BRAINwaves

The Newsletter of the Brain Foundation incorporating the Migraine Newsletter. **Winter 2004**

CHANGES TO THE BRAIN FOUNDATION BOARD

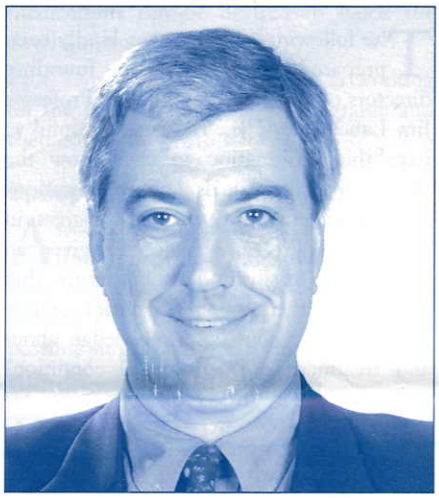
At the AGM last November, long serving President, Tony Grey handed over to Professor Philip Thompson of the University Department of Medicine and Department of Neurology at Royal Adelaide Hospital.

Mr Grey remains on the board and his six years as President was gratefully acknowledged by fellow board members. In particular, under his leadership, last year saw the completion of advanced Web sites for the Brain Foundation and for Migraines and Headaches. Another change was the resignation of Dr Kevin Bleasel AO. His resignation was reluctantly accepted as Dr Bleasel has supported the Brain Foundation for over 30 years in his capacity as a director.

The new appointments to the board were: Professor Max Bennett of Sydney University. Professor Bennett is one of the founders of the Brain and Mind Institute at Sydney University. Dr Bill Carroll of Perth. Dr Carroll is a former president of the Australian Association of Neurologists. Assoc Professor Marcus Stoodley of the Prince of Wales Hospital, Randwick was elected as the Neurosurgeons Society of Australasia representative. Professor Michael Pender of rhe Royal Brisbane and Womens' Hospital is the Queensland representative and Dr Dominic Rowe of Royal North Shore Hospital will now be on the board as well the NSW Committee.

They have joined the re-elected members of the board. They are: Professor Geoff Donnan, National Stroke Research Institute; Assoc Professor Nick Dorsch; Department of Surgery, Head Injury and Stroke at Westmead Hospital; Mr Jim Graham, Tasmania; Mr Tony Grey, Sydney; Professor Michael Halmagyi, Vice-president Medical, Royal Prince Alfred Hospital, Sydney; Professor James Lance AO, CBE, Sydney; Lady Sonia McMahon, Sydney; Mr Garry Meggison, Adelaide; and Dr John O'Sullivan, Victoria;

Professor Thompson welcomed the new appointments and the accumulated



Professor Philip Thompson

experience and knowledge of re-elected members. He feels that the time is right for a review and renewal of the Brain Foundation's strategic direction and that any new direction should reaffirm the genesis of the Foundation as the Australian Neurological Foundation of the Australian Association of Neurologists and the Neurosurgical Society of Australasia. The Brain Foundation's strengths on a nation-wide basis, will remain its ability to encourage and support junior clinicians, to top-up funding for meritorious projects where other sources have been insufficient and to be a first point of funding for established researchers.

The Brain Foundation will also continue its work to bring wider knowledge to those suffering neurological disorders and brain injuries and their carers by further development of the websites, conducting seminars and distribution of other materials. Professor Thompson expects that the board will examine new ways of meeting its objectives and explore new opportunities.

The new President also introduced a new, more efficient structure for the National and NSW Offices and announced the appointment of Gerald Edmunds RFD, M Bus, BA as the new National Executive Director from February and passed on the appreciation of the board and all the Foundation's members to Ms Louise Alexander for her contribution during her time in that position.

Professor Thompson extends his thanks to all members of the Brain Foundation and recipients of this newsletter for their generous support in the past and hopes that even more of you will be able to take advantage of the tax deductibility for donations and make a contribution this year so that the Brain foundation can improve and increase its research, carer and education programmes.

Mission

The Brain Foundation was established in 1970 by members of the Australian Association of Neurologists and the Neurosurgical Society of Australasia to reduce the incidence and impact of brain, spinal cord and nervous system disorders, diseases and injuries through the provision of support, community education and research

In this issue

NEWS FROM CANBERRA

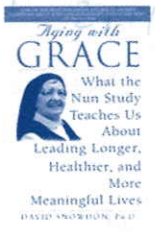
The Minister for Health and Ageing, Tony Abbott has approved the establishment of a Neuroscience Consultative Task Force (NCTF) and associated expenditure. This is to be the government's main response to the Prime Minister's Science, Engineering and Innovation council (PMSEIC) Brain and Mind disorders! Impact of the Neuroscience report.

The report found that brain and mind disorders pose the highest health, economic and social capital attrition burden to Australia of any disease group. These disorders will require novel means of prevention and cost-effective treatment achieved through intensified cross-disciplinary scientific research in order to understand their biological basis. The NCTF is to integrate neuroscience and psychiatric research with social science and frontier technologies to increase Australia's scientific capacity to reduce the burden of brain and mind disorders.

Recognition of these trends by government will highlight the work of the Brain Foundation and our director, Tony Grey has already had informal talks with the Minister, Tony Abbott and our national director, Gerald Edmunds has had a meeting with the Minister's staff and an informal meeting with the Minister.

Book Review by Sue Halmagyi

Aging with Grace by David Snowdon, Bantam Books, 2001



David Snowdon is Professor of Neurology at the University of Kentucky. The book describes his findings as he studied a group of elderly nuns to determine "the causes and prevention of Alzheimer's disease, other brain diseases, and the mental and physical disability associated with old age" (www.nunstudy.org); their findings in summary are that although the "use it or lose it": principle does not affect the incidence of the physical changes associated with Alzheimer's disease; it does protect us from the evidence of the disease in our daily life.

The nuns provided a wonderful complete set of records of their medical and occupational history throughout their adult life; they had many similarities – their lifestyles were similar; they did not smoke; they drank little or no alcohol. These similarities simplified the task of identifying factors that really made a difference.

The nuns who have participated in the study all agreed that they should be evaluated on an annual basis for symptoms of any deterioration in their mental facilities, and that their brains should be available for autopsy after they died. The findings have been most exciting – although there is no evidence that the "use it or lose it" principle applies to the incidence of the disease, it does appear that using your brain in active and creative ways into later life does protect you from showing the signs of the condition.

This finding is being borne out by other researchers in the field.

The book is very readable, and should be read by everyone. It is certainly not a depressing read – it is available from **www.amazon.com,** where there is a very good editorial review.

You can visit the Web site for this study at : **http://www.mc.uky.edu/nunnet/**

You might also like to check out the web page from the **National Institute of Neurological Disorders and Stroke: http://www.ninds.nih.gov/health_and_medical/pubs/dementias.htm**

It certainly appears that there is a lot we can do to keep our brains healthy and active as we age – a problem that is facing all of us since effective treatments have been developed for so many physical diseases. The Brain Foundation is progressing its Healthy Brain Program: you will see some results shortly, and one aspect, "Brain Food", is treated in some detail in this newsletter.

An Overview of Advances from the Brain Foundation's Grants Programme

Brain Foundation Sponsored Research Outcomes.

The following summary has kindly been prepared by one of the founding directors of the Brain Foundation, Professor Jim Lance AO CBE. It is most helpful to have this information to show how the money that individuals and organizations have contributed has enabled progress in many areas. Professor Lance has given an overview, in easily understood terms, that draws together smaller studies where applicable to show how knowledge about and treatment of neurological conditions is improving in the continuing quest for cures.

Parkinson's Disease.

Natural history. What is the outlook for patients with Parkinson's disease? The neurological team at Westmead Hospital followed 149 patients closely for 10 years. Of these, 67 were still surviving, most of whom had remained intellectually intact. Patients with onset at less than 55 years of age were still employed after 5 years. Comparison with studies done before the introduction of levodopa show that this medication, although alleviating the symptoms of Parkinson's disease, has not increased life expectancy.

Causes of symptoms. The parts of the brain responsible for muscular rigidity, tremor and intellectual changes are being identified by collaboration between the Prince of Wales Medical Research Institute (PoWMRI), Royal North Shore and Westmead Hospital. These researchers have found a chemical change that promises to predict whether a family member of a sufferer will develop Parkinson's.

The nature of Lewy bodies which are scattered through the brain in Parkinson's disease has been established by Dr. Bill Blessing at Flinders University. This opens up a new line of investigation of the cause and potential treatment.

A method of analysing the tremor of Parkinson's disease has been devised by A/Prof Jim Colebatch to distinguish it from other causes of trembling. He has also worked with a group from Monash University to study brain function in Parkinson's disease by PET (Positron Emission Topography)scanning. They have shown that the mental imaging of a projected movement is intact in most patients but the difficulty in carrying out the movement lies in motor centres below the cortex of the brain.

Treatment. New surgical methods of stopping tremor and other involuntary movements have been pioneered at St Vincents Hospital, Sydney. Wires are inserted by a stereotaxic instrument accurately into the parts of the brain causing tremor. The movements can then be switched off by a pacemaker inserted under the skin. Neuroprotective drugs and some agent resembling "Ecstasy" are being studied to improve treatments in Parkinson's disease.

Inherited disorders.

A/Prof Garth Nicolson heads a team at the Sydney University Molecular Medicine :Laboratory at Concord Hospital. They have discovered that the gene for a common form of inherited neuropathy (Harcot-Marie-Tooth disease) causing weakness of the hands and legs, lies on chromosome 17. More recently, they found the gene responsible for compression paralysis in families with sensitivity of peripheral nerves to pressure. They are now working on hereditary forms of Parkinson's disease.

Ageing and Alzheimer's disease.

A risk factor in Alzheimer's disease, known as Apo E4 has been found in the serum. Professor Patricia Armati at the University of Sydney is studying the way that brain cells take up this substance.

A/Prof Bruce Brew at St Vincent's Hospital, Sydney is conducting trials of agents that block a toxic substance released in the brain by immune reactions. These are thought to play a part in Alzheimer's disease and other degenerative disorders in the brain.

The only defects produced by ageing alone aere found to be slowness of movement, difficulty in looking upwards and perceiving vibration in 700 patients of 75 years and older studied by Prof Tony Broe at Concord Hospital. The causes of falling in the elderly is being studied by Prof Simon Gandevia and his team at PoWMRI. He has also examined the causes of progressive weakness in people who suffered from poliomyelitis as a child. Their increasing disability appears to be related to secondary changes such as osteoarthritis in weakened limbs rather than a further fall-out of nerve cells.

Peripheral Nerves

Research workers at the PoWMRI have looked at the way in which pain is caused by over excitability in nerves of the arms and legs. The way in which drugs control this pain acts as a model for over-excitability of nerve cells in the brain causing epileptic fits

Head Injury, Stroke and brain operations.

A grant from the Brain Foundation enabled the Neurosurgical Society of Australasia to complete a report on methods of handling head injuries. Spasm of brain blood vessels may have a detrimental effect after strokes, cerebral haemorrhage, head injury and brain operations. Dr Nick Dorsch and colleagues at Westmead Hospital have demonstrated flow changes by transcranial Doppler apparatus and the studied build up of carbon dioxide in the post-operative period which can cause brain swelling and epileptic fits. The use of equipment bought with the aid of Brain Foundation grants has enabled these abnormalities to be detected and corrected with resulting improvement in patient care.

Researchers at the Sir Charles Gardiner Hospital in Perth, the Austin Hospital in Melbourne and the John Hunter Hospital in Newcastle are investigating the ways top increase the amount of surviving brain tissue after a stroke.

Professor Noel Dan at Concord Hospital has used ultrasound during operations to enable brain tumours to be identified more readily and to provide a check on complete removal of tumours. The localisation of tumours is being refined by Dr Briellmann in the Brain Research Institute in Melbourne and new treatments are being studied in Queensland and NSW.

Dr Geoff Herkes at the Royal North Shore Hospital has studied the electroencephalographic changes after the brain has been deprived of oxygen (e.g., after cardiac arrest or respiratory failure) and found that global changes predict the neuropsychological outcome.

Professor Anne Cunningham is studying neural stem cells as replacements for damaged nerve cells at the Sydney Children's Hospital.

Assoc Prof. Marcus Stoodley is a leader in the field of operations to treat arteriovenous malformations in the brain and cystic changes in the spinal cord (syringomyelia). His work is supported by the Brain Foundation.

Migraine Headache

The novel treatment for migraine headache, sumatriptan (Imigran), was developed in the U.K. because Dr Patrick Humphrey was stimulated by work done at the Prince Henry and Prince of Wales Hospitals showing the relationship of a chemical transmitter serotonin to migraine headache. This opened the way for a new series of migraine treatments, the "triptans" (Imigran, Zomig and Naramig). Recent studies from the group on peptides causing the cerebral blood vessels to dilate during migraines and cluster headache may open up a new line of treatment. The pathways in the brain responsible for feeling head pain are now being investigated to find the transmitters involved in each stage so that medications can be devised to block the development of headache.

Prof. Lyn Griffiths in Brisbane is working on the genes responsible for migraine and their connection with strokes.

Epilepsy

Assoc Prof Annie Bye used her award from the Brain Foundation to invent a new technique for brain imaging that assesses children with severe epilepsy for possible surgery to correct the condition.

Blindness: The Bionic Eye

Professor Minas Coroneo in Sydney has initiated research into a technique to transfer an image of surroundings to the seeing part of the brain in totally blind people.

Muscle disease in children

The Brain Foundation has supported research into weakness caused by muscle disorders by Dr Sue North and Dr S Cooper in Sydney.

Brain function: The Healthy Brain

Mapping functions of the cerebral cortex has been carried out by Dr John Watson and A/Prof. Jim Colebatch in Sydney to increase understanding of the way a healthy brain works. This uses Positron Emission Tomography (PET) scanning to show the areas of brain that become active during sensation form skin and muscle.

Vertigo

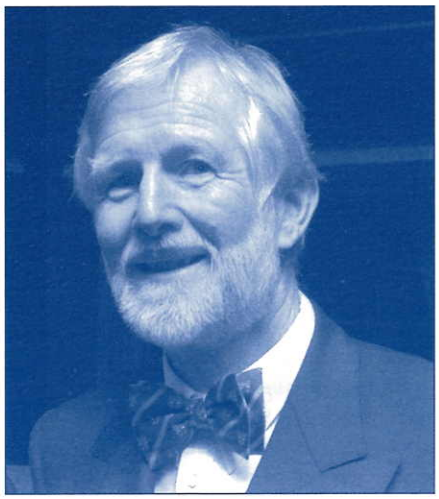
Causes of giddiness are being investigated at the Royal Prince Alfred Hospital in Sydney.

Distribution of Funds

While the bulk of money raised in New South Wales has supported research in that state, substantial grants have been made for research to be carried out in Queensland, Victoria, the ACT and Western Australia and the scientific committee that reviews all the submissions makes its decisions wholly on the basis of merit.

NATIONAL OFFICE

I am delighted to have been appointed as the new national executive director. I am looking forward to working with the board, members and subscribers to take the Brain Foundation forward. My background, after the Navy, was in Marketing and Management Consulting and I have worked



Gerald Edmunds

on a range of projects for organizations including; heavy industry, mining, government departments, financial institutions, event-management and large developments.

My role is to develop and implement a business plan to build upon our strengths, enlist the help of our supporters like you, our readers, and raise the profile of the Brain Foundation so that our share of corporate grants will increase.

The first priority has been to refine our websites and introduce a subscribers' only section. This development is underway so that there will be new, separate discussion forums for different interest groups, regular bulletins about advances in research, treatments and "wellness" programmes. I hope that you will all subscribe to the websites and invite others whom you know to do so.

The money raised from subscriptions goes to maintain and hopefully increase our carer, community education and research programmes. This is the time of year when we close off applications for our annual research awards and, with your help we will be able to fund more programmes. The total of all the submissions submitted this year is just over $1 million. We would need each reader to contribute at least $50 to have enough to lift our current funds to that level.

Please send your donations straight back so you can claim your deduction in this year's tax return.

An equally high priority is to bring the research being conducted on how to achieve and maintain a Healthy Brain to a stage where we can launch the entire programme. Initial information has been provided in earlier newsletters, but there is much more detailed information to follow. This issue will provide more about "Brain Food". The most important and exciting thing is that people who follow the whole programme can avoid some of the debilitating mental

symptoms of ageing if they start and maintain the programme early enough.

I am looking forward to the challenge of working with you and for you to advance the mission of the Brain Foundation. I have already been grateful to receive offers of support from the AMA (NSW), The Pharmacy Guild, PricewaterhouseCoopers and in particular, further help from Pfizer Australia who have helped defray the costs of this newsletter after last year meeting the development costs of our websites. I recently attended a function at which Pfizer announced grants totalling $500,000 to 10 upcoming Neuroscientists which is a further demonstration of that company's high level of involvement with the medical and medical research communities.

In a further development with the Brain Foundation, Pfizer has launched a "Stroke Pad" which provides information for GPs and a separate section for their patient that advises them to refer to the Brain Foundation for further information.

Gerald Edmunds

NEW SOUTH WALES

Activities in NSW are overseen by the national director, and the initial months have been a very busy time. Two events were held on behalf of the Foundation. First, the Artist, Diarne Wiercinske devoted an Exhibition of her and fellow artist's works to raising funds for us. The other, quite different, a fine gesture by the vintage tractor movement who were planning to bring 2,000 tractors or more to Cootamundra, including quite a few that were being shipped in from overseas, to set a new world record.

Golf Day

The next event planned is a Golf Day Monday the 15th November at the Pymble Golf Club. Golf will start at midday followed by a Barbecue. I hope all the keen golfers will call in to book a round straight away as there will be a limit.

Eli Lilly European School of Oncology, ACE Journalist Award.

The CEO, Gerald Edmunds, was a judge for this award. It carried a prize of $5,000 and a trophy. The winner and highly commended finalists were entered in the European Final that has a prize of $10,000 euros and first class trip for two to Vienna to collect the prize. Mr Edmunds is shown in the picture above with the Australian winner, Jill Margo of the Financial Review and Deborah Fitzgerald of Eli Lilly.

QUEENSLAND

The Foundation plans to renew its presence in Queensland. Considerable

Mr Gerald Edmunds, Jill Margo of the Financial Review and Deborah Fitzgerald of Eli Lilly.

interest came from many regional centres in the weeks leading up to Brain Awareness Week and each was provided with materials for displays and information about the medical data available through our two websites.

One letter of thanks for some information that I provided contained a poem from Paula Penrose of Toowoomba who is using our information to help others. She agreed that we could publish it.

Migraine

The pain in your head is horrendous,
You cope without much said,
Noise and light pose a problem,
Should have stayed in bed.

People understand when
they see a leg in plaster,
They cannot see migraine pain,
for sufferers, a disaster.

You don't say much about it,
To hide it is an art,
Looked on as a misfit,
From the very start.

We are human and intelligent,
it's the pain that gets us down,
To say you have a migraine,
upon us people frown.

We hope one day they will see the light,
Kind to sufferers, realize their plight,
Until such time please read this poem,
For migraine sufferers who remain
unknown.

This is why we keep trying to raise more funds for research. The following report indicates that the need for improved treatment of migraine and headache is getting more prominence internationally.

Report on Headache International Conference

Victoria's CEO, Margaret Smyth, represented the Brain Foundation at the World Headache Alliance (WHA) Convention in September 2003. I am able to say that the Brain Foundation, through its many years of involvement and experience in headache & migraine is well placed to take a lead role nationally and internationally, with improved coordination and partnerships with organisations and individuals affected by headache.

Margaret Smyth

Secondly, the XI Congress of the International Headache Society, Rome 13-16 September 2003 that followed the WHA Convention attracted 2,200 delegates. While this was a spectacular conference in size and organisation the general view from a number of neurologists and organisations was that it was disappointing as there were no new findings from a scientific perspective. This was replaced by a major debate about the efficacy of the top 7 triptans. But it was a great display of the breadth and strength of the international headache society.

World Headache Alliance Convention, Rome, Italy:

The Convention held 13-16 September in Rome scoped the global data on migraine for the Burden of Disease Study (epidemiological) commissioned by WHO and presented a best practice framework for headache policy and program development.

This comprehensive research and development was undertaken by director and Co-founder of WHA Dr Timothy Steiner, a leading UK headache doctor and researcher

And Dr Mathilde Leonardi, Paediatric Neurologist, Italian National Neurological Institute in Milan both of whom together with Dr Fred Sheftell Chairman of WHO (appointed by International Headache Society) were the key presenters. Dr Steiner said that this work would reach out to all layers of the audiences touched by headache - policy makers, neurologists and people affected by headache.

World Headache Alliance

The WHA consists of 40 organisations representing 26 countries. Australia is represented by the Brain Foundation and the WA Migraine Support & Severe Headache Group (incorporated) a part of WA Brain Foundation. The WA group is led by Beth Eggleston in a volunteer capacity. Beth is a newly elected councillor of WHA. The WHA call is for greater involvement with government agencies that have responsibility for international health policy to put in place strategies that will reduce the global burden of headache through a joint campaign to be launched in March 2004 in Copenhagen.

Key Issues for Brain Foundation:

A major objective of the WHA is on forming volunteer, self-help, patient and family support for those affected. This is a major development towards activities that include people more than relying just on organisations to speak on behalf of those affected. There are many great examples within the WHA membership of how organisations are partnering with the people in forming support groups and involvement in contributing to how these groups are formed. Getting the "people movement" off the ground and to be seen to be attracting membership is a powerful way of changing the dynamics towards reducing the burden.

VICTORIA

Headache & Migraine -

The Victorian Branch of the Brain Foundation conducted an information seminar on Headache and Migraine on April 3rd 2004 for sufferers and their friends and family. Presentations were given by Dr John Heywood, neurologist, and Dr John O'Sullivan, general practitioner. Dr Heywood spoke on Headache Management and Dr O'Sullivan spoke about Preparing for Doctor's Appointments. There were 52 participants who attended on the day and the feedback was that the session was very "interesting" and "informative" and reassuring. During question time a major focus was on medication:

Brain Foundation Victoria is conducting its second Headache and Migraine training seminar on June 5th 2004 as a professional development education session for general practitioners in partnership with the Epworth Hospital. Issues raised by the sufferers will be presented as part of the day.

Stroke

Plans are being made for Stroke Awareness Week 2004, which is in September. Last year we held two simultaneous Information Sessions, one at Caulfield General Medical Centre and one at Royal Talbot Rehabilitation Hospital. This year we hope to develop another information site, in addition to our existing partners.

These sessions are available to those people who have recently been discharged from hospital, rehabilitation and for those who are looking for support in preventing a secondary event. Carers and family member are included

1) Carer Support Program

The Brain Foundation Victoria Ltd receives funding from the Federal Government's Carers' initiative to provide an informative and supportive program for friends and family members who are caring for a relative or friend, who has had an acquired brain injury or degenerative neurological condition. We work in partnership with Australian Huntingdon's Disease Association; Motor Neurone Disease Association of Victoria; Multiple Sclerosis Society of Victoria; Muscular Dystrophy Association (Inc) and Parkinson's Victoria Inc and Villa Maria-Carer Services

As an educational and motivational tool, the program aims to raise carer's awareness of their rights and the importance of their role in the community. We recognise that caring is a critical role, requiring specialised knowledge, skills and commitment. It is often difficult and lonely work. This is often not a job of choice for most people so they have no idea where to begin or what to expect in the future.

The program also provides an opportunity to meet with other carers in a similar situation. This allows carers to develop peer support groups and networks; nothing is ever quite as frightening once you are no longer alone. One Carer said, *"this for me was a very rewarding experience where I benefited in confirming my role of a Carer, and knowing that I am not alone, and more importantly where I can seek further support"*

The program features a wide range of service providers and health care professionals who address key topics relevant to carers. These include presenting and discussing current research findings and self care strategies, coping with grief and loss and dealing with physical or behaviour changes. They provide knowledge of services, which can support the Carer, and the person they care for.

The program message is clear, supporting and educating carer's. This helps to reduce the emotional, social and health consequences of caring. One Carer reported that, *"my involvement in the program enabled me to discuss issues with doctors, family and friends with much more ease and confidence".*

2) ABI and Children

BFV has recognised that parenting a child with an ABI can bring joys and rewards as well as uncertainty and anguish. As such we are proud to announce that our "Parents Guide- Growing up with an ABI" is available on our **www.brainfoundation.org.au** and will soon be available in book form on the request of families and service providers. The guide aims to support and strengthen parents and other carers in meeting the challenges they face and to help them understand their child's special needs. Growing up presents its own unique challenges under the best of circumstances, an ABI interrupts and complicates this process. The guide aims to help parents build on their child's strengths and assists with a happy healthy and productive passage from adolescence to adulthood.

SOUTH AUSTRALIA

Lisa Taplin, Executive Director, Brain Foundation South Australia.

The South Australian Branch has just conducted a very successful lottery and introduced a new event for that state. The new event was an evening of debate between celebrity personalities. One team taking the "Brains" and the other the "Brawn". The chairman, Gerry Meggison believes that given a specific purpose to get together, people will contribute significantly to a good cause.

These successful events will add to an additional, tagged bequest from the Simpson family of $100,000, the returns from which are accumulated to be distributed every two years. This amount will be topped up with the proceeds from a special 70th birthday event for Mrs Simpson arranged by the Brain Foundation and SA was also planning a third, 'short' lottery for the first time.

SA is sorry to report that A/Prof Rick Burns had resigned from the Board after many years.

TASMANIA

Brain Foundation Tasmaina Ltd

Lynne Creswell, Executive Officer, Brain Foundation Tasmania.

Brain Foundation Tasmania has been fortunate enough to obtain a one off community grant from Department of Veterans' Affairs allowing the Brain Foundation to commence a Stroke Prevention and Support Program in rural areas of Tasmania. As you can well appreciate Tasmania has many small towns and people who have suffered stroke find it not only difficult but stressful to travel to major centres for support and information, eg Devonport Launceston and Hobart.

The stroke support groups which are for both veterans and residents gather together stroke people and carers from the community. Brain Foundation provides lunch and a guest speaker of interest, eg Public Trustee talking on Enduring Power of Attorneys, Community Police, Carer Respite Centre, and many other people of interest not just for the person who has had

the stroke but also the carers. The second stage to commence from the support groups are other specialised groups, eg art, gentle exercise, laughter groups and computer classes. I am hoping that volunteers within the community with this expertise will assist. I have no doubt that this will be readily available.

The prevention program entails travelling the state talking to community groups, support workers, hospital CEOs and anyone who wishes to learn about the prevention of stroke. Tasmania has developed a Stroke Support Kit that is copyrighted to Brain Foundation, Tasmania and consists of five sections regarding what happens to a person who suffers a stroke and the progression through hospital, rehabilitation and home. It also describes some of the areas of the body and mind affected by stroke which is of great benefit to the carer./family. Brain Foundation also has a number of handouts, brochures and other fact sheets on stroke.

My first stroke support group had already been established some seven years ago but was about to fold due to the illness of the dedicated volunteer who had been coordinating this group for that time. Brain Foundation stepped in and we now meeting on the third Tuesday of each month at the Punchbowl Christian Centre in Kingsmeadows. The time frame is 2.00pm to 4.00pm. There are approximately 40 members which includes carers. Other stroke support groups which Brain Foundation Tasmania has developed are in Deloraine for the Meander Valley region, meeting every third Monday of the month and on the East Coast of Tasmania, St Helens, Bicheno and Swansea.

During July/August the Huon Valley will be visited and the necessary meetings etc to commence groups there will be organised.

A migraine awareness program is being developed which we hope to take into secondary schools and colleges for not only the staff, administration staff but students and parents as well. Migraine is a common ailment which is often not easy recognisable by those who do not suffer.

Brain Foundation Tasmania is working hard in the community to help prevent stroke to as many people as possible by making them aware. The three "Rs" Recognise, React and Respond.

Lynne Creswell, Executive Officer, Brain Foundation Tasmania
Email: brainfoundationtas@netspace.net.au

Healthy Brain

by Gillian Gregory

There was an outline of the components of the complete Healthy Brain Programme in the last Newsletter. The seven parts were identified, but, for most people, following the seven-point plan will involve a change; doing something different to what you are currently doing. That is a big challenge for everyone. REMEMBER, you must do something different to get a different (better) result.

We will be expanding upon another part of the Healthy Brain Programme in the next issue. Please adopt the recommendations below by then so you will be ready to move onto the next one.

Healthy Brain

Brain Food

Point 3 of the Brain Foundation Healthy Brain Program

Research suggests that a diet for a healthy brain is very similar to a diet for a healthy heart.

The concept that dietary factors can influence cognitive function and subsequently the risk of dementia is growing. Current research suggests that antioxidant intake is associated with a lower risk of dementia. Saturated fat and cholesterol intake have been found to be associated with higher dementia risk[1, 2]. Many of the risk factors for AD, such as cholesterol and fat, and risk reduction factors, such as whole grain cereals and vegetables, are the same as those for ischemic heart disease[3]. A diet composed of the correct ratio of carbohydrates to proteins, as well as the inclusion of sufficient vitamins, (especially folate, vitamins C and E), and minerals (iron and zinc), is important not only to maintain general health but also to improve cognitive function[4, 5].

So, how do we optimise our diets for the sake of our brains. Outlined below are different foods and supplements believed to be important in maintain a healthy brain.

Things to look out for:

Facts:

Antioxidants include vitamin E, vitamin C, and beta carotene (a form of vitamin A), as well as other minerals and compounds found in food. These nutrients have been shown to help reduce oxidation, a process that can cause damage to cells and may contribute to aging, including the cognitive decline that typically develops with age.

Berries and Coloured foods:

Research by Dr Jim Joseph and collaborators from Tufts University in the USA, suggest that the dietary addition of berries, particularly blueberries, can help to improve cognitive performance. In his best-known set of experiments, aging blueberry-fed rats showed actual improvements on cognitive and motor-skills tests. "I call the blueberry the brain berry," says Dr Joseph, who attributes the effects to its antioxidant and anti-inflammatory compounds. Tufts scientists measured the antioxidant levels of 50 fresh fruits and vegetables, and found the highest levels in berries. Much of the antioxidant strength comes from the anthocyanin pigments that tint berries red, purple and blue. The darker the berry, the stronger the protective pigments.

Dr Joseph recommends eating a diet full of coloured foods. He eats 1-2 cups of blueberries a day and suggests that we all add berries to our diet. They can be both fresh and thawed, however try not to use the microwave, as this will remove any nutational value from the food. Other coloured vegetables and fruits believed to be beneficial to our cognitive performance are:

Green leafy vegetables - Spinach, Bok Choy etc; Plums, Avocado, Beetroot, etc; Other Berries: Black-, Rasp-, Straw-, Cran-berries

Fish:

A principal component of membrane lipids in the brain is the n-3 polyunsaturated fatty acid (PUFA) docosahexaenoic acid (DHA). High levels are found in the more metabolically active areas of the brain and it is important for neuronal function and viability. Fish has been found to be a direct source of preformed DHA.

Animal studies have shown that diets enriched with n-3 PUFAs increase neuronal functioning, whilst reducing ischemic damage to neurons. Behavioural studies on animals show superior learning and memory performance over animals fed control diets.

Population studies have shown that fish consumption has been inversely associated with the risk of incident AD. Those that consumed one fish meal or more per week had 60% less risk of AD than people who eat fish rarely or not at all 6. Eating fish has also been inversely associated with cognitive performance at middle age, indicating the

importance of the protective effect of omega-3 PUFAs throughout life 7.

Alcohol:

The strikingly low incidences of coronary heart diseases (CHD) in France, despite intake of a high-fat diet, (termed the "French Paradox") have been attributed to the consumption of red wine containing high levels of polyphenolic compounds. Polyphenols such as resveratrol, are only found in plants, are abundant in grapes and are generally known to possess potent antioxidant properties.

How do these compounds protect against the onset of diseases? The answer lies in their intrinsic biochemical properties. Scientists consider that the modification of fats such as cholesterol in the blood vessels is a prime factor in the initiation of heart disease. One such modification is oxidation. Grape and wine polyphenols possess the capacity to retard this process by acting as anti-oxidants.

In recent years, understanding the "French Paradox" has stimulated new research interest to investigate whether polyphenolic antioxidants may offer protective effects beyond the cardiovascular system, and whether polyphenols from other botanical sources may similarly offer beneficial effects to human health. Studies have found that resveratrol, an important component of grape polyphenols, shows protective effects on neuron cell death induced by alcohol and other oxidative agents 8. This would suggest that the protective mechanisms of polyphenols extend beyond the cardiovascular system, and that the moderate consumption of red wine, is not only good for the heart, but good for our brains too.

Vitamin and Mineral Supplementation:

As more and more people take multivitamin/mineral tablets, marketing hype and consumer confusion have increased. Of course, it's possible and preferable to get your nutrients from a healthy, balanced diet. However, surveys consistently show that large groups of people tend to fall short in a variety of key vitamins and minerals in their diets.

Reasons to consider taking vitamin supplements

- Many, if not most, people over 60 don't get the nutrients they need, for a variety of reasons. For instance, aging itself may make it more difficult to absorb and utilize certain nutrients. The major problem nutrients for older people are vitamins D, C, B-6, and B-12, and folic acid, as well as minerals such as zinc.

- Anyone else not eating a balanced diet (at least five fruits and vegetables a day, as well as whole grains, low-fat dairy, and small servings of lean meat, poultry, or fish) may not be getting enough folic acid, B-6, and B-12.

Some studies suggest that deficiencies of essential nutrients, especially vitamin B6, B12, beta-carotene and folates, and antioxidant deficiencies (vitamins E and C) are risk factors for cognitive impairment 9. Outlined below are some important vitamins and supplements that have been implicated in influencing cognition. The amount of supplements on the market promising to promote greater memory retention or stop cognitive decline is just enormous. It was impossible to investigate all of these different products, so instead the focus is predominantly on those vitamins and food groups that have been the subject of detailed medical research.

Vitamin A (Beta-carotene)

The ability of Vitamin A to enhance the aging brain remains to be determined. However supplementation of this vitamin could be considered a cheap and safe option to insure against cognitive decline. Vitamin A is fat soluble, but unfortunately can be toxic. The smart way to ensure that you're getting enough Vitamin A is through beta-carotene, which is converted in the body to Vitamin A. Beta-carotene is plentiful in vegetables and fruits, and is beneficial in this form. High levels of beta-carotene in the blood have been associated with better memory performance in the elderly population 10.

Vitamin B-12

Vitamin B-12 is very important for the brain, our nerves, and our blood system. People who are vitamin B-12 deficient can develop numbness, weakness, problems seeing, poor memory, confusion, tingling in the hands and feet, difficulty walking, and anemia (large red cells). The main risk factor for vitamin B-12 deficiency is being aged 60 or older, because as we age we are less able to digest and absorb B-12. Vitamin B-12 is found naturally only in animal foods such as liver, meat, poultry, fish, eggs, milk, cheese, and other dairy foods. Vitamin B-12 is not found naturally in plant foods such as fruits or vegetables.

From the Wellness Guide-University of California Berkeley (www.berkeleywellness.com)

In recent years experts have become more concerned about vitamin B-12 in people over 50 and those following a strict vegetarian diet. This vitamin is important to life and health, and to almost every cell and system, including the blood and the nervous system. If you eat moderate amounts of dairy products, fish, poultry, meats, and/or fortified foods, you probably don't need to worry about B-12. The liver is able to store large amounts of the vitamin, and even if you stopped consuming it for months, you would not become deficient.

Low levels of B-12 have been associated with increased risk of Alzheimer's disease and cognitive decline in a number of studies. Other research has shown improvements in cognitive function after B-12 supplementation 11.

Folate-homocysteine

Folates are vitamins essential components of the human diet and are produced by micororganisms and plants. Leafy vegetable, fruits, mushrooms, yeast and animal protein are all rich sources of folates. Prolonged cooking (more than 15mins) destroys 60-90% of a food's content of folates. In adult life folate deficiency is known to produce a form of anaemia known as "megaloblastic'. Degrees of folate inadequacy not severe enough to produce anaemia, have been found to be associated with high blood levels of the amino acid homocysteine. Elevated levels of homocysteine in the blood have been linked with the risk of dementia and Alzheimer's disease. The recommended daily intake is 100micrograms (mg) for adults which rises to 500 mg during pregnancy.

Epidemiologic findings suggest that high-calorie diets and folic acid deficiency increase the risk for Alzheimer disease and Parkinson disease. Studies of animal models of these disorders have shown that dietary supplementation with folic acid can reduce neuronal damage and improve behavioural outcome 12.

Studies in humans are still inconclusive and supplementation should only be used when the diet doesn't provide enough. In other words, make sure you diet consists of good amounts of vegetable, fruits and animal proteins.

Vitamins C & E

Studies looking at the supplementation with vitamin E have found mixed results, with some showing a delay in the onset of Alzheimer's disease, and increase resistance to oxidative injury associated with exercise 13, whilst other studies of patients with Alzheimer's disease and Parkinson's disease found that vitamin E did not offer any significant memory benefits.

Scientists have found vitamins E and C may protect the ageing brain - but only if taken together. The researchers from the Johns Hopkins University in Maryland, found that taking a combination of vitamin E and C seemed to have a protective effect. People taking both vitamins were 78% less likely to show signs of Alzheimer's than those not taking the combination. They found no

benefit from taking either of the vitamins in isolation, or from taking multivitamins alone.

BBC NEWS: Published: 2004/01/20
http://news.bbc.co.uk/go/pr/fr/-/2/hi/health/3409221.stm

Most multivitamins contain 100%, or even 200%, of the Daily Value of vitamins C and E, but this is not enough to provide the full antioxidant effects and other potential benefits of these vitamins. The University of California Berkeley's Wellness Guide recommends that everyone consume 200 to 800 IU of E and 250 to 500 milligrams of C a day and say that the best and easiest way to get these vitamins is in tablet form.

Ginkgo biloba

The ginkgo tree is believed to be the oldest living tree species. The active components of ginkgo biloba consist of flavonoids, terpenoids and terpene lactones (ginkgolides and bilobalide). The ginkgolides and bilobalide are unique to ginkgo biloba. The typical daily dose of ginkgo biloba is 120 mgs of dried extract in two or three oral doses. The standard ginkgo extract is known as Egb761.

Ginkgo biloba has been used in China as a traditional medicine for a range of conditions including asthma, bronchitis, heart dysfunction, for at least 5000 yrs. Dr Schwabe introduced Ginkgo biloba into Germany in 1965 where it is prescribed extensively for cerebral insufficiency, a diagnosis that can cover a range of conditions including memory and concentration problems, confusion, depression, anxiety, dizziness, tinnitus and headaches. It is believed that the medicinal properties of Ginkgo biloba are due to a combination of effects and that it acts by increasing blood supply by dilating bloody vessels, reducing blood viscosity, by modification of neurotransmitter systems and by reducing the density of oxygen free radicals. The main use is in the treatment of cerebral dysfunction. Ginkgo biloba extracts are prescribed for a number of symptoms, particularly memory impairment, in elderly patients. It is postulated that because of its pharmacological actions, this treatment could prevent the decline of cognitive function 14.

Many investigations to date have examined the cognitive effects of ginkgo in humans, but many of the research reports are in non-English publications or in journals with very restricted distribution, making assessment of the findings difficult. Studies with Alzheimer's disease patients have shown that those who receive ginkgo performed 10-20% better on various cognitive tests than did patients who received a placebo 15. Improvements were seen in attention, short-term memory and reaction time. A recent 6-week trial of ginkgo in a population of healthy aged individuals showed that ginkgo provides no measurable benefit in memory or related cognitive function. 16 An important question in regards to the treatment is whether the studies showing positive effects actually improved cognitive abilities in AD patients or merely slowed their deterioration. Further studies have raised the possibility that short-term, rather than long-term biological actions provide the basis for ginkgo's reported effects on cognition. Far fewer studies have examined the cognitive effects of ginkgo biloba on healthy young adults. Those that have show that improvements were at best only short term providing only minor support for the view that ginkgo may enhance cognitive functions in young people 15.

Cautionary Note:

The world of antioxidants is complicated. There are many types of antioxidants, and they do different kinds of work. What marketers of supplements never tell you is that not all of it is good work. Information on dietary supplements today comes far more from folklore than experimental findings. The US Food and Drug Administration does not regulate herbal treatments, meaning that manufacturers are not required to test the effectiveness or safety of their products. In Australia, many complementary medicines, which includes vitamins, minerals and supplements, are listed on the Australian Register of Therapeutic Goods (ARTG). Essentially, any product for which therapeutic claims are made must be entered in the ARTG before the product can be supplied in Australia. The ARTG is a computer database of information about therapeutic goods for human use approved for supply in, or exported from, Australia. Products assessed as being low risk (most complementary medicines) are assessed for quality and safety. In assessing the level of risk, factors such as the strength of a product, side effects, potential harm through prolonged use, toxicity and the seriousness of the medical condition for which the product is intended to be used, are all taken into account. This does not include those items sold over the internet from overseas.

It is important not to assume that any supplement "can't hurt, might help" or that antioxidants are always beneficial. The nutrients and other healthful compounds in foods work in a fine balance, which scientists are only beginning to understand. There's also a delicate balance between free radicals and antioxidants in the body.

It is therefore important that we eat a balanced diet, one with lots of fresh vegetables and fruit, fish and protein that will provide the vitamins and other nutrients that benefit our daily cognitive function. RDI of vitamins C and E are associated with reducing the effects of free radicals and B vitamins such as folic acid have also been shown to be beneficial for mental alertness.

In eating well we not only help to create a healthy body, but a healthy mind.

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A total of 24 grants were awarded last year so I have had to make an arbitrary selec tion.
Anne Cunningham, Editor

New Therapies for Neurological Injuries and Diseases Based on Neural Stem Cells

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The University of New South Wales

Background to the research project: Our experiments have two broad goals: firstly, to develop ways of grafting adult neural stem cells into brain and spinal cord to replace damaged neurones; and secondly, to potentially use this knowledge to activate the dormant repair mechanisms of brain and spinal cord in order to promote self-recovery, i.e., we hope we may be able to teach the nervous system how to self-repair.

Progress: A key question is whether the neural stem cells we are studying, which are harvested from the olfactory region, are committed to the olfactory lineage or, alternatively, have the potential to reconstitute neurones of many different phenotypes, e.g. dopaminergic neurones, cerebellar Purkinje cells or spinal motor neurones. In the first phase of this project, we have focussed on comparing neural stem cells from the olfactory system to central neural stem cells harvested from brain, regarding their growth factor requirements, pluripotentiality and progeny. These preliminary experiments have indicated that the olfactory neural stem cells appear committed to becoming cells of the olfactory lineage, under the conditions we have tested to date. We have exciting new data about their expression of growth factors and growth factor receptors, which we will now apply experimentally to modify their growth and differentiation.

Outlook: We are optimistic the basic research area described in this project will have relevance to the development of new therapies for brain and spinal cord injury, both traumatic and non-traumatic, and so ultimately benefit Australian patients.

Diagnosis and treatment of atypical benign paroxysmal positional vertigo.

Chief Investigator: *Dr Swee Aw*
Co-Investigators: *Prof. Michael Halmagyi, Mr Michael Todd, Mr Leigh McGarvie, Ms Grace Aw.*

Background to the research project: The aim of this project is to study the pathological activation of the balance or vestibular system in atypical benign paroxysmal positional vertigo that involved more than one semicircular canal, in order to improve diagnosis and thus treatment of this condition.

Benign paroxysmal positional vertigo, first described by Barany (1921) and popularised by Dix and Hallpike (Dix and Hallpike 1952), is now a curable, or at least controllable balance disorder. Its mechanism, otoconial debris moving in a semicircular canal duct resulting in abnormal activation of the semicircular canal receptors during changes in gravitational head position causing vertigo, abnormal eye movements or nystagmus and imbalance. It is the single most frequent disorder of the balance system; e.g. about 30% of ~2500 patients seen last year at the Royal Prince Alfred Balance Disorders Clinic were suffering from benign paroxysmal positional vertigo or its complications.

Techniques of three-dimensional eye movement vector analysis that my collaborators and I have developed with National Health and Medical Research Council project grant and Brain Foundation support over the last 5 years was applied to detect which semicircular canal was activated by the otoconial debris from the disease.

The progress had been excellent. We tested 41 patients with clinically diagnosed benign paroxysmal positional vertigo that had more than two unsuccessful particle repositioning treatments in the Balance Disorder Clinic. Eleven patients were found to have benign paroxysmal positional vertigo involving more than one semicircular canal. Four had bilateral posterior canal involvements, six had involvement of the lateral and posterior semicircular canals on the same side and one patient had involvement of both posterior canals and also one lateral canal.

The Brain Foundation funding enabled us to employ a third year UNSW medical student Grace Aw part-time to analyzed the three-dimensional eye movement data in order to determine which semicircular canals were affected by the disease. Using the diagnostic information we had learned, we were able to successfully treat the patients with the 2-axis rotator (Fig. 1). The manuscript titled: "Atypical positional nystagmus in benign paroxysmal positional vertigo: 3D study of 41 patients" has been submitted to Neurology and is currently under review.

Role of Insulin-Like Peptide-3 (Insl3)/Lgr8 Receptor System in Function and Survival of Key Thalamic Nuclei Damaged in Parkinson's Disease

Dr Andrew Gundlach, Howard Florey Institute, University of Melbourne, VIC.
Dr Jasmine Henderson, Dept of Pharmacology, University of Sydney, NSW.

LGR8 receptors in thalamic CM-Pf complex of rat and human

Insulin-like peptide-3 (INSL3) is a peptide hormone of the relaxin-insulin family that activates a former-orphan, G-protein-coupled receptor - LGR8. Leucine-rich repeat-containing, G-protein-coupled Receptors (LGRs) represent a unique group of receptors that mediate characteristic, long-lasting effects on cell activity. INSL3 has been shown to alter production of the cellular messenger, cyclic AMP and to inhibit 'programmed cell death' (or apoptosis) in cell lines and testicular germ cells. LGR8 gene expression was earlier detected in brain, but its distribution and effect on neuronal activity and/or survival have not been investigated.

In this respect, histochemical studies by Dr Gundlach and colleagues revealed the selective expression of LGR8 mRNA by

neurons in the parafascicular (Pf) complex and adjacent posterolateral nuclei of adult rat thalamus. Subsequent studies revealed similar or stronger expression of LGR8 mRNA in the same thalamic nuclei during postnatal development (Figure).1,2 In contrast, production of INSL3 gene/peptide by brain neurons located in areas that project to the centromédian-parafascicular (CM-Pf) complex in the thalamus has not be demonstrated, suggesting that brain levels of INSL3 may be very low and that INSL3 may act as a neurotrophic factor in brain, with effects on nerve survival mediated by long-lasting activation of LGR8 receptors by low concentrations of INSL3. Thus, our working hypothesis is that the INSL3-LGR8 system is associated with the regulation of neurons in the CM-Pf complex - now known from Dr Henderson's research to be selectively involved in the pathology of Parkinson's disease (PD).

We predict our studies* will demonstrate: (i) expression of LGR8 by neurons in CM-Pf in normal human brain and loss of receptor-positive cells in PD brains; (ii) effects of unilateral lesions of midbrain-dopamine and thalamic-glutamate pathways (or combined) on LGR8 expression in the Pf of rats; (iii) effects of INSL3 infusion into the Pf complex of normal/lesioned rats on different parkinsonian-like behaviours; and (iv) effects of INSL3 on the activity of LGR8-positive Pf neurons (Figure)1,2 and their survival and LGR8 expression. After optimising the surgical procedures, rats are currently being injected with saline or INSL3 (0.1-51µg in 1µl) unilaterally into the Pf to assess effects on behaviour. .

In addition, Dr Henderson's group have further characterised behavioural changes after CM-Pf lesions3 a and recently discoveredy of altered rotational behaviour after acute apomorphine challenge in parkinsonian rats with CM-Pf lesions, relative to rats with only 6-OHDA lesions. These findings suggest thats degeneration of the CM-Pf may affect a PD patient's likelihood of developing dyskinesias on L-dopa. anti-PD medication.3

**Colleagues assisting us in these studies include Katayoun Sedaghat (new PhD student, HFI), Dr Pei-Juan Shen (HFI), Haydn Allbutt (U Sydney), Prof Glenda Halliday (POWMRI) and Dr Kevin Phelan (UAMS, USA).*

Communications and publications arising from this Brain Foundation Australia-funded project

1. *Shen P-J, Fu P, Phelan KD, Sedaghat K, Scott D, Layfield S, Tregear GW, Bathgate RAD, Gundlach AL. Restricted expression of LGR8 in intralaminar-, posterior- and epi-thalamic nuclei of adult and developing rat brain suggests a role in sensorimotor systems. Relaxin 2004 Meeting, Wyoming, USA (submitted).*
2. *Shen P-J, Fu P, Phelan KD, Sedaghat K, Scott D, Layfield S, Tregear GW, Bathgate RAD, Gundlach AL. Restricted expression of LGR8, a relaxin family receptor, in intralaminar and other thalamic nuclei of adult and developing rat brain: Role in sensorimotor systems? SfN Meeting 2004, San Diego, USA (submitted).*
3. *Henderson JM. The thalamus and Parkinson's disease: Clinical, pathological and experimental observations. In: Scientific Basis of Treatment of Parkinson's disease. Galvez-Jiminez N (Ed). Pergamon, NY (in press).*

Trishomocubanes-Potential Neuroprotective Drug Therapies for Parkinson's Disease?

Dr Jasmine Henderson[1] and
Dr Michael Kassiou[1,2]
Department of Pharmacology1, University of Sydney and Department of PET and Nuclear Medicine2, Royal Prince Alfred Hospital.

Background

This proposal is concentrating on characterising the effects of a novel potential therapy using trishomocubanes, drugs which may prove to have both neuroprotective and antiparkinsonian properties using an animal model of Parkinson's disease. Neuroprotective drugs could halt the progressive death of cells which is part of the disease course in PD. By the time a patient dies, approximately 95% of dopamine-containing cells have died and this deficiency of dopamine is associated with symptoms such as muscle rigidity, tremor and slowing of movements. It may be possible in the future to administer drugs which could therefore slow the progression of the disease so that patients do not deteriorate as markedly over time. One such possibility are trishomocubanes which are drugs that have been shown to increase locomotion when administered to normal mice and which are structurally similar to some neuroprotective compounds the use of which, however, has been limited by toxicity. Until now, no studies have previously evaluated the effects of novel trishomocubane compounds on chronic parkinsonism. In this project, generously funded by the Brain Foundation, we are comparing two of the trishomocubane drugs in a rat model of Parkinson's disease.

Progress/Outlook

To-date we have:

1) Synthesised the drugs (Dr Kassiou).
2) Produced the model of Parkinson's in the rats and performed detailed studies to characterise the behavioural changes (Dr Henderson, Mr Haydn Allbutt). The rats are slower to react to stimulation, they have changes in posture and in locomotion (movement), changes which are are typical of those expected in this model and comparable to some symptoms of Parkinson's disease.
3) We have been administering the trishomocubanes to groups of parkinsonian rats and comparing the effects on parkinsonism using a range of different tests (including posture, balance, locomotion, reaction time) with rats treated with vehicle (solution containing no trishomocubanes).
4) So far we have found that trishomocubane CTDP32108 has biological activity at two different doses (1mg/kg and 3mg/kg) in our model. We have not experienced any major toxicity problems. The main effect is on locomotion and we are currently investigating this in more detail in the animals. Whilst preliminary, we are feeling optimistic since this is the first time this has been demonstrated in a chronic animal model of Parkinson's disease.
5) Upon completion of the behavioural study we will examine the brains of treated vs untreated animals for evidence of neuroprotection (decreased cell loss).

Migraine and Stroke – Are There Common Risk Factors?

Chief Ivestigators
Professor Lyn Griffiths, Director, Genomics Research Centre, Griffith University
Dr Rod Lea, Research Fellow, Genomics Research centre, Griffith University
Assoc Professor John MacMillan, Clinical Geneticist, Royal Childrens' Health Service, Brisbane

Lay Summary:

Migraine is a painful disease affecting millions of people worldwide. Suffering from migraine significantly increases ones chances of also suffering a stroke in later life. Both migraine and stroke are known to involve predisposing genes. Our research will determine whether the same defective genes are responsible for causing both migraine and stroke. Identifying the defective genes that are common to both of these important diseases, may provide valuable clues about their cause and how best to treat and prevent these disorders.

Project Outline:

Migraine is a painful, debilitating neurovascular disorder that affects at least 12% of the Caucasian population. Migraine has a strong genetic basis, although at present the number of genes involved in the disorder has not been defined. Epidemiological studies have consistently shown migraine to be a risk factor for cerebrovascular disease (stroke), particularly in females. Indeed, certain pathophysiological features of a migraine attack, such as neurological disturbances, reduction in cerebral blood flow and headache are also characteristic of a stroke episode. This leads

to the hypothesis that the genes implicated in risk of stroke may also influence migraine susceptibility. We will test this hypothesis by utilising a novel stroke-related, multilocus genotyping assay in a large group of migraine sufferers (n=600) and unaffected controls (n=600). We will determine whether stroke-related genes also influence migraine, by undertaking gender-specific, clinical severity and genetic interaction analyses. By identifying the stroke-risk genes that also predispose to migraine, our research may provide valuable clues to the shared molecular mechanisms that increase susceptibility to both of these diseases. In turn, this may allow predisposed individuals to receive more effective patient-specific treatment for migraine and important presymptomatic risk assessment for stroke.

Progress:

This study supported by the Brain Foundation involves an analysis of the MTHFR gene as a risk factor for migraine. We are currently investigating an MTHFR gene variant in a large case-control population of ~1200 individuals. Currently we have genotyped most of these samples and are now undertaking statistical analysis of the results. We have also commenced investigation of a second MTHFR mutation and are genotyping this marker to provide more data regarding MTHFR variation in migraine. This large dataset will provide adequate statistical power to also allow us to undertake detailed gender-specific and clinical severity analyses. We have also undertaken interaction analysis of the original MTHFR gene variant with another variant in the ACE gene. These results indicate that the two DNA markers are causing an interacting effect. Our initial MTHFR results have just been published, as shown below [1] and our MTHFR-ACE interaction paper is now under review [2].

Our results are in strong support of a role for the MTHFR gene in migraine susceptibility and they also indicate that other genes are influencing this risk. We are currently continuing to finalise these MTHFR studies but are also trying to find a commercial partner to aid in clinical trials. The MTHFR gene mutation results in higher homocysteine levels and it has previously been shown that additional dietary folate and increased Vitamin B levels can have a important effect reducing these levels. Since the MTHFR mutation has been implicated in migraine susceptibility, it is possible that appropriate dietary additions could also influence migraine onset and severity. We are hence, hoping to extend our genetic MTHFR studies to see if there are real clinical implications from these results.

Publications:

[1] Lea, R.A., Ovcaric, M., Sundholm, J., MacMillan, J. and Griffiths, L.R. 2004. The methylenetetrahydrofolate reductase gene variant C677T influences susceptibility to migraine with aura. BMC Medicine 2:3, 1-8

[2] Lea, R.A., Ovcaric, M., Sundholm, J., MacMillan, J. and Griffiths, L.R. 2004. Genetic Varients of Angiotensin Converting Enzyme and Methylene Tetrahydrofolate Reductase May Act in Combination to Increase Migraine Susceptibility. Molecular Brain Research (submitted 01/04/2004).

Related publications:

Heux, S., Morin, F., Lea, R.A., Ovcaric, M., Tajouri, L., and Griffiths, L.R. 2004. The methylentetrahydrofolate reductase (MTHFR) gene variant (C677T) as a risk factor for essential hypertension. Hypertension Research (under re-review 27/05/04)

Tajouri, L., Martin, V., Gasparini, C., Ovcaric, M., Curtain, R., Lea, R., Csurhes, P., Pender, M.P., and Griffiths, L.R. 2004 Genetic investigation of methylenetetrahydroxyfolate reductase (MTHFR) and catechol-o-methyl transferase (COMT) in multiple sclerosis. Journal of Neurological Science (under review 26/01/04)

Does Increased Activity of the Sodium-Calcium Exchanger Ion Channel Protect the Brain from Stroke?

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Background to Project

The sodium-calcium exchanger (NCX) is a membrane ion transporter protein responsible for regulating intracellular calcium levels. There are three NCX genes, NCX1, NCX2 and NCX3 and multiple splice variants that give rise to different NCX isoforms. The exact role of the different NCX isoforms in neurons under normal and pathological situations, such as stroke/cerebral ischaemia is not fully understood. We have previously demonstrated up-regulation of NCX in the rat brain following global cerebral ischaemia. As the NCX has a key role in calcium transport in neurons and as deregulation of intracellular calcium homeostasis is a pivotal event in ischaemic neuronal injury determining the role of NCX in cerebral ischaemia/stroke is important.

The specific focus of this project is to generate transgenic mice overexpressing NCX in the brain. These animals will then be used to determine whether NCX has a neuroprotective or a neurodamaging role following stroke. The demonstration that NCX activity enhances neuronal survival or exacerbates ischaemic neuronal injury will provide a rational therapeutic target for the development of drugs to reduce neuronal injury following stroke.

Progress - Outlook

NCX transgenic mouse

In order to assess the role of NCX overexpression on neuronal outcome following stroke we will generate a transgenic mouse. The NCX transgenic mouse will be produced by Ozgene, a Western Australian company specialising in the production of transgenic and knockout mice. We have selected the NCX2 isoform as the transgene to be overexpressed, as this is the major isoform in the brain. In addition, at a recent conference (American Neuroscience Meeting, November 2003) another laboratory reported increased brain damage following stroke in a NCX2 knockout mouse. Therefore experiments with our NCX2 transgenic mouse will complement the NCX2 knockout findings and delineate whether increased NCX activity is neuroprotective following stroke.

With respect to the NCX2 isoform we have cloned its cDNA and inserted it into a custom built expression cassette. The expression cassette consists of the Rous sarcoma virus (RSV) promoter and the woodchuck post-transcriptional regulatory element (WPRE). We have found the RSV promoter to produce strong gene expression in neurons and the WPRE to enhance gene expression. We are currently in the process of amplifying the NCX2 expression cassette in order for Ozgene to commence generating the NCX transgenic mouse, which takes 13-16 weeks.

Mouse stroke models

In readiness to perform the stroke models on the NCX transgenic mice, Dr Sharon Lee, a Masters student in our laboratory has been working to establish the focal and global cerebral ischaemia stroke models in mice. This has involved modifying the surgical procedures we use in our laboratory to induce focal and global cerebral ischaemia in rats. Sharon also spent time with Dr Peter Crack from the Monash Institute of Reproduction and Development in Melbourne to further gain experience in performing the mouse stroke models. Once the mouse stroke induction techniques have been established and the transgenic mice are available, Sharon will assess whether NCX transgenic mice have increased or decreased brain damage compared with wild type mice following stroke.

Up to Date Records

We are currently updating our records. In particular, we are trying to get as many Email addresses as possible, so that, if you chose, we can send you information electronically - for example, your copy of Brainwaves. This will cut our costs and leave more money for our research, carer and education programmes. The information we would like are the contact details on the separate appeal page.

If you still have the envelope in which Brainwaves was delivered, you will see that on the top line there is a code that started with "BW0401 / XXXX" where "XXXX" represents the number by which we can identify you in our computer records.

Please add this number to the address details in the separate appeals page, and kindly consider making a donation when you confirm your address and phone details.

And there's MORE. If you subscribe to our website, you will have access to the discussion forums, regular notices about advances in research and treatments and "wellness" programmes that we are introducing.

In Memoriam

The President and Directors pass their condolences and gratefully acknowledge gifts in memory of the following:

Vinko Bozanic; Bob Derry; Alice Halmagyi; Maria Coffa; Lois Webster; Anthony George; Carlo Pepicelli; Joy Porter; Vera Lena Kennon; and Cameron Urquhart

The board is also grateful to the following who have donated to the Foundation in private memory of their late family members and friends. They are:

Mary Agius; Gerard Ailan; Jeanette Bard; Oliver Baldry; Vic Burgess; Child Family; Margaret David; Mr S Hill; James Montgomery: Mary Morton; Lucy Rosani and Charlie Green; Frances Timothy Russell; Sydney Shepley: and Tony Sullivan.

The board also is grateful for the donation from, "Physiotherapists 'Year of '64'

Please contact us for more information about bequests and please consider nominating a donation to the brain foundation as your preferred tribute for loved ones.

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