

# Submission to the National Neuroscience Consultative Taskforce

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<i>Date of Submission</i>
28/10/04

  

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## **SUBMISSION**

### **Australian Association of Gerontology Submission to**

### **National Neuroscience Consultative Taskforce**

#### **Introduction and background**

The Australian Association of Gerontology (AAG) has a broad multidisciplinary membership of academics, researchers, government administrators, service providers and others interested in the issues of ageing. The AAG is the multi-disciplinary umbrella organisation for individuals and professional bodies involved in *ageing research* and in the translation of *ageing research* into policy and practice. Through a grants program it has taken a lead role in promoting emerging researchers. As may be expected, given the high levels of dementia and other neurological impairments common in older Australians, the AAG membership has a very strong interest and expertise in neuroscience, both from a research perspective and also from the perspective of translating research into clinical practice and community based management of older persons with neurological impairment.

Neuroscience research is in the national interest because disorders of the brain and mind pose the largest health, economic and social capital burden to Australia of any disease group – well ahead of cancer and heart disease. Brain disorders are chronic and debilitating and affect both the young and the elderly. Moreover with the increasing proportion of older persons in Australia these diseases are set to increase rapidly. Collectively, these disorders take a major

slice of the health care budget. In Australia this is currently estimated to be in excess of \$4 billion and this expenditure is expected to rise dramatically over the next 40 years.

Neuroscience is itself a large interdisciplinary field that links the biological and psychological sciences through its central focus on the biology of the brain. However because of the social and behavioural issues associated with cognitive and movement disorders, neuroscience research is intrinsically associated with broader research fields, particularly those associated with management of cognitively and behaviourally impaired people, within the community and health sectors, with development of health services, and with carer support services. The AAG has a major role in facilitating multi-factorial research, which requires dynamic linkages between researchers in multiple disciplines, local communities and service providers. AAG therefore welcomes the initiative for the Neurosciences Consultative Taskforce and proposals which enhance the interconnectedness of those involved in neurosciences research; while stressing that such research should not be silo based and should involve researchers from a wide range of disciplines, particularly those involved in health services research and management of the cognitively impaired.

### **Neurodegenerative Diseases and Older People**

In the developed world, a majority of those who survive to 80 years and over will go on to develop neurodegenerative diseases before death. A progressive delay in age of onset, and a decline in mortality from the systemic degenerative diseases (such as cardiovascular and lung diseases) has been described as the fourth transition of “delayed degenerative diseases”. (Olshansky & Ault) We are now seeing yet another substitution of mortality due to later onset neurodegenerative disorders, such as dementia and Parkinson’s disease. It is predicted that the neurodegenerative disorders will gradually replace the systemic degenerative disorders as the major causes of both death and morbidity in the 21<sup>st</sup> century. (Broe & Creasy)

### **Impact of Demographic Transition on Neurodegenerative Disease morbidity**

Declining fertility rates mean fewer children and older populations. Rapid population ageing is now a worldwide phenomenon. Australia has aged rapidly in the past 30 years with rapid growth in numbers of the “young-old” – those aged 65 to 75 years. However more rapid population ageing in Australia will result from “ageing of the aged”, as our mortality rates decline in the over 70s to 90s. Population ageing will then greatly accelerate from the 2020s, when the baby boomers reach 75 years. Average survival in NSW is now over 80 years (83 years for women and 77 years for men) and human life span will continue to rise relentlessly. Average life span is projected to reach 100 years for women by 2060, with men slowly closing the gap. Absolute numbers of the “oldest-old” (85 years and over) will increase exponentially over the decades to 2051 - by 50% to 2011, by 440% to 2051 with 1.3 million people aged 85 years and over - while the total Australian population grows by just 30% from 20M to 26M people (ABS). On prevalence and incidence data from the Sydney Older Persons Study (1992-2002), given the present level of neurodegenerative disease in the over 85s, it is estimated that 70% will have a disorder of gait, balance and movement with 8% having Parkinson’s disease, and 70% will have a disorder of cognition with 32% having frank dementia.

There remains a brief window of opportunity to prepare for the coming exponential growth in numbers of very old people that will confront health aged care and medical services in coming decades. Population ageing can be dealt with most effectively through policy structures which are designed to engage all concerned parties, and which integrate public policy with public sector, private sector and non-government organisation activities and

initiatives. Research and education as well as health, hospitals, housing and aged care are crucial issues for a successful ageing policy.

## **Age-related neurodegenerative disorders**

As a class, the neurodegenerative diseases are primary neuronal disorders, i.e. not secondary to known metabolic, vascular, inflammatory, malignant, toxic or other causes. Their defining feature is selective neuronal loss in a pattern that tends to be specific to each disease. Many neurodegenerative diseases manifest as a rare familial young onset form and a more common late onset sporadic form, which increases exponentially in incidence with advancing age over 70 years. The late-onset neurodegenerative diseases include the dementias, movement disorders and sensory loss.

The two most important late-onset neurodegenerative disorders, for the determination of mortality and morbidity data in the older population, are dementia and Parkinson's disease. Also defined as a neurodegenerative disease are age-related macular degeneration (ARMD) and the almost universal age-related sensori-neural deafness. Despite their very high prevalence in the "old-old", the neurodegenerative diseases are, in general, poorly defined and diagnosed compared to the common systemic degenerative diseases (heart disease, stroke, chronic lung disease and cancer) and there is a high current level of under-ascertainment of neurodegenerative disease mortality, particularly in the very old. Multiple pre-clinical syndromes commonly exist in older people and have been shown to predict subsequent dementia; these include cognitive or memory impairment (not reaching criteria for AD), motor slowing (not reaching criteria for PD) and evidence of vasculopathy.

The major diseases are:

- Alzheimer's disease [AD],
- dementia with Lewy bodies [DLB]
- Parkinson's disease (PD)
- fronto-temporal dementia [FTD]
- Motor-neuron disease (MND).
- Age-related macular degeneration (ARMD), MND or amyotrophic lateral sclerosis.
- Vascular brain disease contributes to the burden of neurodegenerative dementia and gait disorder in older people
- Mixed senile or late-onset dementia is the commonest dementia syndrome in older people with elements of AD, DLB and Vascular dementia
- The term is also used for a host of less common familial and sporadic neurological diseases of unknown cause, including progressive supranuclear palsy (PSP), cortico-basal degeneration (CBD) and the spino-cerebellar atrophies (SCA), many of which appear to be age-related.

## **Multi-factorial "Geriatric Syndromes"**

Because of multiple pathology in the "old-old", the neurodegenerative disorders outlined commonly present as multi-factorial "Geriatric Syndromes", rather than as specific neurological diseases amenable to specific diagnoses on death certificates. Many of the "Geriatric Syndromes" have a high mortality rate including: "immobility" with underlying

parkinsonism and dementia; “instability and falls” with underlying impairments of balance gait and vision; “delirium” with underlying mild cognitive impairment and dementia; and “aspiration pneumonia” due to underlying brain and oesophageal-motility disorders. However, the underlying causal diagnoses rarely appear on death certificates

## **Incidence**

Data from the Sydney Older Persons Study (SOPS) showed high overall prevalence rates of neurodegenerative disorders in the 75 and over population, ranging from a prevalence of 50% for gait ataxia and 43% for visual impairment to 38% for cognitive impairment, 19% for gait slowing, 17% for dementia and 5% for Parkinson’s disease (PD). (Wade et al) All 6 neurodegenerative disorders examined showed a steep and highly significant increase in prevalence and incidence with advancing age from 75 to 93 years. The late-onset neurodegenerative disorders cause increasing morbidity towards the end of the increasing human life span. For example Alzheimer’s disease is the commonest dementia, and shows a doubling of incidence every 5 years from 65 to 90 years of age.(Jorm) There has been controversy as to whether dementia incidence plateaus off over 90 years of age, with 2 meta-analyses producing conflicting results. Systemic disease related disability is being replaced by a new wave of disability due to neurodegenerative disorders, which are increasing exponentially in the most rapidly growing sector of the population, the “old-old”, forming a new disease transition. in developed countries. This process parallels the exponential increase in the numbers of those surviving into their 80s and 90s. This is the age at which the neurodegenerative diseases show their greatest increase in prevalence and incidence, and the age at which the chronic systemic diseases show static or falling rates. From SOPS neurodegenerative disorders were major causes of disability in personal care (ADL), domestic care (IADL) and mobility. As predicted they were the major contributors to severe ADL disability and were responsible for an increasing proportion of disability with increasing age. On current figures (SOPS): 80% of the over 85s need assistance in domestic care; 30% require personal care (bathing, dressing, toileting); 70% are mobility impaired (high falls risk) and 70% are cognitively impaired (high delirium risk). They are vulnerable to acute illness, disability & hospitalisation. Their carers are vulnerable to social losses, stress, depression, poor health & economic loss

## **Life Span and Compression of Morbidity**

Based on a human life span of around 85 years, it had been predicted by Fries and Olshansky (xxx) that chronic systemic disease, and consequent disability, would be delayed and compressed to the end of life by ongoing changes in life style and risk factors such as reduction in smoking, improved diet and more exercise. Recent data support this association. However, with further increases in human life span, it remains possible that morbidity is simply being delayed to later decades of life rather than compressed, i.e. from the “young-old” to the “old-old” or from the 70s to the 80s and 90s. A shift to a new epidemiologic transition of later-onset neurodegenerative disorders would result in additional causes of morbidity as well as mortality at advanced ages. While morbidity related to chronic systemic diseases appears to be declining, or being compressed to the end of life, the morbidity related to neurodegenerative disease, particularly the dementias, is increasing with advanced old age.

## **Population ageing, preventive and neurodegenerative disease research**

1. An essential issue to address is the current and projected incidence of neurodegenerative diseases. If current incident rates continue then the ageing of the population will create an epidemic of dementia, with the associated demand for care and assistance. The possibility that healthier old age, better education and increased mental and physical activity, will reduce the incidence of such diseases is one positive scenario which needs thorough study: as does the more negative scenario that suggests the age related incidence of neurodegenerative diseases may in fact be increasing. Factors such as changes in the levels and timing of diagnosis and reporting could artificially inflate such incidence figure but research is urgently needed to determine underlying disease incidence and trends.
2. The neuronal systems involved in the neurodegenerative disorders do not appear, on current evidence, to be susceptible to the same life style or risk factors that devastate other body systems (e.g. nutrition, diet, smoking and cardiovascular and lung diseases). Other risk/protective factors for these diseases may be found. For example, potentially modifiable risk or protective factors suggested, but unproven, for Alzheimer's disease include anti-inflammatory drugs, statins, red wine, metal binding agents, oestrogens, education and mental and physical activity, and the role of anti-oxidants in age-related neurodegeneration more broadly.
3. Neuroscience is one major area of particular relevance to the health and well being of older people. However demographic transition is generating major research challenges across a wide range of economic, financial and policy areas. With rapidly changing demographics, we are largely in uncharted territory in terms of our understanding of the many interrelated factors influencing the quality of life for older Australians. Equally if not more vital, is understanding the social factors influencing well-being of older people, including suitability of care and support models and effective social participation. The emphasis of this neurosciences initiative is on biomedical scientific research, however it must be recognised that this should not ignore the population health, community service and social agendas. Divisions at the research level often impede proper delivery of care and services at the community level. Use of terms such as brain and mind may divert focus from the more general needs for research focusing on optimising communities for supporting all types of brain impairment.
4. Moreover there is increasing evidence of direct interaction between the social/educational environment and brain health itself. In terms of human life span, it is proposed that brain function responsible for the human capacities for learning, cognition, insight and social knowledge, is one determinant of longevity in human populations. Socioeconomic status, educational level, and mental ability or intelligence are closely linked. A cohort effect of increasing fluid intelligence, as measured by psychometric tests of verbal reasoning, spatial orientation and inductive reasoning, has been demonstrated. This effect, which has been attributed to improvements in education, parallels observed changes in both education and longevity over the same period. Although no causal links have previously been suggested, it is arguable that improvements in education and fluid intelligence are in part responsible for increases in longevity.
5. It must be recognised also, that while important research goes on into causes and prevention of neurological disease, there will be many older persons still suffering and who will need optimum care from health professionals. Any partnership/ research

approach should recognise those for whom the advances of cause/prevention science will be too late. Moreover the multifactorial nature of most degenerative cognitive impairment means that a silo driven research into specific biochemical/genetic brain disorders may not yield practical benefits, since the problems of one type of impairment may simply mask other degenerative neuronal conditions. Long term care for the cognitively impaired ageing is still to be expected and care should be taken to avoid the belief in neurosciences research as offering a “magic bullet” to avoid the costs and difficulty of managing our aging population. The investment in research related to appropriate care practices and environments is also essential. Unlike much traditional health and scientific research, *Ageing Research* does not apply a single issue, reductionist research model. It recognises the complexity of ageing and the multi-factorial causality of age-related health and decline. It requires cross-disciplinary research, building capacity in medical, psycho-social, nursing and allied health areas. It will include study of multi-factorial preventive and clinical outcomes including social, environmental & biological factors responsible for late life decline.

It must be stressed again that whatever model is developed for promoting direct research into the biology of the brain, it must not be at the expense of other ageing research more focussed on the multifactorial issues involved in causation and in management of older peoples needs.

### **Research capacity**

There is an urgent need to build Australia’s capacity in ageing research. A strong research and development focus, supporting skill development and career opportunities for researchers will be a national resource in addressing an ageing population over the coming decades. Neuroscience research will of course be one major component of such research. Australia has an established strength in medical research including neurosciences but the research effort is severely under-funded. Research funding is major problem for all areas of research in Australia, with Universities increasingly constrained in research budgets. Research infrastructure in all institutes and universities across Australia has been progressively run-down over the years and major items of equipment have not been upgraded to keep pace with advances in the field. Problems will always be most acute in areas of research reliant on high cost instrumentation, powerful data management technology or expensive laboratory and set up. Much medical research will fall into this category. Urgent and substantial support is required for such high cost research.

For successful research outcomes it will be necessary to harness all the existing expertise as well as promoting the development of additional expertise. This development of young human capital is an essential output of this kind of initiative, and will stand Australia, and the region, in good stead into the future. It will also be important to tap into existing research programs. Currently substantial support may be available for high profile researchers or those with extensive track records, and support is becoming available to emerging (early career) researchers. However, less attention is given to researchers that are outside these two groups – researchers that with some support could make a more significant contribution to knowledge in Australia. This group could be networked into existing research hubs or developing ageing research collaborations.

To date, traditional research funding bodies, such as the NH&MRC and ARC, have not funded ageing research in proportion to Australian population ageing and the growth in absolute and proportional numbers of very old people. While existing Research Institutes and Foundations cover heart and lung diseases, arthritis, diabetes, cancer, mental illness and neuroscience, no public or community bodies at a State or Commonwealth level exist with

capacity to promote or fund multifactorial *Ageing Research*, as a defined research process, aiming at a defined body of knowledge. While the neurosciences initiative is strongly supported it should not be at the expense of similar initiative in the broader field of ageing.

#### **Key research foci**

1. One initial focus of neuroscience must be on research outcomes for the population whose numbers are increasing most rapidly and who carry the greatest burden of acute illness, chronic disease, disability and social need - the “old-old” or people aged 75 to 100 years and over. For ageing research it is commonly the *status of the old-old* that is the outcome variable of interest, whatever the issue, condition or age-group under study. While the outcome of *Ageing Research* is the well being of the general population of older adults, there may also be a need to examine ageing across the whole life span.
2. Gait, sensory and cognitive (neurodegenerative) disorders are prevalent in the old-old. These disorders cause 70% of all disability and the limited research so far has found few proven protective factors. There can be little doubt that research into the causes, prevention and management of cognitive impairment is a priority area for ageing research focus. This is also true for research into multifactorial movement and gait disorders associated with advanced ageing. However, this needs to be broader than discipline defined research into specific movement disorders (such as Parkinson’s disease in the young-old).
3. In conjunction with a focus on the avoiding or treating neurological disorder in the old-old, there must be research into the care and support needed for this group. As previously noted, on current figures (SOPS): 80% of the over 85s need assistance in domestic care; 30% require personal care (bathing, dressing, toileting); 70% are mobility impaired (high falls risk) and 70% are cognitively impaired (high delirium risk). They are vulnerable to acute illness, disability & hospitalisation while there has been very limited study or quantification of the impact on carers, who are vulnerable to stress, depression, poor health as well as considerable social & economic loss.
4. Research should be multi-disciplinary (bio-psycho-social paradigms) to ensure that knowledge gains have value in informing constructive action. For example amongst older persons, understanding of productivity and independence in later life, must jointly consider health, employment, and family issues. Ideally research should include participation by key stakeholders (older people organizations, NGOs, government agencies, industries and services, etc) in the development, conduct, and application of research.
5. All research should be of sufficient scale, quality, and continuity to bring together collaborative teams and build substantial bodies of knowledge.

#### **Organisational arrangements**

The issues associated with neuroscience research were addressed recently by PMSEIC and in a report entitled “*Brain and Mind Disorders: Impact of the Neurosciences*” specific recommendations were made to develop an enhanced basic neuroscience research effort in Australia. The issues addressed included the need for better networks, including involvement with international developments and effective collaboration between research teams. The development of well funded Centres of Excellence characterised by internationally recognised centres of research effort and networking of smaller research groups was canvassed as was the development of a “Brain Alliance”. Clearly any endeavour which

improves the research effort in Australia and promotes collaboration is to be fully supported and in this context the initiative of the PMSEIC is welcomed.

## **Brain alliance**

It is not clear just what the PMSEIC intended by the term Brain Alliance. Such an alliance may be somewhat narrow in focus and alliances and collaborations across all disciplines including the social sciences are generally preferred.

## **Centres of excellence**

The development and support for centre of Excellence is strongly supported. Such Centres allow groups of experts to gather and can provide the type of support, leadership and mentoring needed for new researchers to emerge and develop. Equipment can be shared to maximise cost effectiveness of research and there is opportunity for easy exchange and sharing of information which will maximise the overall effectiveness of the research effort.

### *The Centre for Population Ageing Research*

In order to promote targeted multi-factorial research The AAG supports the proposal for a Centre of Excellence (CoE) built around the economic health and social implications of population ageing. It is assumed that the Centre will be located within a University with alliances with research expertise in other universities; Such a centre could focus on economic, financial, workforce and policy dimensions of ageing and health issues with selected research involvement from epidemiology, gerontology, neuroscience and community health experts. Funding of the type and scale available under the CoE program will enable a unique research program to be built which will move economic and financial research on population ageing to a new level of integration and co-ordinated understanding. The proposed centre will seek to bring together academic, policy and private sector experts to promote understanding of the wide range of challenges which the evolution of population ageing throws up, in an environment in which complementary research is ongoing on related issues in other disciplines. Equally important, it will nurture a new generation of young researchers, through PhD scholarships and Post-Doctoral fellowships, in gaining expertise in these research areas. This development of young human capital is an essential output of this kind of initiative, and will stand Australia, and the region, in good stead into the future.

The development of other centres of excellence in areas with an impact on ageing and neuroscience is also fully supported, therefore CoEs with a focus on neurosciences will be welcomed. Once again it is useful to stress that any such centres not have a “silo” approach and ensure multifocal research to maximise overall benefit.

## **Institutes**

Institutes provide an effective means of cross disciplinary collaboration and also allow for and overview of priorities and funding needs amongst a group of research centres. Structures which are designed to engage all concerned parties including the private sector, and which integrate public policy with private sector activities and initiatives will be most effective in promoting well targeted research. Moreover by their nature Institutes are well placed for

collecting funding and sponsorship from external bodies including the private sector. Institutes are also effective means of promoting networks amongst researchers.

The formation of a Commonwealth funded Institute of Ageing, with a focus on Health and Medical Research, is seen as an early step in this process. Such an institute would promote, facilitate, assist and fund (but not conduct) *Ageing Research*, defined as research aimed at improving health status, health care and quality of life for the increasing numbers of people reaching advanced old age and for their carers.

## **Collaborations**

New approaches to conducting research are needed that complement traditional investigator-led efforts by individuals and discipline based teams: In particular promotion of collaborations is an intrinsic part of ageing research. In order for research to have a significant impact on the lives of older people, we need to bring together researchers from multiple areas to work together in addressing issues of ageing. There has been limited incentive or ability for social scientists and medical and health researchers to collaborate on research projects. Barriers to multidisciplinary projects such as single-discipline grant assessing panels could also be addressed. In this context the types of brain focused collaborations proposed by the PMSEIC may be too narrow.

## **Networks and information exchange**

Promoting networks amongst researchers is an essential part of research. Problems are emerging with the traditional network mechanisms (Conferences, journals, associations) largely because of the rapidly expanding body of knowledge increasing specialisation of disciplines and the vast size of many international conferences. Solutions to this problem are not easy and it is not clear that narrow alliance on specialty research areas will prove sufficient.

In terms of effective information exchange it is essential that research summaries be readily available. This needs to be at several levels of technical detail. For example Not only do geneticists need to keep up to date with advances in biochemistry or clinicians with brain research, so do those involved in economics, or social sciences need to have understandable summaries of research findings. Centralised support for funding such research summaries could be an effective means of promoting collaboration.

Although no single effort will solve this problem of effective information exchange some key elements are:

- Ensure adequate funding is available for researchers including emerging researchers to attend conferences. Subsidising some major conference could assist.
- Encourage cross disciplinary conferences which maximise opportunity for interchange of ideas and scope for collaboration
- Ensure availability of research summary information either through published reviews of current material or perhaps specifically organised review conferences

### **Specific Research Priorities**

Mechanisms need to be developed for identifying research priorities which ensure that the overall benefit to Australia is optimised. This task cannot be undertaken in isolation and it is essential that as wide a range of researchers, policy makers and those involved in

management of the elderly and sick in the community are involved in the process of identifying research priorities. In the case of neuroscience research the groups which must be involved in setting such priorities must include

- Clinicians involved in the diagnosis and treatment of the cognitively impaired
- Those involved in the day to day management of patients with clear understanding of the current real needs
- Demographers and social scientists who can provide input to the needs of Australia over the next 50 years
- Bean counters and policy makers who will be responsible for implanting policy long term and who will be responsible for funding both the research and also managing the consequences of an increasingly cognitively impaired older community.

Although priorities will change over time the areas of neuroscience research which can now be identified as priority Include

- Genetic epidemiology and molecular biology research into causes of degenerative neurological disorders in the aged with particular attention to the common disorders of Alzheimer's Disease, Parkinson's disease, gait slowing and sensory disorders.
- The effectiveness of specific drugs or other therapies in management of neurological disorders
- Longitudinal studies and associated data collections of the ageing population to get a better understanding of the disease patterns both now and in the future.
- Environmental and Genetic Risk Factors in the Neurological disorders of Old Age and associated methods of prevention or delay. Specifics might include the role of education and learning as a preventative for dementia
- The current and projected incidence of neurodegenerative diseases. Can compression of morbidity extend to the very old?
- Multi-disciplinary research into the complex causation, prevention and clinical management of the common multifactorial "Geriatric Syndromes" (gait instability and falls, acute confusional state and delirium, cognitive decline and dementia, slowing and reduced mobility, incontinence, depression) that create co-morbidity, prolong length of stay and increase disability following acute systemic illness.

## **Conclusion**

Ageing research must be a major focus of health and social research for the foreseeable future. It is to be expected that the priorities and key tasks will change over time in the light of new data, new technologies, medical advances, changing social trends and improved overall population health. It is important therefore that avenues of research remain flexible and capable of turning attention to new needs and circumstances as they arise

The important question for ageing research is not simply “is this degenerative process ageing or disease?” but, more significantly, “can this degenerative process be modified, prevented or delayed, without significant risk, by manipulation of environmental and/or genetic risk factors”. The aim of ageing research remains one of compression of morbidity, towards the end of life and the prolongation of the period of healthy non-disabled life. This aim may, or may not, be consonant with increased longevity. The challenge facing ageing research is to seek new and modifiable risk factors to delay the onset of disorders, which are reducing quality of life in advanced old age.

The Australian Association of Gerontology has a strong focus on ageing research and education across many fields. Its members have considerable expertise in both in-depth medical, scientific and social research, as well as in cross-disciplinary projects. The Association welcomes the opportunity to contribute to further development of the Australian ageing research agenda, both now and in the future. Support for neurosciences research will remain a major component of any such research.

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