brainWAVES

The Newsletter of the Brain Foundation. *Summer 2012*

2012 Research Grant Results and Christmas Edition

The Directors and Staff of the Brain Foundation would like to sincerely thank our supporters and wish you all the very best for the upcoming holiday season.
This year we are glad to announce that we were able to award 16 Research Grants to applicants throughout Australia. Read all about them in this issue.
We would also like to extend a very warm welcome to all of our new Headache Australia Register members. With your involvement we hope to continue to be at the forefront of Headache and Migraine research in Australia.

Our Fundraisers are the Heart of what we do

Everybody knows that the Brain rules! But without a heart, we would not be who we are. The Brain Foundation is blessed to have some outstanding fundraisers who work tirelessly to raise funds towards our research grant programme. We would like to sincerely thank them all for their outstanding efforts this year.

Rachael Stephens and the team from Caulfield Grammar, Wheelers Hill Campus

Rachael and her family suffered a huge loss several years ago when her mother, Donna, succumbed to a brain tumour. Now in Year 12, Rachael wanted to do something positive to remember her mum and to contribute to the increasingly important area of brain tumour research.

With the backing of her school mates and teachers, Rachael teamed up with the Victorian Cross Country League to hold a 'fun run' in August at Lysterfield Park. Luckily the weather was kind when over 150 runners and walkers assembled to take part in a 6km course or a 16km 'not very fun' run. With the enticing aroma of a BBQ, it was not long til everyone was enjoying a sausage on a roll and comparing times. With sponsorship of the runners, Rachael and her schoolmates raised over $7,500

We would like to sincerely thank Rachael for her determined efforts to make the day such a success, the VCCL for their help hosting the event and the teachers, students and families of Caulfield Grammar Wheelers Hill Campus, for their support.

The whole team

Rachael with Gary Tyler, head of Senior School, Paul Runting, head of Wheeler Hill Campus & Michael Robinson, Co-captain, Shaw House

The Brain Foundation wins Gold in the 2012 City to Surf

This was big year for the Brain Foundation in the City to Surf fun run.

Having taken a Gold Sponsorship, we were pleased to be able to offer the coveted 'gold' places to a wonderful team who were running in memory of their sister and daughter, Stephanie.

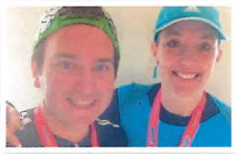
'Team Steph', looked awesome in their special t-shirts and brainy caps and received many compliments along the 14km course. The 7 member team was outstanding in their efforts, raising more than $9,200

Team Steph

'The Tumourous Two' – Cecil and Simon ran to support a couple of mates going through a difficult time. They certainly looked like they enjoyed themselves in the race and we certainly 'enjoyed' the support they were able to give to our research programme - over $2,800

David McCarthy chose to run for us after going through a personal difficult time. Not being beaten, he was not going to let his 'heartbreak hill' get the better of him either. Surpassing expectations, David contributed $1,000 to the total.

The Tumourous Two



David & his running partner

Sue Bisson wanted to 'run in her husband's footsteps' as a tribute to their long life together. A fit man who loved running marathons, John is missed every day.

Natalie Shoonraad also has had close family experience of just how quickly life can change when struck by one of the many brain disorders.

Sue and Natalie both easily exceeded their fundraising expectations contributing another $1000.

Altogether over $14,000 was raised on our behalf. An outstanding effort by everyone.

The Brain Foundation support crew

Contact the Brain Foundation
PO Box 579, Crows Nest NSW 1585
Telephone: 02 9437 5967 or 1300 886 660 Fax: 02 9437 5978
Email: info@brainfoundation.org.au
Visit our websites www.brainfoundation.org.au and www.headacheaustralia.org.au

More Fundraisers

Andrew is a Superstar

Andrew Tomlin featured in our last issue but deserves another big thank you for his efforts. Having been diagnosed with an aneurysm when he was 13, Andrew wanted to raise awareness of this condition and thank the people who looked after him. Now getting back to sport and life as it was before his diagnosis, Andrew used Everyday Hero to raise $6,000 on our behalf.

Andrew loves his spare brain!

Class mates remember a good friend

The students from Gleeson College in S.A. had some sad news early this year when a year 12 student collapsed from an aneurysm. Rushed to hospital, sadly she did not make it through the operation.

Wishing to remember their friend by raising funds for research into aneurysms, the students from Stage 1 Business and Enterprise Studies decided to hold a "marketplace" during a lunchtime at school.

Organised into groups, they developed a business name, business plan and a product to 'market' to the other students. Goods offered for sale included show bags, hot chips, hot dogs, lollies and ice cream.

The event was a great success and raised $800 on the day. The students should be congratulated on their fantastic efforts.

Oktoberfest = fun! Dystonia = not fun!

One of our long term supporters and sufferer of Dystonia, Lee Pagan, has put together an Oktoberfest celebration day to help raise funds to go towards Dystonia research. Assisted by her friends, Lauelle from Gleneagle Gables and Kathy from Quota, a great day was had by all. Lee used Everyday Hero to promote the event and along with donations from the day raised nearly $2,000. (See two Dystonia projects funded in this year's awards later in this issue.)Thank you all so much for your hard work.

Pictured is Lee, at right, with Laurelle and Kathy.

Our corporate sponsors: Zombies for the day!

Well, I wonder what the bosses would think!

Our corporate sponsor, The Docs and Coversion Team from Suncorp Bank joined the very popular **Brisbane Zombie Festival Day and Walk** this month. And what a day they had, all dressed up among the zombie hoard and making the most of the event. The team has been raising funds for the Brain Foundation through various events and using Everyday Hero, and have raised close to $3,000.We are thrilled that we are their Charity of Choice.

If you or your company are looking for a charity to support through your workplace, please give us a call in the office to see how we can help you!

Zombie Kim!

Would you buy a cake from this zombie?

Well, plenty of people did.

Charmaine and Kimbly Hollywood supported us at the **Sydney Zombie Walk**, but they wanted to do more. Using Go Fundraise and holding a cake stall with a raffle and lots of 'gooey' treats at their local shopping centre, they have raised $500 and still counting.

We didn't think Zombies ate cake!

Birdies at our golf day!

Once again our sincere thanks go to our director Val Gibson and the team from Bullant Sports, Gary and Matt, for another wonderful day of golf at Pymble. With a full compliment of players, this year we had 5 ladies teams to give the fellas some competition!

The Charity Challenge Gala Dinner at the end of the month will cap off another successful year!

Pictured is the Ladies Winning Team - Sandy, Pippa, Shaun and Jen.

Dementia awareness week

The Brain Foundation joined Alzheimers Australia in Martin Place, Sydney, for Dementia Awareness Week. Raising awareness of dementia in our society, information and mind game demonstrations, (courtesy of our partner Ric, from the Brain Food Factory) kept the workers entertained in their lunch break and gave them some 'food for thought'!

Pictured is Caroline (Brain Foundation) with Andrew Mills, General Manager Marketing, Alzheimers Australia.

Headache News

In 2005, the Brain Foundation awarded a grant to Professor Lyn Griffiths of Griffith University to support her Phase 1 trial investigating the effects of vitamin B/folate supplementation on migraine frequency, severity and disability. The results of the trial showed that supplementation significantly reduced migraine disability in people with a specific genetic mutation. Following this trial, the Genomics Research Centre at Griffith University is conducting a larger, 6 month trial to be completed by the end of 2014 for female sufferers with aura. They are currently in the process of recruiting people and if you would like to see if you qualify, please contact the University on (07) 5552 9201.

We are pleased to have again funded Professor Griffiths in her migraine studies and you can read about her latest project elsewhere in this issue.

We are TV stars!

Well, not really, but it was great to participate in a Today Tonight episode in September where migraine was discussed. Professor Griffiths also had a starring role along with our President, Professor Michael Halmagyi and Brain Foundation Secretary General, Gerald Edmunds. But, what followed from the story was that many sufferers of migraine contacted our office to let us know that they had had significant relief by reducing or completely eliminating gluten from their diet. Remember, everyone has different triggers, but as all of these people had the same story, if you haven't tried it perhaps it could work for you too. Let us know if you have success, or, better still, go on our forum.

And, don't forget to join our Headache Register. Details on the web site:

www.headacheaustralia.org.au

Headache Australia

Did you know?

Healthy Brain

Did you know that a diet for a healthy brain is very similar to a diet for a healthy heart. A diet that consists of carbohydrates, proteins , sufficient vitamins (especially folate, C and E) and minerals iron and zinc, is important to maintain general health and improve cognitive function.

The top ten brain foods are: Blueberries, salmon, flax seeds, mixed nuts, avocados, eggs, whole grains, broccoli and believe it or not, coffee and chocolate In moderation. Who said diets had to be boring!

So, now you have the ingredients for a healthy diet, you need to keep your mind active too. Check out the web site for **Brain Food Factory** and sign up for their free monthly puzzles

www.brainfoodfactory.com

We have a sample puzzle on the back page of this issue. The solution will be published on our web page and Facebook page from December 16 (or we can mail or fax one to you on request).

For our supporters who **love to travel** but have a mobility issue, perhaps as the result of a stroke or an injury, there is a travel agent specialising in your needs. Check out the web site for Cane and Able – they have some great places to visit information on getting around and getting the assistance you need.

www.caneandable.com.au

2012 Research Grant Awards

The Brain Foundation receives many applications each year for funding. The successful applicants are selected by members of the Scientific Committee and are awarded to those projects with the potential to make the greatest advances in their respective areas of research.

The Award Ceremony was held in October in the Great Hall at Sydney University and once again was an event enjoyed by all who attended.

We would like to take this opportunity to thank the members of the Scientific Committee who volunteer their time to assess each application received and also to thank our donors and fundraisers, without whom the awards would not be possible.

The Cause of Whispering Dysphonia

Chief Investigator:
Professor Carolyn Sue

Co-Investigators:
Associate Professor Robert Wilcox
and Professor Christine Klein

Dystonia is a neurological movement disorder characterised by abnormal posture due to an imbalance of muscle contraction. It can be associated with abnormal twisting or repetitive movements in the absence of stiffness or mechanical abnormality. Abnormal movements may affect the arms, legs, trunk, face and neck. Dystonia can be caused by a number of different genetic or environmental factors.

Mutations in several genes have been identified to cause different types of dystonia. However, the disease cause in the majority of patients is still unknown. In this project, we collected DNA samples from eight affected and nine unaffected members of a large family with spasmodic (whispering) dysphonia. The phenotype of this family has been classified as dystonia 4 (DYT4). We used state-of-the-art sequencing techniques (so-called next generation sequencing), to identify the novel genetic cause of DYT4 in affected family members. We will test the effect of these genetic mutations in a number of tissues sampled (under local anaesthetic) from affected and unaffected patients from the DYT4 family.

Using this strategy, we hope that our project will identify novel targets to develop new treatments options for patients suffering this condition.

Inflammation in newborns as a cause of cerebral palsy

Chief Investigator:
Dr Michael O'Callaghan

Co-Investigators:
Professor Alastair MacLennan,
Dr Catherine Gibson,
Professor Eric Haan and
Ms Gai McMichael

Cerebral palsy is a developmental disorder affecting movement and posture and is the result of white matter brain damage occurring before birth or early in life. It affects 1 in 500 babies born in Australia and for most cases there is no known cause. Our group's ongoing research program at the University of Adelaide has provided genetic evidence for an altered fetal immune response as a contributor to cerebral palsy. The aim of this research study is to extend our knowledge by examining protein level changes in inflammatory related mediators. The study will screen a large number of inflammatory mediators in cord serum from babies later diagnosed with cerebral palsy to assess which factors are most important.

The group has extensive experience linking to pregnancy outcome registers and cerebral palsy registers and has previously accessed cord serum samples in the Adelaide Women's and Children's Hospital. The proposed study uses a large cohort and the tests proposed are robust and well validated.

Identification of specific inflammatory mediators associated with cerebral palsy may allow more precise and targeted prevention strategies or could be useful for early prediction of cerebral palsy outcome; both of which are high priorities for families affected by this brain disorder.

Multimodal interventions to cerebellum as a treatment for Cervical Dystonia

Chief Investigator:
Dr Lynley Bradnam

Co-Investigators:
Associate Professor Michael Ridding and Dr Michelle McDonnell

Recent evidence supports a role for the cerebellum in the pathogenesis of dystonia. Cervical dystonia is a debilitating, painful neurological disorder that is known to reduce quality of life in affected people. Our research has found that increasing the excitability of the cerebellum with non-invasive brain stimulation in a single session restores inhibition in the primary motor cortex and improves functional writing tasks in both cervical and focal hand dystonia. We now intend to conduct a clinical trial in people with cervical dystonia. The aim of our new study is to assess effects of repeated sessions of cerebellar stimulation combined with training to further challenge cerebellar motor functions on global measures of dystonia, quality of life, range of movement, motor dexterity, motor learning and brain neurophysiology. Participants will attend for 10 sessions over 2 weeks to have theta-burst stimulation (a form of repetitive transcranial magnetic stimulation) applied over the cerebellum bilaterally or sham stimulation. Following stimulation, all participants will perform cervical range of motion and proprioception exercises using a task-orientated motor learning approach delivered by a video. Participants will be trained in implicit motor learning tasks and motor sequencing tasks at each session. In addition, they will record their subjective measurement of pain, ease of movement and static head posture using visual analogue scales. We hope the results of this clinical trial will provide data to support the development of a efficacious, cost effective alternative treatment intervention for people with cervical dystonia in Australia.

Measuring neurodegeneration using Transcranial Magnetic Stimulation in Progressive Supranuclear Palsy

Chief Investigator:
Dr Kelly Bertram

Co-Investigator:
Associate Professor David Williams

Progressive Supranuclear Palsy (PSP) is a rapidly progressive neurodegenerative disease for which there is currently no diagnostic test or any treatment. It affects around 7 people in 100,000 over the age of 40 causing frequent falls, eye movement abnormalities and intellectual difficulties. The average time from disease onset to death is eight years.

The diagnosis of patients with PSP, and differentiating it from Parkinson's disease, relies on clinician experience. To ensure that clinical trials in PSP can be designed with reliable end-points, an objective measurement of disease severity is urgently needed to supplement the imperfect clinical measures currently being used.

Transcranial Magnetic Stimulation (TMS) uses a handheld magnetic coil to induce an electrical field, providing a simple, non-invasive method to measure brain dysfunction. With our collaborators in Rome, we conducted a pilot study which showed abnormalities in PSP could be measured using TMS. Importantly we made discoveries that may: (1) provide a method for measuring disease progression by directly measuring the evolution of brain dysfunction in PSP; and (2) provide a technique for separating PSP from other Parkinsonian syndromes.

The intention of this project to be funded by the Brain foundation is to confirm these findings in a larger group of people with PSP and compare the responses to these TMS paradigms in people with clinically similar conditions, that is, Parkinson's disease and Multiple System Atrophy. This will help determine if these findings are reproducable and disease specific.

The earlier, accurate diagnosis of PSP by objective means would be useful clinically, but would also enable possible treatment options to be studied more accurately and efficiently. The principles of treatment of PSP have implications for possible treatment options for other neurodegenerative diseases including Alzheimers disease and Parkinson's disease.

2012 Research Grant Awards

Rewiring the brain after stroke : how to promote it and measure it

Chief Investigator:
Dr Penelope McNulty

Co-Investigator:
Ms Christine Shiner

Currently the lifetime risk of stroke is 1 in 6, leading the World Health Organisation to target stroke as a critical non-communicable disease and one of the largest crises facing world health. More than 50% of stroke survivors suffer profound disability which limits their independence and reduces quality of life. With no cure for stroke, rehabilitation is the only means of promoting recovery and lessening the burden of disability for survivors and their families. Thus developing more effective rehabilitation strategies and maximising recovery potential by improving our understanding of how and why such strategies work has become an imperative. In 2009 Dr McNulty developed Wii-based Movement Therapy, a novel rehabilitation protocol that is cheap, effective, overcomes poor patient compliance, and can be implemented in the home. To optimise the impact of Wii-based Movement Therapy we need to deepen our understanding of how this rehabilitation strategy mediates improvement.

Given the growing evidence for conventional post-stroke therapies, it is likely that Wii-based Movement Therapy similarly promotes recovery through brain 'reorganisation'. In this study we will quantify brain reorganisation and identify the mechanisms that are associated with functional recovery after a brief, but intense 14-day protocol of Wii-based Movement Therapy. Magnetic resonance imaging (MRI) is the current gold standard for studying brain reorganisation, however the implementation of routine scanning is limited by cost and access to services. We will investigate alternatives to MRI in this study by comparing MRI results to those from a cheaper, more accessible assessment tool, transcranial magnetic stimulation (TMS). Using MRI and TMS to uncover the mechanisms by which post-stroke rehabilitation facilitates recovery will enable us to more specifically tailor Wii-based Movement Therapy to individual patients and their deficits, optimising therapy efficacy. This presents an opportunity to significantly reduce the debilitating social and economic burden of stroke.

Ms Christine Shiner on behalf of Dr Penelope McNulty

To identify and characterize molecules released from platelets that protect brain cells

Chief Investigator:
Professor Robert Medcalf

Co-Investigators:
Ms Amanda Au and Dr Andre Samson

"Stroke is the second leading cause of death and the leading cause of disability in adults. An ischaemic stroke occurs when there is a blood clot occurring in a vessel in the brain, causing death of neurons and other brain cells due to lack of oxygen and glucose. Clotting occurs when the coagulation cascade is activated normally in response to damage to blood vessel walls. Clotting is a complicated process, but one of the major elements in the clotting cascade are platelets. Platelets are very important as they play a major role in coagulation and release many molecules essential for clotting to occur in a timely fashion.

Clotting can occur at inappropriate times causing blood vessel blockage. If this occurs in a blood vessel in the brain, a stroke occurs. At present, therapeutic options to treat stroke are limited and there is a clear need to improve current clinical practices to prevent and treat stroke.

In this project, we will investigate the unsuspected protective effect of platelet products on brain cell survival. Although it is well known that platelets release factors important for clot formation, many other factors are released from platelets with unknown function. In preliminary work we showed that unidentified platelet derived factors were able to protect brain cells (neurons) from injury induced by various damaging agents. This was an unexpected finding and opens a number of possibilities.

The funding we will receive from the Brain Foundation will allow us to further explore the protective effect of these platelet derived factors (referred to as "PRF's") on brain cells in vitro and also in our well developed in vivo models of brain injury. We are particularly interested in identifying the active molecule(s) that are responsible for this protective effect. A number of candidate factors have already been identified using mass spectrophotometric analysis. We will also determine whether these protective PRFs also have beneficial effects in other brain disorders, including traumatic brain injury".

Assessing a new Deep Brain Stimulation target in the brain to alleviate symptoms of postural instability in Parkinson's disease

Chief Investigator:
Dr Wesley Thevathasan

Co-Investigator:
Mr Thushara Perera

Over 64,000 Australians have Parkinson's disease (PD) – and this number is rising along with our aging population. A major problem for patients with PD is postural instability – impairment of the reflexes that maintain upright stance. Most patients with PD will develop postural instability, which causes falls and impairs quality of life. Unfortunately, postural instability is often refractory to treatment including medication and conventional forms of deep brain stimulation.

Deep brain stimulation is a rapidly evolving therapy, where electrical stimulation is applied to specific brain regions via implanted electrodes connected to a battery - akin to a heart pacemaker. A new form of deep brain stimulation, targeting a brainstem structure called the Pedunculopontine Nucleus (PPN), has been found to help gait disturbance in PD. PPN stimulation is also proposed to help postural instability – but the impact is uncertain.

To clarify if PPN stimulation can help patients with postural instability, we have recently conducted a multicentre experimental study. We assessed patients with PD implanted with PPN stimulation (for gait disturbance) – and measured the impact on postural control using objective neurophysiological measures. Postural control was assessed both off and on PPN stimulation and compared to controls. Funding from the Brain foundation will allow us to apply mathematical modelling to this data - to characterise postural instability and assess whether PPN stimulation improves it. These findings could be rapidly 'translated' to help patients.

Ms Colette McKay accepting the award on behalf of Dr Wesley Thevathasan

FoxM1 and melanoma cerebral metastases

Chief Investigator:
Dr Timothy Siu

Co-Investigator:
Dr Hong Duong

Melanoma is one of the deadliest tumours known to humans with the highest propensity of all primary cancers to metastasize to the brain. Despite recent advances in targeted therapy for metastatic melanoma, the average survival of patients with metastatic brain disease remains less than 10 months. In search of a new therapeutic target, a recently established cell cycle regulator, FoxM1, that is found to be aberrantly expressed in many solid tumours, holds great promise in delivering more effective therapy.

FoxM1 is a signaling agent in the cell that is fundamental for normal cell growth and development. It is only present in growing cells and is switched off in mature cells. Abnormal gain of FoxM1 function has been found in many types of cancer and by targeting FoxM1, new treatment may be developed that could interrupt multiple signaling pathways critical for the development of brain metastases. With an across-the-board strategy to suppress cancer signaling while sparing other mature cells, anti-FoxM1 treatment may be more effective in halting the progression of brain metastases while producing less toxic effects.

Our project aims to evaluate the role of FoxM1 in the growth of melanoma cancer cells in a test tube environment. The overall goal is to characterise the expression of FoxM1 in melanoma and to determine its functional role in cell invasion, migration and angiogenesis. Our plan is to first acquire relevant in-vitro data through the use of human melanoma cell lines to assess the expression of FoxM1 in melanoma brain metastases. We will then conduct various tumorigenic assays with inhibition of FoxM1 to ascertain the effects of loss of function of FoxM1 on the development of various metastatic phenotypes. This basic research would form the groundwork for progressing to real life experiments in animals and ultimately to human clinical trials.

2012 Research Grant Awards

Utilisation of glioma stem cells to investigate novel therapies for glioblastoma multiforme

Chief Investigator:
Dr Wayne Ng

Co-Investigators:
Dr Andrew Morokoff, Associate Professor Kate Drummond, Professor Andrew Kaye, Dr Giovanna D'Abaco

Glioblastoma multiforme (GBM) is the most common malignant brain tumour and has a very poor survival (7-15 months) despite current best treatment (surgery, chemotherapy and irradiation). Glioma stem cells (GSC) are a new concept in glioma research described as representing the 'life source' of GBM by providing the tumour with an unlimited capacity to renew. This capacity likely underlines its inevitable recurrence, thereby ensuring its poor prognosis. Preliminary studies in the Royal Melbourne Hospital Department of Surgery Brain Tumour Laboratory have established a number of these human tumourderived GSC lines. These cells have been confirmed to possess the quality of self-renewal/immortality making them an ideal platform to further investigate this form of brain tumour.

These GSC lines will be incorporated into a mouse model with 'glowing' GSC which will allow non-invasive realtime assessments of tumour growth and response to treatments in live mice. Early work with one of the GSC lines has confirmed that GSC are able to recapitulate tumours within brains and provide a working in vivo model.

Brain tumour treatments encounter a problem which distinguishes them from other cancers. The brain exists in an insular environment which seals and separates it from the rest of the body. Therefore, by utilising this brain tumour model we will also provide important information about the ability of drugs to be delivered into the brain beyond the blood brain barrier. This model will therefore form the basis of future experiments to test new drugs. This research will also greatly promote our scientific understanding of GSC and their behaviour within an in vivo environment and could form a powerful basis for future clinical cancer drug trials.

Investigating new genetic causes of muscular dystrophy

Chief Investigator:
Dr Nigel Clarke

Co-Investigator:
Professor Kathryn North

The muscular dystrophies are genetic conditions that cause life-long disability from progressive muscle weakness. It is important to identify the specific genetic cause in each family as this allows doctors to plan health care and give accurate genetic counseling. Finding the specific gene mutation that is causing muscular dystrophy in a family is often difficult. One of the reasons is that there are over 40 different known genetic causes and the testing process can take years. Another reason is that it is likely that many disease genes that cause muscular dystrophy remain undiscovered. The Institute for Neuroscience and Muscle Research, based at the Children's Hospital at Westmead, has been a leading research laboratory for muscular dystrophy for over 10 years. Through previous and ongoing projects, the INMR has provided over 100 muscular dystrophy families with genetic diagnoses and has contributed to finding many disease genes.

Through a technique called whole exome sequencing we have found two new likely causes of muscular dystrophy in different families. To confirm that these two new genes truly cause muscle disease, we will test 100 muscular dystrophy patients who remain without a diagnosis, aiming to find other families with mutations in these genes. We will also test whether some patients who have been diagnosed with limb-girdle muscular dystrophy (an umbrella term for over 20 different muscular dystrophies) in fact have myotonic dystrophy type 2 (DM2). DM2 affects people in similar ways to LGMD and is relatively common in many parts of Europe but is rarely diagnosed in Australia. We think DM2 may be under-recognized in Australia and some patients are mis-diagnosed with LGMD. To investigate this, we will test 60 LGMD patients who remain without a specific genetic diagnosis for DM2. The aim of these projects is to improve the ability of doctors to diagnose the genetic causes of muscular dystrophy to help with the care of affected people and their families.

The excessive calcium leak into dystrophic muscle

Chief Investigator:
Dr Bradley Launikonis

A child born with Duchenne muscular dystrophy (DMD) is not physically distinguishable from any other baby in regards to their ability to move at this very early age. However with the increasing mobility of the growing child, delays in movement milestones such as crawling and walking are noticeable. The disease progression through the first decade of life is very severe, the child loses normal posture and the use of limbs, resulting in confinement to a wheelchair. This continues through the second and third decade of life, with the patient likely succumbing to respiratory or cardiac failure in this time. The underlying cause of the disease is a genetic one, but the progression of the disease is associated with contraction-induced damage to the muscles. Underlying this damage is the entry of calcium into the muscle that most likely activates deleterious pathways in the muscle, reducing normal function.

Calcium is dissolved at very high concentrations normally in the bodily fluids and has many important roles in the healthy body. Inside muscle (and all other tissues and organs) it is present at very low concentrations when the muscle is not contracting. In DMD too much calcium enters the muscle from that in the bodily fluids, upsetting the normal levels of calcium inside the muscle. What could further improve the outlook for DMD patients would be treatments or drugs that would redress the normal calcium balance across the surface of the muscle. By imaging calcium in muscle fibres with new techniques developed in our lab we aim to identify the way that calcium enters muscle fibres normally and how this changes in DMD. This information could provide potential ways to prevent calcium overload in dystrophic muscle.

Treatment for nerve fibre loss in diabetic neuropathy

Chief Investigator:
Professor Adrian West

Co-Investigators:
Professor Bruce Taylor and
Dr Lisa Foa

Diabetes commonly causes problems with nerves in the hands and feet and limbs of patients. This may be a simple loss of sensation or it can be burning or itching, ranging up to quite intense pain. It appears to be caused by loss of some of the fine nerve fibres near the skin surface. The actual cause of this is unclear, but the nerve fibres seem to be unable to regenerate successfully, once they start to degenerate. The nerve problems can cause very significant suffering for diabetic patients in the long term, and are currently incurable. Existing treatments are aimed at minimising or masking the irritation or pain, rather than treating the underlying problem.

Our research group has been working for some years on a small naturally-occurring protein – metallothionein – which has potent effects on nerve fibres and nerve cells. Metallothionein can induce nerve fibres grown in culture to regenerate when cut. It can also act as a chemical "lure", attracting regenerating nerve fibres towards its site of administration. We have also shown that metallothionein has potent effects on nerve cell regeneration when injected into the brains of animals which have received an injury – this type of injury in the brain generally does not regenerate.

We therefore hypothesize that metallothionein might help to regenerate nerve fibres in the skin of diabetic patients, both by switching on regeneration (nerve fibre growth) and by directing the fibres towards the site where the metallothionein has been applied (e.g. a region of little or no sensation on the patient's skin).

To test this hypothesis, we will examine diabetic rats which have the typical loss of nerve fibres in their skin. We will identify regions of nerve fibre loss (with fine fibres which stimulate the skin), apply metallothionein, and then analyze the nerve fibres for signs of regeneration. We will also test the skin of the animals for any signs of a return of sensation. Analysis of which nerve fibres regenerate will throw light on the molecular mechanisms by which metallothionein acts, and upon why the nerve fibres start to degenerate in diabetic patients in the first place. Most importantly, we will be encouraged to develop further synthetic analogues of metallothionein which are suited to topical administration and can be used as a therapy for neuropathy.

2012 Research Grant Awards

Testing various approaches for treating McArdle's Disease using a mouse model

Chief Investigator :
Associate Professor Kristen J Nowak

Co-Investigator :
Professor Nigel G Laing

McArdle Disease is one of the most common genetic skeletal muscle diseases, affecting up to 1 in 100,000 people (~1 in 158 people are carriers). McArdle Disease patients can have critical episodes of early fatigue when exercising, muscle pain (myalgia), myoglobinuria (when muscles break down and release myoglobin in urine, making it brown/red in colour), and then subsequent kidney failure.

Patients with McArdle Disease cannot utilise their glycogen energy stores in their skeletal muscles, due to a defect in the gene that produces the necessary enzyme. Despite a great deal of intensive investigation, no effective treatment for McArdle Disease has been found. Therefore there is a huge need for further research in this area.

We previously studied a naturally occurring sheep model of McArdle Disease, and were involved with investigating replacing the missing enzyme using a modified virus. This study yielded promising results. Since then, great improvements have been made using viruses to treat muscle diseases. Thus there is now even more impetus to pursue viral therapy for McArdle Disease.

However, a McArdle Disease mouse model to more readily and efficiently facilitate the evaluation of therapeutic approaches has been missing until now. Our collaborators in Spain (Drs Ramon Marti and Tony Andrew) recently created the first McArdle Disease mouse model which closely mimics the human disease. Our collaborative project will test delivering the missing enzyme to McArdle Disease mice using an adeno-associated virus (or delivering the fetal (brain) version of this enzyme), and we will target mice at different ages.

If successful, our research will be a significant step forward for the field, especially as this therapeutic approach should be effective for essentially all patients with McArdle Disease. We would eventually hope to test any positive treatment regime in the McArdle Disease sheep in Western Australia, which would be the next crucial step towards human clinical trials.

Neural basis of adolescent recovery post brain injury

Chief Investigator:
Dr Janine Cooper, PhD.

Co-Investigators:
Professor Vicki Anderson and
Ms Ashley Di Battista

Of all the issues that face a child or adolescent after traumatic brain injury (TBI), one of the most common and challenging to their quality of life (QoL) is a failure to recall personal memories involving the self, known as autobiographical memory (ABM). In moderate to severe cases, many cannot lead a normal life and show problems at school, college and in the workplace where they fail to recall previous events and timelines and are unable to make future plans. Many require regular supervision, which affects their ability to form strong friendships at a crucial stage of personality development. These factors have a huge impact on their sense of autonomy and the overall mental health of the adolescent and their family. Current methodology for identifying problems with ABM is limited and few treatments are available.

In direct response to the high prevalence of TBI, the lack of support to aid memory problems in younger people and the resultant negative impact that this has on QoL, we have developed a computerised rehabilitation system. Treatment is delivered by an avatar/ virtual reality peer and includes systematic instructional methods in a contextsensitive approach, with relevance to everyday life, which will assist with the maintenance of skills and provide opportunities for generalization of learnt skills. A great strength of this system is that rehabilitation can be delivered remotely and have a wide reaching effect to help those who cannot travel to hospitals and rehabilitation

centres. It directly addresses a need for greater access to rehabilitation of cognitive impairment after brain injury for children/adolescents. The research will also use structural and functional neuroimaging to provide clinicians with a greater understanding of brain related changes associated with this treatment at a time of development when the brain is thought to have greater adaptability to injury.

Long-term effects of sports-related concussion

Chief Investigator:
Professor Christopher Levi

Co-Investigators:
Associate Professor Peter Stanwell,
Dr Frances Kay-Lambkin and
Dr Andrew Gardner

Participation in sport is an extremely popular activity among individuals of all ages. While there are considerable benefits to engaging in sporting activities, one of the potential consequences is concussive injury - which has a rather large prevalence among contact sports athletes. Although most athletes experiencing a concussion recover with several days of injury, a proportion of individuals may develop long lasting symptoms or long-term consequences. Exposure to repeated concussive and subconcussive blows, such as those experienced by athletes of collision sports, has been proposed as the genesis for chronic traumatic encephalopathy. Despite considerable focus of this particular topic, there have been no prospective studies published in the literature at this point.

The current research study proposes to examine the long-term consequences of sports-related concussion in a group of current and retired professional sports athletes. The retired athletes will be placed in two groups (short-term retired [≤10yrs] and long-term retired [>10yrs]). Current athletes will form one group. A well matched control group, screened for neurological, cognitive and psychiatric conditions, will also be recruited to the current study as a basis for comparison. We propose to conducted neuroimaging, cognitive testing and psychological/psychiatric assessment of each participant in order to examine whether those athletes with a greater number of reported concussions perform significantly different from those with less exposure and also to determine whether significant group differences are observed across the age ranges.

The findings of this research has the potential for a far reaching impact in terms of the management of sports-related concussion across all age ranges, in terms of return-to-play decision making, management of acute concussive injury and limiting an athlete's further exposure to concussion.

Dr Andrew Gardner on behalf of Professor Christopher Levi

Identifying migraine gene mutations in a large genetic isolate pedigree population

Chief Investigator:
Professor Lyn R. Griffiths

Co-Investigators:
Dr Bridget Maher and
Dr Rod A. Lea.

Migraine is a complex, debilitating neurovascular disease that imparts considerable economic and social burdens on sufferers and their families. The disorder is common in westernised countries – approx 12%, and shows a marked female preponderance (~3:1). A tendency for migraine to run in families also suggests a strong genetic influence on the disorder. We have been involved in migraine genetic studies for over 15 years and our group was the first to map a common migraine gene, and has subsequently identified a number of genes that influence migraine susceptibility.

Recently we undertook a genetic study of the large pedigree from Norfolk Island - in which ancestry can be traced back to the 'Bounty' mutineers and Tahitian women who were the original founders of the population. The Norfolk Island population is uniquely suited for pedigree based studies of migraine not only due to the relationships of the cohort but also due to the high number of migraine sufferers. Migraine prevalence was determined to be 25.5% in this population, compared to 12% seen in general populations, interestingly the female preponderance remained consistent in the Norfolk population.

Using this population cohort, we recently identified a novel migraine locus on the X chromosome in a large pedigree from the Norfolk Island genetic isolate. This locus contains a potential migraine candidate gene - the Hephaestin gene, which is in involved in iron transport. We now propose to undertake a study to deep sequence this susceptibility region to further investigate this chromosomal region. The objective of this project is to follow-on from our Norfolk X chromosome study by completely sequencing the Hephaestin gene in migraineurs from the Norfolk Island pedigree in an effort to identify functionally relevant genetic variants associated with migraine predisposition in this and also other migraine populations.

Fundraising

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The Brain Foundation is proud to announce our partnership with Funeral Alliance Solutions (FAS) in Sydney. Losing someone close is always a very difficult time in the lives of loved ones. It is a time of grief, and confusion relating to the organising of the necessary arrangements can arise. This is where FAS can help. Bringing together all the relevant steps for this very difficult time, they take away any additional stress and can guide you through the entire planning process. You can contact FAS on 1300 550 367 or see their web site **www.fasolutions.com.au**

Funeral Alliance Solutions

Supporting us is easy!

If you would like to support our Research Grant Programme, you can hold your own event, as some of the people featured in this issue have done, or, join a public event, such as a fun run or bicycle ride and create a fundraising page on one of our partner fundraising sites:

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You then e-mail your friends and family and link to facebook, and you are fundraising! Easy! We would like to thank more fabulous supporters who have chosen to use the above sites for their fundraising: Check out some of their pages!

Elicia Fowler who is using **Go Fundraise** to raise funds in lieu of birthday gifts.

Tracie Crombie, Patrick Fogarty, Mai Mary, Karen Thorpe, Eliza Fowler, Natasha Carroll, Katie and Lauren Higginson and Amanda Ward who are all using **Everyday Hero** to raise funds for lots of different reasons.

Together these wonderful supporters have raised a further $9,000 to go to our Research Grant Programme.

Remember, 100% of your donation goes to our Research Grant programme!

Don't forget, you can shop with us too!

Check out our web site – we have our 'brainy caps' aprons and Ambre Hammond's beautiful piano CD's. And, don't forget to get your 2012 Entertainment Book too.

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In Memoriam

We would like to gratefully acknowledge these gifts in memory and thank the families for their support at this very difficult time.

Debbie O'RIELLY
Nestor BRAGANCA
Don SCHUTE
Bruce ELLIS
Katrina SCHAEFER
Margaret GIBBENS
Lynette HART
Zelio SALVALAGGIO
Donna STEPHENS
Leslie GARLAND
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An Active Brain is a Healty Brain. Test your powers on this puzzle.

Healthy Brain

9 into 6 - Place the 9 letters below each box into the 3x3 grid to make six valid five letter words

	C	B	S	
F				K
H				N
G				E
	K	N	E	

C O R P O R E A L

	I	P	S	
F				K
D				M
T				R
	M	S	N	

I N O C U L A T E

	D	U	A	
M				Y
A				E
A				D
	T	P	T	

M E S S I E U R S

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