency on the healthcare system. Due to ineffective treatment regimes, these neurodevelopmental disorders are currently an important focus for research, as improved treatments and outcomes are likely to lead to more productive lives, not only for patients but also for their carers.

With our expertise in clinical phenotyping, databases and data collection, neurogenetics and neurodevelopment and multi-disciplinary capability, Australia holds a unique place internationally. We propose to integrate these strengths into a cohesive entity to rapidly and collectively answer questions integral to growing and maintaining a healthy brain and consequently a healthy population, notwithstanding the challenges of disease, disability and ageing.

RECOMMENDATIONS

Three key concepts underpin all four of the recommendations outlined below. Firstly, the concept of an '**institute without walls**'. The recommendations rely on broad, national collaboration with a national funding mechanism, national standards and national leadership to inspire a culture of teamwork, partnership and alliance across Australia in the field of brain research. Secondly, the concept of '**systems biology**'. This fundamentally relies on a holistic approach to research, in which complex interactions within and between systems are interrogated and integrated. Finally, the concept of '**big theory**', where as much emphasis is placed on the development of ideas as on the generation of data. That is, a focus not just on what

the brain looks like and does but how and why it develops this way.

BIG DATA

Australia is internationally recognised for its large, cohort-based, longitudinal data collection in research. However, one of the consequences of using the latest technologies for genetic analysis is the vast quantities of data produced from genome sequencing. Genome sequencing generates 10 to 200 GB of data for each sample, requiring significant computing infrastructure and support for effective storage and analysis. Furthermore, these experiments are expensive and performed on preciously small and limited amounts of clinical samples. A national collaboration to enable data sharing between researchers would allow individual researchers to interrogate existing data rather than conduct repetitive and costly experiments for each new project. For example, a national resource of genome sequences from a collection of control (unaffected) subjects could be used across multiple studies.

Big data also has other advantages, such as enabling researchers to answer multiple questions not evident at the time of initial data collection; facilitating identification of the causes of rare disorders (only evident when similar cases are found) and drilling down on subtle but significant endophenotypic differences between patients, allowing narrow segmentation of diseases to better define therapeutic targets. Within the healthcare system, big data facilitates personalised medicine. Data can be used to track therapeutic interventions and lead to pre-emptive minimisation of side effects. Critically, it may help reduce the number of unsolved paediatric cases. In the USA alone, use of big data resources is expected to lead to savings in the healthcare system of US$300–450 billion annually[1].

To facilitate the use of big data, we propose:

- undertaking a national review of neurogenetics data science to estimate growth rates in the generation of big data
- achieving consensus on what neurogenetics data need to be captured and how they should be stored and shared, e.g. generating requirements for the functionality and essential features of a purpose-built scale-out network-attached-storage system
- establishing a national repository to store this big data, such as setting up a cloud-computing platform that can safely store vast amounts of genomic and clinical data together with dedicated computing staff to assist users and curate the data.

EMBRACING eHEALTH NATIONALLY

Australia has the potential to lead the world in the gathering, storing and ethical dissemination of clinical (patient) data. This would enhance patient care and provide opportunities for integrating clinical data across systems in order to make new discoveries about individuals and the population as a whole. Major improvements are possible that would cement our national system as a world leader. These include:

- committing to eHealth across Australia (one individual health record and unique number for each patient to replace the fragmented system currently in place). This system could allow for the possibility of limited access by specific individuals (for example, mental health data might only be accessible by mental health professionals). Individuals should also be able to access a version of this information for their own records
- drawing together research and clinical data to create a cultural shift that will enable data integration and access for clinical purposes and research purposes. The Western Australia data linkage program represents a wonderful example of this (**www.datalinkage-wa.org**). With the creation of a single system for both clinical and research purposes, we anticipate an improvement in the quality of patient history reporting and a reduction in costs and errors associated with the duplication of clinical information for research purposes
- exploiting our already excellent healthcare system to update current methods of sample collection, documentation and bio-banking through the incorporation of a simple-to-use nationally interconnected system with national standards for data definitions, collection, storage, access and deletion.
- integrating health information across disciplines such as imaging, genomics and mental health to enhance holistic, integrated care.

ENHANCING THE SYSTEMS THAT SUPPORT COLLABORATION AND ANALYSIS

Although Australia has world-class bioinformaticians, the need for collection, storage and creative analysis of data has already far surpassed the existing labour force. Outsourcing data analysis to computer companies, such as Systems Biology Institute Australia, has merits

1 Kayyali, B, Knott, D and Van Kuiken, S (April 2013) *The big-data revolution in US health care: accelerating value and innovation*. McKinsey Global Institute, www.mckinsey.com/insights/health_systems_and_services/the_big-data_revolution_in_us_health_care

but is only a bandaid solution unless expanded. Therefore we recommend:

- initiatives to train bioinformaticians from multiple backgrounds, such as computer science, mathematics and biology, so that Australia can compete worldwide in this critical and underappreciated field
- long-term strategies to fund bioinformatics research services
- that individuals with bioinformatics expertise be included early on in discussions about the integration of existing data (such as those involved in the cloud-computing infrastructure discussed above).

A range of additional strategies will also enhance translation of data into molecular and therapeutic advances:

- **intellectual property protection and biotechnology spin-off companies**. This requires legal (e.g. patent lawyers) and business consultants (e.g. venture capitalists) to initially advise on the suitability of each individual patent application and business venture
- **consortiums/Cooperative Research Centres/ Linkage projects** that bring together industry and clinical and basic science – specifically tailored to bring multidisciplinary groups together over long periods of time and including patient involvement
- a **national registry of researchers, clinicians and patient advocacy groups** with expertise and interest in the components of translational brain research to help 'matchmake' interested parties and collaboration across fields
- **national research priorities** guiding the training of our graduates. Attractive scholarships are required for interdisciplinary training, where PhD students are expected to perform a subset of their training in a different discipline while still retaining relevance to their core project.

A PROACTIVE ETHICAL APPROACH

Electronic data sharing, research and personalised medicine all have inherent ethical risks. In particular, access, storage and dissemination of genetic information are hotly debated topics. To store and share such data (and thus realise the benefits), proactive ethical leadership is required. Key stakeholders should include patients and their families, patient advocacy groups, clinicians, research scientists, politicians, ethicists, Australian biotechnology companies, insurance companies, Indigenous representation and clinical service providers. In addition to this, we propose:

- direct public engagement and public benefit. These are vital to ensure the investment and support required to establish and maintain the database
- an opt-out system for individuals in which, unless they opt out, their de-identified information will be accessible for research purposes
- a single, national ethics committee solely responsible for reviewing and approving research access to the national database.

GROUP C

ARTIFICIAL INTELLIGENCE, MATHS AND MODELLING

Chairs Professor Steve Furber, Professor Stan Skafidas

Rapporteurs Associate Professor Andreas Fouras, Dr Elizabeth Holliday

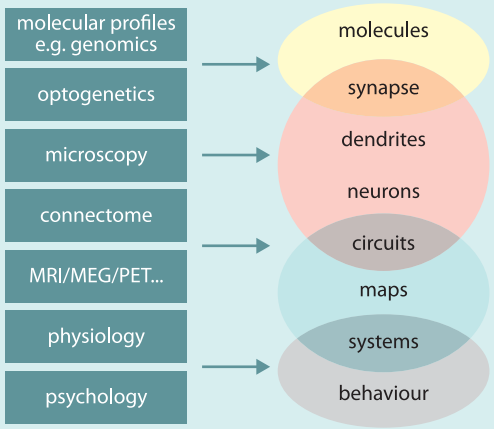
INTRODUCTION

Understanding how the human brain works is one of the most important and challenging endeavours of modern science. The brain is the most critical organ of the body, and yet we still do not know how the brain generates thoughts that guide intelligent decision-making and truly autonomous behaviour. The consequences of malfunction of the thought process are obvious to us and disastrous for the sufferer. Mental illnesses such as depression and schizophrenia, neurodegenerative disorders such as Alzheimer's disease, and developmental disorders such as autism are all recognised as malfunctions in how the brain creates rational thought. Progress in curing these very complex disorders is limited by the fact that we still do not have a detailed working model of how the neural circuits of the healthy brain generate thoughts. Understanding the brain is truly a grand scientific challenge. The human brain demonstrates profound complexity, with our highest-level cognitive abilities dependent on extensive biochemical networks spanning multiple anatomical brain regions and scales of function. Systematically mapping such complexity requires an unprecedented scientific effort.

To address this grand challenge, two ambitious international projects have recently been launched in the USA and Europe (see Appendix A). These two projects involve an enormous and unprecedented commitment to measuring and mapping the human brain. They will generate massive new datasets and resources, which we can expect to be open access. The opportunities for new knowledge are vast, and will likely lead to technological advancements across a range of fields. For Australia the question is: how can we best respond to this new era of 'big neuroscience'?

RECOMMENDATIONS

We argue that the Australian neuroscience community should not focus on an attempt to model and map the entire human brain, but on mobilising Australia's existing significant and unique neuroscience expertise around the new emerging neuroscience resources to comprehend, simulate and abstract the biological basis of thought.



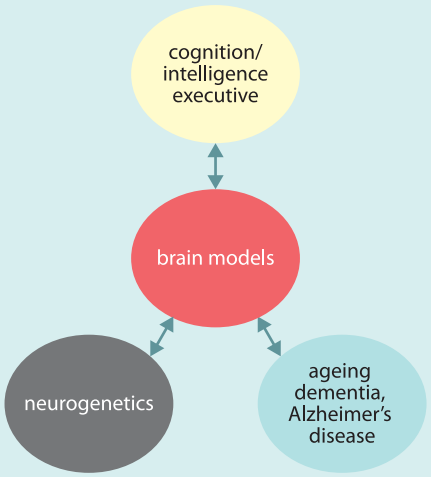
The multiple scales of structure and function of the brain. The US and European brain projects propose compiling data from diverse disciplines to model the brain at many different biological scales.

The program will fuse fundamental neuroscience with novel computational platforms, cellular-based substrates, mathematical modelling and computer simulation to develop models of human thought. It will analyse simple animal systems for the basic circuit principles of autonomous decision-making, and iteratively abstract and simulate the thought process to inform both models of brain function and machine intelligence. This research would be highly interdisciplinary, bringing together scientists from anatomical and functional neuroscience, neuroinformatics, neuroimaging, molecular genetics, computer science, mathematics/statistics and psychology. The program will have two key objectives:

- gain a detailed understanding of the process of thought in a biological brain
- translate this understanding into computing, to create a machine that can truly think. We will develop a bio-inspired artificial intelligence built around the principles of biological brain function: a **bionic brain**.

These two objectives are interwoven. Analysing how intelligent thought and rational decisions emerge from biological circuits will inspire new approaches to machine intelligence. As the bionic brain develops it will also provide a platform with which to test hypotheses about biological brain function and the basis of mental illness.

If we really want to understand what is happening in the brain and solve problems of brain dysfunction,



Brain-based models of thought have the capacity to act as a unifying force in neuroscience, bringing together data, knowledge and skills from all other areas. In return, the bionic brain provides incredibly powerful tools that promise to accelerate progress in all of these fields.

we have to be able to understand the biological mechanisms underpinning thought to the level at which we can replicate it.

If we could understand and simulate even a simple brain, the contributions to machine intelligence and the progress towards understanding the human brain would be enormous. Even simple animals like ants or bees are more behaviourally autonomous, robust, fail-safe and efficient than any machine we can currently build on a similar scale. We propose that rapid progress could be made by an initial focus on understanding and simulating the operation of simple animals with small brains. An exciting outcome will be a machine that will be more autonomous, more creative and more fail-safe than any machine built before.

Just as the human genome project saw the creation of new disciplines, new discovery, new medicine and new intellectual property, so the brain projects will similarly transform neuroscience. Australia cannot afford the cost of opting out of this global initiative. The Australian neuroscience program would leverage the programs in Europe and the US to rapidly create a unique Australian product: a thinking machine. This research has high value for Australia with applications in every part of our society and every sector of our economy. In the same way that programmable machines (computers) transformed our lives in the 20th century, our lives in the 21st century will be transformed by machines that are beyond programmable, and are truly intelligent, directable and reasonable.

EXECUTION

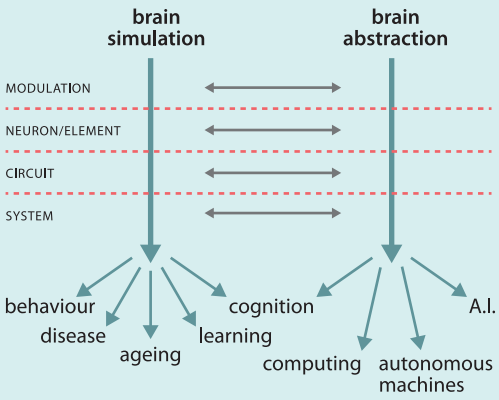
This project cannot be realised without a dedicated injection of funds. In terms of funding, 'business as usual' for the Australian neuroscience community will not do. Within our community there is great concern about the widening gap between the funding scopes of the NHMRC and ARC. Many of the scientists working towards a greater understanding of the brain and thought have a background in the physical sciences (e.g. computer science, mathematics or engineering). While their work provides the underpinnings for subsequent medical breakthroughs, it lacks the immediate translational application increasingly desired by the NHMRC. Conversely, neuroscience projects are often viewed by the ARC as yielding human health outcomes, and therefore not appropriate for this funding agency.

As argued by proponents of the European brain project, a focused and integrated effort is required to ensure meaningful progress. The fragmented efforts of individual research groups will not produce important advances in either knowledge or technology. But a coherent drive from our community, enabled by a significant boost in dedicated funding, will see Australian neuroscience lead the world and provide enormous economic, healthcare and societal returns.

We estimate that the total cost of creating a **bionic brain** would be approximately $200 million, distributed over 10 years. Dedicated and stable funding is crucial in order to achieve real, tangible outcomes. Funding would be provided in the context of a concerted national program aimed at enabling big neuroscience. Core funding would allow the program to sustain a critical mass of personnel and activity.

Funding will be required across four domains:

- **People**. Funding for scientists across all career stages will be necessary and could be provided as 3- to 5-year scholarships or fellowships. Fellowships would be awarded to junior, mid-career and senior scientists who demonstrate their intention to conduct interdisciplinary research, describing a team with representation from multiple specialist fields. This would help to ensure forward thinking and creative approaches to problem solving and achieving research outcomes. Projects must align with the program's two core goals, and synergies to other projects in the program must be explicit. In awarding scholarships to graduate students, we suggest these students be required to undertake multidisciplinary training, gaining expertise in at least two complementary fields (e.g. biostatistics and computer science). The supervisory team should also reflect the multidisciplinary nature of their proposed research project.



Understanding thought by both simulating the brain and abstracting brain function. The program will develop a bionic brain capable of simulating brain function at various key levels of complexity. This will become a tool for testing new hypotheses about brain function and disorder. In parallel new findings of brain function will be abstracted to computational systems to further machine learning and the development of a thinking machine.

- **Project**. Adequate project funding will ensure the availability of tools and reagents for research, including computational, electronic and biological resources. As specified for people funding, applications for project funding should be required to demonstrate a multidisciplinary research proposal, involving the application of techniques from multiple and distinct scientific fields.
- **Infrastructure**. Dedicated infrastructure funding will be necessary to support a fundamental shift from silo-based research to multidisciplinary research. Research teams will need to acquire a range of specialised instruments and tools to support novel research applications.
- **Coherence**. We envisage a massively transdisciplinary project. Funding will be needed for mechanisms to support meaningful collaboration, unify project efforts and ensure delivery of outcomes.

ECONOMIC AND CLINICAL BENEFITS

Nearly one half of all Australians will suffer a disorder of brain or mind during their life and the financial costs are enormous, with conservative estimates exceeding $20 billion annually[1]. There are also substantial, albeit less tangible, effects upon families and society.

Research that delivers new solutions to mental illness will provide substantial health and societal benefits. Delivery of a bionic brain supporting an intelligent machine would transform existing industry and create new technologies:

- Analysis of the thought processes of biological brains will provide increased understanding of normal behaviours, attention and volition and inspire new treatment strategies for cognitive disorders by grounding treatment of brain dysfunction in a thorough understanding of healthy cognitive function.
- A bionic brain built on biological principles will be a unique computer asset. Unlike conventional computers the bionic brain will have a capacity for thought and independent intelligent decision-making. The potential applications of such a device cannot be overstated. The first true programmable computer (created in the 1950s) was viewed as a research tool and little more, but the capacity of programmable computers generated their own industries and transformed every aspect of life, science and innovation in the 20th century. Imagine the capacity of a machine that transcended programmable, and could instead actively contribute to thinking through the solution to a problem.
- The development of a thinking machine built on biological principles would transform our comprehension of decision-making and rationality. It would provide a modifiable platform that could be used to explore the thought process. Behavioural disorders such as psychosis, addiction and anxiety could be simulated within a bionic brain. This would then yield a computational platform with which to understand pathologies and test new therapies. This would allow the development and initial testing of treatments more rapidly than possible in the clinic.

We propose galvanising Australian neuroscience toward the goal of comprehending thought and creating the first bionic brain. Richard Feynman famously said 'What I cannot create, I do not understand'. We propose understanding thought by creating a machine that can think.

1 Australian Bureau of Statistics (March 2009) *Mental health*. ABS report 4102.0 – Australian Social Trends. www.ausstats.abs.gov.au/ausstats/subscriber.nsf/LookupAttach/4102.0Publication25.03.094/$File/41020_Mentalhealth.pdf

GROUP D
AGEING, DEMENTIA, ALZHEIMER'S DISEASE AND END-OF-LIFE ISSUES

Chairs Professor Colin Masters,
Professor Julian Savulescu

Rapporteurs Associate Professor Elizabeth Coulson,
Dr David Nisbet

INTRODUCTION

As Australia celebrates having one of the world's best life expectancies, dementia, including Alzheimer's disease, is emerging as a major challenge for our healthcare system. Dementia is the third leading cause of death in Australia, and there is no effective treatment. By 2050 Australia is expected to have more than one million people living with dementia, costing 3.3% of GDP[1].

In order to address the burden of disease and dysfunction caused by mental health issues and neurodegeneration, there are a number of challenges: we need to understand the problem, and that includes understanding what changes occur in the brain during normal ageing and how these are different to neurodegenerative conditions. We need to understand what it means to age well, and whether it is possible to turn ageing off. We need to understand the fundamental processes that keep a brain healthy or result in neurodegeneration and then find ways to interfere with those processes. In addition, we also need to address the social and ethical implications of managing an increasingly ageing population. While other international initiatives propose to **map the brain**, clearly a mission that is both important and fundamental, we propose an Australian initiative should aim to **understand the brain**. How can we logically try to restore memory loss when we are only on the brink of understanding how a memory is formed and stored, let alone tackle bigger questions such as 'What are hallucinations?'

RECOMMENDATIONS

Any Australian brain initiative, we posit, needs to address three core areas: biological, medical and ethical considerations, which we have addressed here using ageing and dementia as examples.

1 Access Economics (for Alzheimer's Australia) (2003) *The dementia epidemics: economic impact and positive solutions for Australia*. www.fightdementia.org.au/research-publications/access-economics-reports.aspx

BIOLOGICAL

To understand the fundamental processes that keep a brain healthy or result in neurodegeneration and find ways to interfere with those processes, we need comprehensive biological studies and systems analysis of **healthy** and **abnormal** ageing brains. This specifically includes comparative analyses between healthy and abnormal, at genetic and epigenetic, molecular, cellular, circuit, brain and population levels in a range of animal models and human studies. Such studies should use a variety of frontier techniques like in vivo wireless freely moving stimulation and recordings of neurons and groups of neurons, as well as using more traditional, established methods. One area of need that has been identified is improving methods to measure brain activity in awake subjects (animal and human), with the hope for such methods to be translatable between animal models and humans where possible.

Investment in interdisciplinary research technology, including cutting edge animal models and big data analytical capacity, is also essential to understand the fundamental processes of ageing, including being able to decipher genetic susceptibility and predispositions. Three key areas were identified as being particularly in need of such investment.

1. Access to affordable **animal model generation and use** requires further investment in and subsidising of genetically modified animal models to bring us up to world level. To be competitive in answering novel questions of gene function, be it 'How does this protein function?' or 'How does this genetic change cause a disease phenotype?', researchers need inexpensive options with short turnaround times for generating new genetically modified animals models. This access is currently limited financially for most researchers in Australia, compared to, for example, researchers at National Institutes of Health in the USA.
2. Increased investment in **imaging, sequencing, and analysis infrastructure** is also required to facilitate the biological assessments of healthy versus abnormal brains. In particular, central data storage and increased databasing of results, improved access to data already gathered, and access to advanced methods for data mining (e.g. modelling and building on data storage and access as provided by the Allen Brain Atlas [www.brain-map.org]).

3. The final key to delivering this outcome is provision of **basic medical research and people support**. We call for major investment in talent-based innovative, creative research and researchers, to bridge the widening gap between NHMRC and ARC funding, presumably driven by dwindling research investment by successive governments. In particular, the recent policy changes of these two major agencies are perceived to have reduced the funding of basic science of medical research. The ARC excludes proposals for 'research primarily and substantially aimed at understanding or treating a human disease or health condition'. By contrast, the NHMRC, although broader in its definitions of what is fundable, in essence requires the research to 'result in a significant advance in knowledge in the field which addresses an issue of significant importance to human health, and to be likely to translate into fundamental outcomes in the science and/or practice of clinical medicine, public health or health policy' in order to be funded. It is perceived that such definitions could exclude the funding of important interdisciplinary research areas such as the use of applied mathematics to study brain dysfunctions, or the development of data analyses to measure brain activity, because they fall within this funding gap. While identifying and providing measures to rectify this perceived gap would assist, any new programs should also encourage a new culture of interdisciplinary collaborations between younger and established researchers, including provision of additional support for neuroscience research that covers basic to translational studies, including blue sky ideas. Other groups have specified more concretely particular schemes that could be established. We echo the McKeon Review's sentiments on training, supporting and retaining the (research) workforce through full funding of salaries, and a strong but flexible scheme for career progression[2]. We also support multidisciplinary research teams, but note that a number of key recent discoveries in the neurosciences were made by small laboratory groups led by well funded individuals. Any large group initiatives should not be at the expense of smaller team-based research.

MEDICAL

Building on the fundamental research discoveries and knowledge highlighted above should put Australia in the position to answer the question, 'What does it mean to age well?' This can only be comprehensively answered by discovering biomarkers for early detection and specific diagnosis comorbidities for monitoring *each* neurodegenerative disease. This will build on the basic science discoveries outlined above, which will identify and validate candidate biomarkers from animal models. This endeavour is critically important for separating out the diagnoses of different conditions which have different causes and thus different treatments, though similar clinical presentations. For example, discerning in life the basic pathology of vascular disease compared to neurodegenerative disease, both of which can lead to dementia, is not currently possible. Once established, these discoveries can be used as biomarker endpoints in clinical trials, and later for prognostic use in clinical practice.

In order to characterise what changes occur in the brain during normal ageing and how that is different to neurodegenerative conditions, including validation of human biomarkers of disease, we need longitudinal studies of human ageing. We have a strong Australian healthcare system, and our ethnic diversity is a further core advantage. In this endeavour we should lead the world. The existing CSIRO program, Australian Imaging, Biomarkers & Lifestyle Flagship Study of Ageing (AIBL, **www.aibl.csiro.au**), is world renowned and proves our capabilities in this regard. One key advantage of AIBL over other similar schemes such as the Alzheimer's Disease Neuroimaging Initiative in the US (**www.adni-info.org**) is the strong standardisation of protocols for psychometrics and imaging in this large cohort. While AIBL is predominantly based in Melbourne and Perth, there are other studies running in other centres. However, further national integration and expansion of such important resources is required, including agreement on protocols, subject inclusion criteria and objective diagnosis. One option is the establishment of a national coordination centre to integrate the multi-centred collection of clinical bio and imaging data (linked to brain banks) with the capacity to share data effectively nationally and internationally, based on proven cohorts such as AIBL. Such a centre requires common and *facilitatory* ethics to increase availability of data for research purposes. An opt-out system coupled with public access to de-identified data managed centrally would greatly facilitate clinical research. A further consideration is for subjects to have free access to their own data should they choose to access it, although the ethical implications also require consideration.

SOCIAL AND ETHICAL

To address the social and ethical implications of managing an increased ageing population (and the

2 McKeon Review (April 2013) *Strategic review of health and medical research – better health through research*. www.mckeonreview.org.au/downloads/Strategic_Review_of_Health_and_Medical_Research_Feb_2013-Final_Report.pdf

ethical and psychological issues associated with increased knowledge), there is a need to consider effective employment of advanced health directives and end of life decision-making based on solid scientific data (e.g. genetic biomarkers or imaging). In order for this to be effectively debated, objective measurements of cognitive capabilities and quality of life need to be developed, but will arise partially from the research themes above. Such measures will also empower people to make informed choices about life management. Personal considerations should include early discussions of prognosis, progression management and lifestyle choices between patient, family, and care providers. These discussions may occur in association with appropriate psychological and, where relevant, palliative counselling including the option to discuss available end-of-life options (such as forgoing artificial nutrition and hydration).

To manage an increased ageing population we need evidence based development of ways to enhance independent living and prevent social exclusion. While there is much anecdotal evidence for 'use it or lose it', and beneficial environmental factors such as exercise and brain games, clinical trials are required to validate efficacy of current and emerging interventions. The outcomes of such trials need to be communicated with the public and carers (e.g. in the recently launched Alzheimer's Australia Your Brain Matters Program, **www.yourbrainmatters.org.au/brain-health-program/the-your-brain-matters-program**) and should also inform government policy including whether aids and interventions should be subsidised by government schemes. We also need increased dialogue between health professionals and basic scientists, both to inform the health professionals of the latest knowledge and developments, and to inform and direct research or trials. Research support can be given to develop new technologies, based on pathophysiological knowledge, to assess efficacy of interventions for both subjects and caregivers.

Finally, we advocate the establishment of a strong alliance or trust that coordinates fundamental components of neuroscience research at the national level. We propose that an 'Australian Neuroscience Trust' could hold responsibility for a number of resources. The trust could coordinate a national registry of animal models and facilitate import and/or build an Australian 'bank' to promote collaboration and drive down costs. The trust would hold a skills and techniques database together with funding for fellowships, to promote career development within the neurosciences and collaborative fields. Further, the trust would hold archives containing human participant and study data with structured access, allowing greater awareness and use of existing information. This would facilitate calls for participation and funding through an enhanced understanding of completed, active and required research in Australia, and would build strong connections with stakeholders such as those in the existing Neurological Alliance of Australia (Alzheimer's Australia, Friedreich Ataxia Research Association Australasia, Huntington's Disease Australia, MND Australia, Muscular Dystrophy Foundation Australia, Multiple Sclerosis Australia, Parkinson's Australia, Spinal Muscular Atrophy Australia).

One of the greatest hurdles in clinical research is that of obtaining ethical approvals, particularly for retrospective or data-mining studies. A national trust could provide new institutional mechanisms to facilitate ethical approval of research that provides centralised, timely and facilitatory ethical review for human and animal studies. Furthermore, the trust would promote ethical debate, particularly regarding research on ageing and neurodegeneration, concepts of living and ageing well and end-of-life planning. Through the trust, neuroscientists would have a vehicle for increased communication and dissemination of research to stakeholders and the general public. This would allow increased participant and stakeholder contributions to fundamental research and clinical trial development. As a national body, the trust would act as a trusted adviser for government and play a fundamental role in informing policy and reform, based on current empirical research.

APPENDIX A

THE USA AND EUROPEAN BRAIN PROJECTS

The USA-based **Brain Research through Advancing Innovative Neurotechnologies (BRAIN) Initiative** funded by the National Institutes of Health (NIH) was announced by the Obama administration in April 2013. Its goal is formidable: to map the synaptic connections and electrical activity of every one of the approximately 100 billion neurons in the human brain. Projected estimates of expenditure exceed US$300 million per year for the duration of the 10-year project, costing a total of about US$3 billion. Initial proposed experimental organisms are simpler organisms such as earthworms or fruit fly, scaling up to more complex organisms such as zebra fish and ultimately primates and humans. Functional measurements may utilise nanotechnology and wireless detection methods based on microelectronics or synthetic biology. It is hoped that the resulting 'functional connectome' (a comprehensive map of neural connections in the brain) will provide a link between current functional MRI-based maps measured at the level of entire anatomical regions, and at the opposite extreme, biochemical and electrical measurements of single cells. The project will produce data spanning multiple scales and functional modes with volumes on the order of about 300 exabytes per year. There will be attendant challenges to storing these data and comprehensively analysing them to extract meaningful insights.

The European-based **Human Brain Project** is equally ambitious. Announced in 2012 by the European Commission, it contends that our ability to gain a comprehensive understanding of the human brain is impeded by inadequate coordination between individual brain research projects, and also the data they produce. To overcome this limitation, it argues for an intensive international effort to incorporate available data into a unified functional representation of the human brain. The project plans to integrate neuroinformatics and brain simulation technologies, biological signatures of disease and supercomputing technologies to simulate functions inside the brain. The total investment has been estimated at about €1.2 billion over 10 years.

THINK TANK 2013 PARTICIPANTS

GROUP A
COGNITION, INTELLIGENCE AND EXECUTIVE FUNCTION

Chairs Professor Max Coltheart and Professor Sarah Dunlop

Rapporteurs Associate Professor Alex Fornito and Dr Deanne Thompson

Dr Ehsan Arabzadeh
Professor Michael Breakspear
Dr Thomas Carlson
Dr Andrew Gardner
Dr Bronwyn Graham
Dr Dave Hawkes
Dr Aoife Larkin
Dr Joel Pearson
Associate Professor John Reynolds
Dr Chandanie Senadheera
Dr James Shine
Dr Hari Subramanian
Dr Jana Vukovic

GROUP B
NEUROGENETICS: INHERITED DISEASES AND DEVELOPMENTAL BIOLOGY

Chairs Professor Kathryn North and Professor Trevor Kilpatrick

Rapporteurs Dr Rony Duncan and Dr Guy Barry

Dr Jon Brock
Dr Vibeke Catts
Dr Jan Fullerton
Dr Julian Heng
Dr Thomas Klaric
Associate Professor Simon Laws
Dr Tammie Money
Dr Angela Morgan
Dr Ken Pang
Dr Corinne Reid
Dr Tim Silk
Dr Justin Yerbury
Dr Kaylene Young

GROUP C
ARTIFICIAL INTELLIGENCE, MATHS AND MODELLING

Chairs Professor Stan Skafidas and Professor Steve Furber

Rapporteurs Associate Professor Andreas Fouras and Dr Elizabeth Holliday

Dr Andrew Barron
Dr Girija Chetty
Dr Alexandre Cristino
Dr Mathew Dafilis
Dr Vincent Daria
Dr Yulin Ding
Dr Jurgen Fripp
Dr Emily O'Brien
Dr Sivalogeswaran Ratnasingam
Dr Karen Siu
Dr Jean Yee Hwa Yang
Professor Murat Yücel
Dr Andrew Zalesky

GROUP D
AGEING, DEMENTIA, ALZHEIMER'S DISEASE AND END-OF-LIFE ISSUES

Chairs Professor Colin Masters and Professor Julian Savulescu

Rapporteurs Associate Professor Elizabeth Coulson and Dr David Nisbet

Dr Kristyn Bates
Dr Dana Bradford
Professor Roger Chung
Associate Professor Tracey Dickson
Dr Alex Hewitt
Dr Oliver Jones
Dr Jee Hyun Kim
Professor Pablo Moscato
Dr Elizabeth New
Dr Bilal Sheikh
Dr Ai Huey Tan
Associate Professor Naotsugu Tsuchiya
Dr Yan Yan

THINK TANK 2013 STEERING COMMITTEE

Chair Professor Bob Williamson AO FAA FRS,
The University of Melbourne and Monash University

Professor Trevor Kilpatrick MBBS PhD FRACP,
The University of Melbourne

Professor Colin Masters FAA FTSE MBBS MD FRCPath FRCPA,
Florey Institute of Neuroscience and Mental Health and
The University of Melbourne

Associate Professor Megan Munsie,
Stem Cells Australia

Dr Don Newgreen,
Murdoch Childrens Research Institute

Professor Kathryn North AM MD FRACP,
Murdoch Childrens Research Institute and
The University of Melbourne

Dr Victoria O'Collins,
Florey Institute of Neuroscience and Mental Health

Professor Stan Skafidas,
The University of Melbourne

INVITED SPEAKERS

Professor Max Coltheart AM FAA FASSA FBA,
Macquarie University

Professor Sarah Dunlop,
The University of Western Australia

Professor Steve Furber FRS,
The University of Manchester, UK

Professor Terrie Inder MD,
Washington University, St Louis, USA

Professor Julian Savulescu,
University of Oxford, UK

Professor Patrick Tam FRS FAA FSB,
The University of Sydney

BACKGROUND TO THE THINK TANK

PURPOSE OF THINK TANKS

The purpose of the Theo Murphy High Flyers Think Tank series is to bring together early- and mid-career researchers from a broad range of relevant disciplines to engage in thinking about novel applications of existing science (including social science) and technology to issues of national significance, and to identify gaps in knowledge that should be addressed. These events are a unique opportunity for career development and networking among the nation's next generation of research leaders and their institutions. Think Tanks are one of the premier events of the Academy's calendar and this is the 12th that the Academy has held.

PREVIOUS THINK TANKS

Previous Think Tanks have culminated in reports to government that have been timely, well received and instrumental in influencing policy development (available at **www.science.org.au/events/thinktank/**). Past Think Tank topics have been:

2002 Australia's national research priorities

2003 Safeguarding the nation

2004 Emerging diseases: ready and waiting?

2005 Biotechnology and the future of Australian agriculture

2006 Innovative technical solutions for water management in Australia

2007 Extreme natural hazards in Australia

2008 Preventative health: science and technology in the prevention and early detection of disease

2009 Agricultural productivity and climate change

2010 Searching the deep earth: the future of Australian resource discovery and utilisation

2011 Stressed ecosystems: better decisions for Australia's future

2012 Australia's population: shaping a vision for our future

Inspiring smarter brain research in Australia RECOMMENDATIONS FROM THE 2013 THEO MURPHY HIGH FLYERS THINK TANK

THE ROYAL SOCIETY

Think Tanks are supported by the Royal Society – the national academy of science of the UK and the Commonwealth – through the Theo Murphy (Australia) Fund