The Annual Research Awards Function held in The Great Hall at Sydney University on the 27th September was a highlight of the Brain Foundation’s activities and this year was marked by a number of changes. First, the Board decided to raise the amount to be considered of the order of $40,000 for each project in order to provide more meaningful levels of support for the successful projects. This meant that competition for funding was intense from the 78 applications. It is envisaged the funding base will be gradually lifted over the coming years thereby increasing the number of grants awarded. It was very pleasing that Parkinson’s NSW contributed funds to the pool for our national scientific committee to adjudicate in that area.

This year, after many decades of selfless and highly professional contributions, both Professor Jim Lance AO CBE and Dr Kevin Bleasel AO handed over to members of a renewed national scientific research committee. The committee is chaired by Professor Michael Halmagyi. Professor Halmagyi and Professor Nick Dorsch were joined by Professors Elsdon Storey of Melbourne, John Willoughby of Adelaide and Pamela McCombe of Brisbane.

The committee deliberated according to the following process. After an initial round of ratings, the applications were graded into rankings, they were then reviewed to reach consensus about the finalists. More details about the projects and support teams are shown on the web site. An overview follows with some photographs from the Awards Function. The awards were introduced and presented by Professor Jim Lance AO CBE who described the projects in lay terms for the benefit of the many non-medical people present.

Associate Professor Roger Pamphlett, Consultant Neurologist, Department of Pathology, The University of Sydney, NSW was awarded funding for research into Somatic mutations in Motor Neuron Disease. The research group has set up an Australia wide DNA bank to look for genetic differences in people with MND. A tissue bank will look at changes in cells. The hope is to find genetic changes so that future attempts at gene therapy can be made.

Dr Mark W Parsons, Department of Neurology, John Hunter Hospital, Newcastle, NSW. Awarded for his project on Stroke which investigates: Supplementary oxygen for acute ischaemic stroke: an imaging-based efficacy trial (SOS Trial).

Dr Peter Lock, Department of Surgery, University of Melbourne, Royal Melbourne Hospital, Victoria, awarded a grant to conduct research into tumours with a Pilot Study to evaluate the role of Tks5 in malignant glioma invasion.

FROM THE PRESIDENT – Professor Philip Thompson

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Dr Peter Lock, Department of Surgery, University of Melbourne, Royal Melbourne Hospital, Victoria, awarded a grant to conduct research into tumours with a Pilot Study to evaluate the role of Tks5 in malignant glioma invasion.
Dr Geoffrey A Lambert, Department of Neurology, Prince of Wales Hospital, Randwick, NSW was awarded a grant to conduct research into whether migraine is triggered by a Cortico-Brainstem connection.

Associate Professor David Finkelstein’s grant is to investigate Clioquinol as an adjunct therapy with L-dopa in a novel animal model of Parkinson’s Disease. His co-investigator is Dr Robert Cherry also from the Mental Health Research Institute at Parkville.

Spinal cord cysts form in patients with spinal cord injury and patients with certain types of congenital brain or spine abnormalities. These cysts cause spinal cord damage, but the origin of the fluid in the cysts remains largely unknown. One theory is that fluid leaks out of blood vessels around the cysts. The researcher’s current work is aimed at determining whether such fluid leakage does contribute to cyst formation or enlargement.

Dr Kay Double, NHMRC Senior Research Fellow, Prince of Wales Medical Research Institute, Randwick, NSW, was funded for research into Peripheral isoprenoid changes in Parkinson’s Disease.

The Awards Function was also a milestone for the Brain Foundation because Professor Lance announced that he would resign from the Board at the end of this year. That will end a remarkable 36-year continuous association from being an inaugural director in 1970. Over those many years Jim’s prominence in his profession grew to international standing but he still found time to serve both the Brain Foundation and the Australian and New Zealand Association of Neurologists (ANZAN), the latter as President from 1978 to 1981. In so doing, Jim has built and maintained the very important links between the two organizations.

I wish you all the best seasons greetings and hope that you will give consideration to the Christmas Appeal included with this newsletter.

Philip Thompson
President, Brain Foundation

Associate Professor Marcus Stoodley, Institute of Neurological Sciences, Prince of Wales Hospital, Randwick, NSW was awarded funding to investigate whether a deficient blood-spinal cord barrier contributes to post-traumatic syringomyelia?

STATE OFFICES

Good Health and Beauty Show

The Brain Foundation was again sponsored by the Pharmacy Guild to have a stall at the Good Health and Beauty Show in Darling Harbour in June 2006, run by the Pharmacy Guild of NSW. Attended by some 10,000 visitors and with more than 100 exhibitors over three days, there were lots of opportunities for the Brain Foundation to meet with other exhibitors, sponsors and members of the public and raise awareness of Headache Australia.

Connie Digolis, Manager of the Brain Foundation, Tasmania, is shown giving a presentation about A Healthy Brain which proved a great success to visitors to the show.

Broken Hill Neurological Support Group

Pro Hart, the widely acclaimed artist and inventor was a supporter of the Broken Hill Neurological Support Group which is led by well known local identity, Jamie Mitchell and is sponsored by the Brian Foundation. It was therefore a sad trip to Broken Hill to farewell Pro when he succumbed to Motor Neurone disease. Pro’s iconic Rolls Royce is pictured outside the Broken Hill Entertainment as his casket is being brought out at the end of the State Funeral Service.
The Annual Women of Achievement Awards

This event was organised by the Brain Foundation’s Victorian subsidiary and was a great success again this year. The winner was Claire Vickery from The Butterfly Foundation. The luncheon was attended by National Executive Director, Gerald Edmunds and the Executive Director from SA, Lisa Taplin and Tasmania, Connie Digolis. Lisa is shown with Izabella Kobyłanski, Director Planning Results, Melbourne and Frances Cummings, Adaps Recruitment Melbourne at the luncheon.

Fundraising and Sponsorship

The efforts of every donor to the Foundation are all greatly appreciated irrespective of the amount for we know that you all support us to the maximum that you can and we will be grateful if you will kindly consider making a donation with the appeal sheet enclosed. For those who are working, one of the most cost effective ways to donate is by taking advantage of pre-tax giving. That way, by giving a monthly amount from pay, the tax deduction is given straight back to you so your cost is minimized and the Brain Foundation accumulates a greater amount over the year than one person would usually give in a single donation.

Recently, there have been some special fundraising activities showing great courage and determination from individuals that I hope will be of interest. Some recent success stories: Noa Olian, 22 from Sydney, accomplished a very personal challenge to complete a Half Ironman in Busselton, Western Australia on the 6th May, 2006 to raise money for Parkinson’s disease, a condition very close to her heart as her father was diagnosed in June of last year. The Half Ironman is a triathlon consisting of a 1.9 km open water swim, followed by a 90 km bike ride followed by a 21.2 km run. Her feat is all the more remarkable because she had not been involved in athletic pursuits before and was not a confident swimmer, runner or cyclist.

World’s Youngest Donor

Baby Gilbert Ernest Jones very kindly asked that donations be made to the Brain Foundation instead of gifts for him at his Christening. He is named after his grandfathers who were both sadly lost to neurological disorders.

Fiona’s Sutherland’s Marathon

Fiona kindly used her participation in The Sydney Marathon to attract donations to the Brain Foundation. This is her story.

“This is my first marathon, all 42km’s of it. I have often thought of doing a marathon as I enjoy running, but have not actually committed to one until now. Hopefully it won’t be my last either!”

All money raised is going to go towards research for Parkinson’s disease and brain tumour and the funds raised are being matched by a generous donation from the Macquarie Bank Foundation.

Headache and Migraine

Our web site, headacheaustralia.org.au has recently been upgraded with the help of funds from Janssen – Cilag. There is new information that examines ways of better managing headaches and migraines and discusses preventative measures. We are looking into complementary therapies and drug-free treatments where some positive results have been obtained. Please re-visit the site if you have not done so recently and, if you are not a member of Headache Australia, please consider joining to help us get more leverage when applying for funds for research into headache and migraine.
CLASSICAL MUSIC LOVERS CAN HELP

The Brain Foundation is fortunate that internationally acclaimed concert pianist, Ambre Hammond (pictured) has nominated the Brain Foundation as one of the charities that she promotes.

The Brain Foundation will benefit from our Brainwaves readers purchasing one or more of her CDs. One disk is Rachmaninoff’s Piano Concerto No. 3. This was recorded at a concert in Argentina given by Ambre when she was 17.

The other CD, referred to as the “Liszt CD” is called ‘Devotion’ Solo Piano music by Franz Liszt recorded when Ambre was 16. It includes favourites such as Liebestraum, Hungarian Rhapsody No. 2 and the ‘Dante’ Sonata. The CDs are $25 each including postage and you will be helping to fund research that is searching for cures to neurological disorders. To purchase, ring 1300 886 660

SOUTH AUSTRALIA

A central role of Brain Foundation (SA) is to fund research. This year we are funding four neurological research projects and have also provided two financial scholarships for the support of two people with brain related disorders to continue their post-secondary education within South Australia. It is through the support of our generous donors and our bi-annual lotteries that this worthy work can continue. As our major fundraiser, each lottery takes approximately three months to conduct. Our current lottery will be drawn on 5 December 2006. Through the lottery process we are also able to raise awareness of brain related diseases and disorders and the importance of research.

This year the four successful research grant award recipients are:

Dr Peter Coyle  Zinc treatments modulates genes associated with foetal alcohol related neurological deficits.

Dr Gabrielle Todd  Identification of early markers for Parkinson’s disease.

Dr Emma Parkinson-Lawrence  The molecular basis of neuropathy in lysosomal storage disorders.

Dr John Semmler  Cortical control and fine motor skills in older adults (see report below)

The Sir Charles Bright Scholarship Trust

The Sir Charles Bright Scholarship Trust was established in 1983. It was designed to provide financial scholarships to people with disabilities who are undertaking post secondary education within South Australia, at either university, TAFE or other recognised educational institutions. Each year the Brain Foundation (SA) funds two scholarships to assist two students with a brain injury.

This year the Brain Foundation (SA) Scholarships were presented by the Hon. Jay Weatherill MP, Minister for Disability at a ceremony at Old Parliament House. The recipients were Miss Emma Sinclair and Miss Alicia Uzumcu.

Miss Emma Sinclair suffers from Autism and intends on completing a TAFE certificate in Baking. Miss Alicia Uzumcu is 20 years old and has Cerebral Palsy. This scholarship will help assist her pay for education fees when she undertakes her TAFE studies.

Alicia Uzumcu shown right with the Honorable Jay Weatherill, Minister for Disability at Old Parliament House, Adelaide.

Professor Donald Simpson AO - Committee Member 1979-2006

Professor Donald Simpson AO joined the Brain Foundation Committee in 1979. This certainly led to exceptional commitment and contribution to the interest of the Foundation over the years. In addition to his dedication to the general Committee structure, he has been a member of the Scientific Advisory Committee responsible for the assessment of research grants for the Brain Foundation South Australia. Professor Simpson also acted as its Chairman for many years and the results have led to many truly deserving individuals having an opportunity to spend valuable time in their chosen area of expertise with the hope of adding value to the medical profession.

We are sorry to lose such a greatly respected individual and we wish him the very best in his retirement.

Dr Ahmad Hanieh
Department of Neurosurgery, Women’s and Children’s Hospital and University of Adelaide

South Australian Committee of the Brain Foundation expresses appreciation for the contribution of Dr Hanieh to its Scientific...
Advisory Committee over many years. Dr Hanieh recently retired from the Committee for health reasons. The Brain Foundation benefits greatly from the contributions made by the members of its committees and Dr Hanieh’s contribution has been an important and appreciated one.

**PROGRESS REPORTS ON BRAIN FOUNDATION AWARDS 2005**

In 2005 the Brain Foundation awarded research grants into a number of Neurological studies, including, Parkinsons Disease, Stroke, Schizophrenia, Migraine and Tumour. We are delighted to announce feedback on those ongoing projects.

Chief Investigator: Dr. Rogan Tinsley, Howard Florey Institute, University of Melbourne. Co-Investigator: Prof. Malcolm Horne, Deputy Director (Research), Howard Florey Institute.

**Research**: Development of dopamine D2 receptor knockout mouse as a new animal model of Parkinson’s Disease

The Brain Foundation Grant, awarded at the end of 2005 has provided seed funding for a project examining the molecular causes of Parkinson’s Disease (PD). This disease, most recently given prominence by Michael J Fox, exacts a terrible toll on patients, causing muscle rigidity and tremors. These symptoms stem from the death of nerve cells which produce dopamine. Unfortunately, the cause is still unknown, and our current treatments only address the symptoms of the disease.

The aim of this project was to investigate the changes which occur in dopamine nerve cells, and to examine what makes them vulnerable to death. We have chosen to tackle this problem using a mouse model of Parkinson’s disease. Evidence gathered in the last 12 months indicated that this has been successful. We have shown, for example, that oxidative stress, caused by blocking the cells’ ability to remove free radicals, can cause aggregates to form in the nerve cells of D2 knock-out mice. Protein aggregates are one of the hallmarks of human PD. This work is continuing, and we look forward to further progress next year.

**Dr Kathryn Buller** Perinatal Research Centre, School of Medicine, University of Queensland. Co-investigator: Associate Professor Simon Firfer, Prof. Michael Morgan and Dr Naresh Ramakrishnan of Royal North Shore Hospital.

Funded for research into long-term neuroprotection in the preterm brain: Targeting neuro-inflammatory mediators to reduce white matter damage induced by a hypoxic-ischemic episode.

Hypoxia-ischemia is a major cause of brain injury in the fetus and neonate. A defining feature of hypoxia-ischemia-induced injury in the preterm brain is white matter damage and the periventricular leukomalacia that can develop is a pathological correlate for cerebral palsy. Cerebral palsy occurs in 2.5 per 1,000 live births with the most important risk factors being a hypoxia-ischemia and premature delivery (<37 weeks gestation). It has been estimated that 5-15% of children born preterm will develop cerebral palsy. Our research has been focussing on the mechanisms responsible for the heightened susceptibility of white matter injury in preterm infants exposed to hypoxia-ischemia. We utilise a hypoxia-ischemia model in the rat to determine how inflammation in the brain may contribute to the demise of oligodendrocytes and their progenitors and the subsequent loss of myelinated fibre tracts in the brain. Oligodendrocytes are specialised cells in the brain that form the myelin sheaths around axons and aid conduction of signals in the brain. Hypoxia-ischemia induces excessive release of proinflammatory cytokines and these neuroinflammatory mediators can exacerbate white matter injury. We have been investigating how the early forms of oligodendrocytes, the O1 and O4 progenitor cells, are affected by inflammatory processes in the brain after hypoxia-ischemia. During a hypoxic-ischemic episode, major sources of proinflammatory cytokines in the brain are activated microglia.

A hypoxic-ischemic episode switches resting microglia into an active state and one of the earliest events to occur after hypoxia-ischemia is the appearance of abundant numbers of activated microglia in and around ischemic white matter sites. We have found that activated microglia are still present in the white matter of the brain up to six weeks after hypoxia-ischemia in the immature rat. There is also associated disruption and loss of myelin at this time. In attempts to prevent this white matter damage occurring, we have also been examining whether blocking inflammatory mediators (using ibuprofen) and the microglia themselves (using minocycline) can prevent the loss of oligodendrocytes in the
The outcomes of this study will be particularly relevant in identifying therapeutic interventions that could benefit preterm infants presenting with symptoms indicative of hypoxic-ischemic damage.

**Chief Investigator Dr. Darryl Eyles** Queensland Centre for Mental Health Research; School of Biomedical Sciences; The University of Queensland; Brisbane, Qld
Co-investigator Dr. Tom Burne; Queensland Centre for Mental Health Research; Neurobiology Program, Institute for Cell and Molecular Therapies, Griffith University, Brisbane,

**Research** The impact of low maternal vitamin D on learning and memory in adult offspring. An Animal model of Schizophrenia.

The researchers are developing a model of maternal vitamin D depletion in order to understand the increase in winter/spring births associated with this disease. In 2005 funding from the Brain Research Foundation allowed us to purchase two Gemini fully automated shuttle box avoidance systems from San Diego Instruments CA. USA (depicted here). We have used this equipment to establish 4 cognitive paradigms in rats; one trial inhibitory avoidance, latent inhibition, passive avoidance and light / dark preference as well as learned helplessness in mice. This equipment is now in heavy demand being used on alternate weeks by for a number of projects in our laboratories.

Preliminary data indicating behavioural deficits in our model are promising and we hope to publish these data in early 2007.

**Research** A randomised controlled trial of two serum magnesium concentration targets in the management of intensive care patients with aneurysmal subarachnoid haemorrhage

Chief Investigator: **Dr. Celia Bradford**, Intensive Care Unit, Royal North Shore Hospital

Subarachnoid Haemorrhage occurs when a brain aneurysm ruptures and bleeds. This may be complicated by vasospasm (narrowing of the blood vessels) which if severe may cause a stroke. Magnesium is a chemical found naturally in the blood. This trial is investigating if a normal level or a high level of magnesium is better at reducing the occurrence and severity of vasospasm and may improve recovery in this condition.

Modern intensive care treatment for subarachnoid haemorrhage involves repair of the aneurysm, blood pressure control, the use of drugs and fluids to maintain blood flow to the brain, the use of a drug called nimodipine to prevent vasospasm, and sometimes surgical placement of a monitor of intracranial pressure.

Despite all these measures the patient may still suffer vasospasm and if uncontrolled could lead to permanent brain damage or death.

The magnesium concentration in the blood of patients who have suffered a subarachnoid haemorrhage is always monitored and corrected but the best level to which the magnesium concentration is raised is unknown. In some hospitals the magnesium concentration is maintained at the normal level whilst in other hospitals the concentration is kept slightly above normal levels.

There have been over 50 patients with subarachnoid haemorrhage included in the trial to date. There are two centres taking part: Royal North Shore Hospital and Royal Hobart Hospital. The aim is to recruit 180 patients.

**Research Project** Organotypic Mesencephalic Dopamine (DA) cell cultures; Studies of Cell Death in Parkinson’s Disease.
Associate Professor James Temlett.

**Introduction**

Parkinson’s Disease is a slowly progressive neurodegenerative disorder characterised by the primary loss of dopamine cells, with is a minimum of 50% loss in the substantia nigra (SN) and 80% of striatal (ST) dopamine before symptoms appear. Common pathological hallmarks of Parkinson’s Disease include Lewy bodies (LB), which are observed in the SN pars compacta (SNc) and pigmented brain-stem nuclei in Parkinson’s Disease patients. LBs mostly contain a neuronal presynaptic protein a-synuclein, which aggregate marking damaged dopamine cells. The aetiology of Parkinson’s Disease remains largely unknown but is believed to be due to a combination of genetic and environmental factors.

**Cell Death**

Oxidative stress (OS) has been implicated in the degeneration of DA cells in SNc of Parkinson’s Disease patients. An increase in DA turnover leads to an elevation in peroxide formation, this along with high levels of reactive iron produce hydroxyl formation thus contributing to free radical generation. In Parkinson’s Disease patients there is also a reduced level of glutathione leading to a decrease in the efficiency of hydrogen peroxide clearing thus contributing to further OS. These stressors can disrupt lipid membrane integrity, inhibit mitochondrial respiration via complex I inhibition, and result in cell death.

Neurotoxins such as 1-methyl-4-phenyl-1,2,3,6 tetrahydropyridine (MPTP) and rotenone induce apoptotic cell death. Both toxins induce behavioural and motor symptoms consistent with fully developed Parkinson’s Disease and respond to anti-Parkinson’s Disease drugs such as levodopa/carbidopa and DA agonist drugs. Both toxins induce DAergic cell death in the SN and ST both in vivo and in vitro by producing high levels of reactive oxygen species and hydrogen peroxide.
So far only rotenone has shown to result in intraneuronal fibrillar inclusion containing ubiquitin and α-synuclein, which is similar to human LBs.

**Neuroprotection**

Neuromorphic factors (NTF) have been shown to promote differentiation and growth of neurons. In particular, nerve growth factor (NGF) and glial cell-derived NTF (GDNF) are potent promoters of survival and differentiation of DA in vivo and in vitro. Interestingly, GDNF is capable of providing protection against toxins such as rotenone and MPTP. Growth factors enhanced dopamine cell growth and provide potential treatments in PD, such as successful gene therapy and cell implantation strategies.

**Experimental aims**

We have since 2000 established the growth of DA cells using organotypic culture and study the effects of rotenone and GDNF.

**Methods**

Using the technique as described in Ostergaard et al., 1990 & Plenz et al., 1996; postnatal rat brains to yield mesencephalon (VM) & striatum (ST) were employed. A blade slices brain tissue at 300μm ST slices and 200μm VM slices, before placing each tissue section 1 mm apart on 11 x 22 mm coverslips (Figure 1).

The coverslips are then placed in a flat bottom culture tube under medium and inserted into a roller drum in an incubator set at 36.5°C, for 14 to 48 days. The cultures are fixed every week and stained for tyrosine hydroxylase (TH), a marker of viable DA cells.

**Results**

**Experiment 1**
Indications are that optimal DA cell growth was between weeks 3 and 4 DIV.

**Experiment 2**

Cultures at weeks 1 were added with a range of different MPTP and rotenone concentration for 24 hrs then fresh media was added following day and left to recover. Consecutive weeks post toxin treatment a number of cultures were fixed and stained with TH to observe the DA cells recovery after an insult of OS.

A trend was observed with higher concentration of toxins inducing lower numbers of TH positive cells during recovery period. The young cultures such as 2 weeks or less seemed to be less affected at lower doses of toxin concentration. As for the older cultures between 3 to 4wks, no significant effect at 10-50nM, 1-50μM concentrations was observed when compared to controls and lower doses of toxins.

**Cortical control and fine motor skills in older adults**

**Investigators**

Dr John G. Semmler
and Assoc. Prof Michael A. Nordstrom

Discipline of Physiology & Research Centre for Human Movement Control. School of Molecular and Biomedical Science

The University of Adelaide
RESEARCH

Project Description
Along with a decline in muscle strength, healthy ageing is generally accompanied by impaired hand function, which includes writing, placing keys in keyholes and fastening buttons. The capacity to perform these types of skilled hand movements in humans is largely attributed to the neural pathway from the motor areas of cortex to the spinal cord. However, we do not know how the ageing process affects the operation and integrity of this pathway. The goal of this study is to examine the age-related changes in this pathway and how these changes contribute to the impaired ability of the elderly to perform fine motor tasks with their hands.

We will use a brain stimulation technique that uses a magnetic field to painlessly activate nerve cells in the brain while older adults perform skilled tasks with their fingers. We will use this technique to examine certain connections in the brain that are responsible for switching off unwanted muscle activity, as these connections are believed to be essential for skilled use of the fingers.

This information is important, not only for its fundamental biological significance, but it also may lead to new strategies for interventions designed to retain or improve fine motor control in the elderly.

John G. Semmler, PhD

IN MEMORIAM
The President, Directors and staff pass on their condolences and gratefully acknowledge gifts in memory of the following since the last Brainwaves.
Mrs “Dolly” (Alma) Gavin
Janet Kersey
Leslie James Manning
Harvey Morton
Marjorie Hulton
Marjorie Elizabeth Lang
Vida Milligan
Peter Nikolopoulos

We continue to revere the memory of those for whom gifts have already been made and especially those who have kindly made bequests to the Brain Foundation. Joining the Estates of Toy, Hallam, Young, Hennessey, Coulson and Chard are:
Michael Rogers Stirling, Rex Banks, Lou Lungo and Dorothea Garrett.

If you are kind enough to consider a bequest to the Brain Foundation, please contact us for a special bequest brochure that shows the format necessary to ensure that your wishes are carried out. Alternatively, a copy of the brochure is available in the bequest section of our web site.

Would you also kindly consider nominating a donation to the brain foundation as an additional or preferred tribute for your loved ones. We have personalised forms to facilitate such arrangements.

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