BUILDING A BETTER FUTURE

NeuRA 2013 IN REVIEW

Building on the past, looking to the future

With the opening of the NeuRA building, the first stage of the Neuroscience Research Precinct, we look forward to the future as we explore the remarkable research opportunities that now open up before us.

Today we have an unprecedented opportunity, through the diversity of our research, to become a global hub for scientific investigation and bring about huge changes in the diagnosis and treatment of so many diseases.

If we, as researchers, are like the visionary architects who designed our new facility, we can build on the firm bedrock of our scientific foundation and then the true promise of our research to benefit humankind can be realised.

NeuRA

Discover. Conquer. Cure.

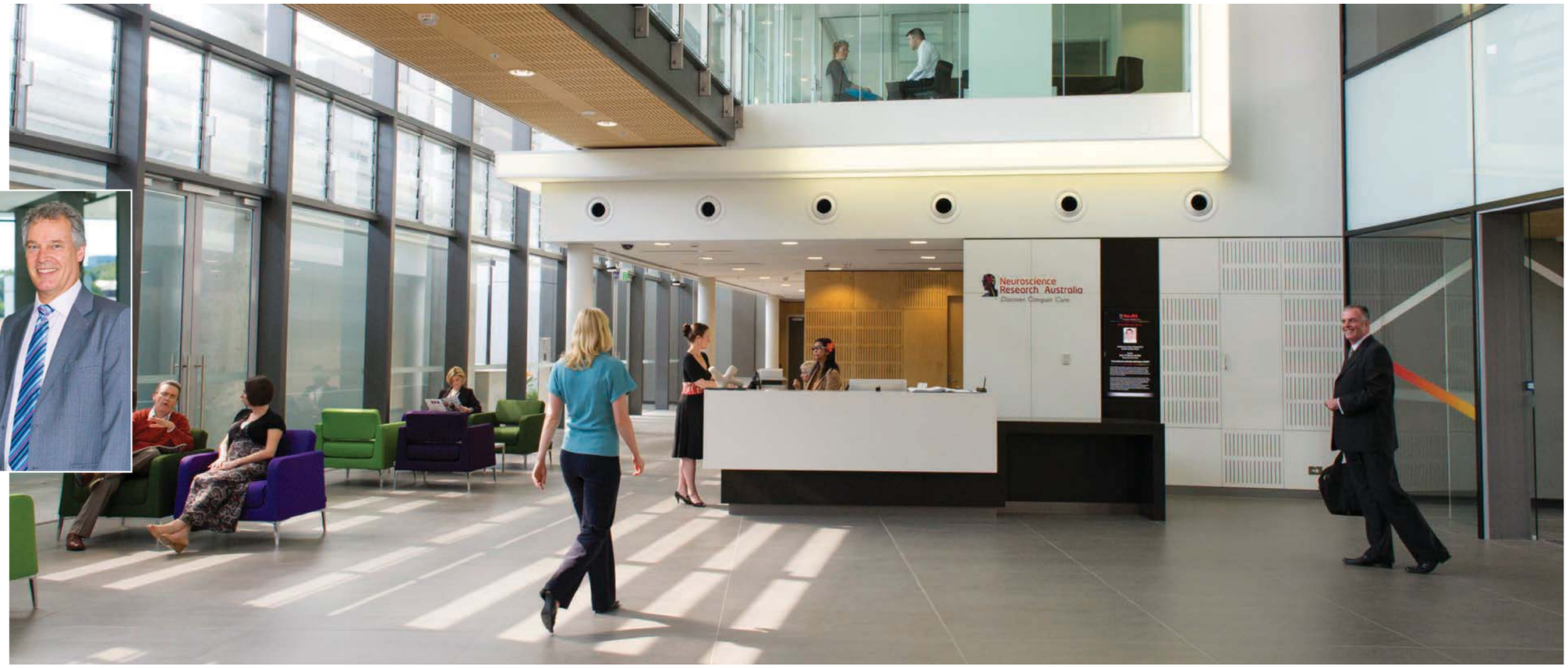
welcome

NeuRA's capacity to discover, conquer and cure the health challenges facing our generation, and those of our children and their children, is the greatest it has ever been.

Paul V Brassil
Chairman

Prof Peter R Schofield
Executive Director and CEO

Main image:
Our new reception



Gains in modern medical research mean that people now live longer than they have at any point in our history. As medicine's capacity to treat and cure infectious diseases and systemic diseases such as heart disease and cancer improves, we will enter a phase in human history where neurodegenerative diseases will be the main cause of death and disability.

Since its establishment 20 years ago, NeuRA has continually grown and adapted and this is important to us in remaining one of Australia's leading medical research institutes. Along with the impressive gains in our physical environment, our researchers continue to make remarkable inroads to understanding the causes of and developing treatments for some of our most devastating diseases.

These milestones include identifying the very first signs of Alzheimer's disease; the creation of digital apps to help clinicians and GPs assess falls in older people; insights into how our muscles fatigue; a paradigm shift in how we view the schizophrenic brain; and an exciting new international collaboration looking at a protein instrumental in Parkinson's disease. You can read more about these in the Profile.

The size and scope of our new building is a sign of the predicted burden that diseases and disorders of the brain and nervous system will have on humanity. We can now engage in cutting-edge research and bring together the best minds in science to address these conditions. Our new clinic and interview rooms, laboratories, research spaces and collaboration zones will unite our research themes and allow for synergies in thinking, methodology and problem-solving.

We have organised this Profile to highlight our research as it relates to you: your memory; your body; your nervous system; your mental health; and your brain.

This is the research that matters to you, and with your help and support we can continue to conquer the health challenges of today, and cure the health challenges of tomorrow.

Paul V Brassil **Prof Peter R Schofield, *PhD DSc***

our 20th anniversary

While many things have changed over the last 20 years, our commitment, initiative and optimism remain central to who we are and how we undertake our research.

Left to right: Construction work in 1992 to turn the site of the Randwick Chest Hospital into POWMRI; The four founders, in 1990, clockwise from top left – Prof Erica Potter, Prof Simon Gandevia, Prof David Burke AO, Prof Ian McCloskey AO; (top) The entrance to POWMRI when it officially opened in 1993; (bottom) The colourful entrance to POWMRI when stage two was completed in 2000; The new NeuRA building on Barker St.

> *"It is a sign of the scale of the medical challenges facing us that a large, dedicated neuroscience facility is required."*

Prof Simon Gandevia is NeuRA's Deputy Director, the last founding scientist still walking our corridors. In 1990, he and three colleagues drew up plans for the nation's then largest experimental neuroscience facility. The idea was bold, courageous and underpinned by incredible foresight. Over the next two years, this founding team secured a site and began the enormous task of launching the Prince of Wales Medical Research Institute (POWMRI).

The site had special significance because it was formerly the Randwick Chest Hospital, an internationally recognised facility for the treatment of tuberculosis. It was established in 1968 in response to the tuberculosis epidemic that had swept the country. Chest hospitals became obsolete thanks to medical research, and so the site later housed a variety of clinics and wards for the Prince of Wales Hospital.

When POWMRI was officially opened in 1993, it comprised fewer than 20 researchers, assistants and students who, in their first year, published 37 journal articles. The institute quickly outgrew the available space and, in the next 17 years, there were refurbishments and renovations and the construction of many new environments for research and learning.

Since its founding, the name of the institute had been confused with that of the hospital and in 2010 it was decided that a new name, reflecting the full scope of its research activity, was needed. The Board reviewed this matter at length and resolved to adopt the name Neuroscience Research Australia and the acronym, NeuRA. This name reflects more accurately what we do, namely neuroscience research, and that the research is directed to the benefit of all Australians.

The new name gave NeuRA space to grow, and grow it has. This year marks the opening of our purpose-built, seven-story building – a place where hundreds of researchers from Australia and the world gather to solve the health crises of today. It is a sign of the scale of the medical challenges facing us that such a large, dedicated neuroscience facility is required.

We find it exhilarating to think about NeuRA's humble beginnings – plans and lists on pieces of notepaper. From there to here in 20 years, one can only wonder what exciting developments and opportunities the coming decades will bring.

your **memory**

Abilities to remember and to think are sacred and deeply personal gifts that are affected by a long list of diseases, and by ageing.

Main image: Dr John Kwok works on the genetics of neurodegenerative diseases.

Inset: (above) a thin section of the cerebellum; (opposite) Dr Muireann Irish investigates memory and future thinking.

> *"We are identifying the causes of these disorders and are working towards developing better diagnostic methods and improved treatments."*

NeuRA is a leading authority on human memory, defining the diseases that attack our brains and minds, and developing biomarkers to measure it, and treatments that may halt devastating changes.

Neurodegeneration is the process by which a part of the brain dies as a result of trauma or disease. Science currently does not know how to prevent or cure neurodegenerative diseases, and our ability to treat them is limited. The causes of Alzheimer's disease and dementia, motor neurone disease and Parkinson's disease continue to elude us.

Diseases that impact the brain and mind, and through these the body, impact severely on your quality of life, as well as that of your family.

The financial cost of these disorders – both to those affected by the disease and the Australian health system – is significant.

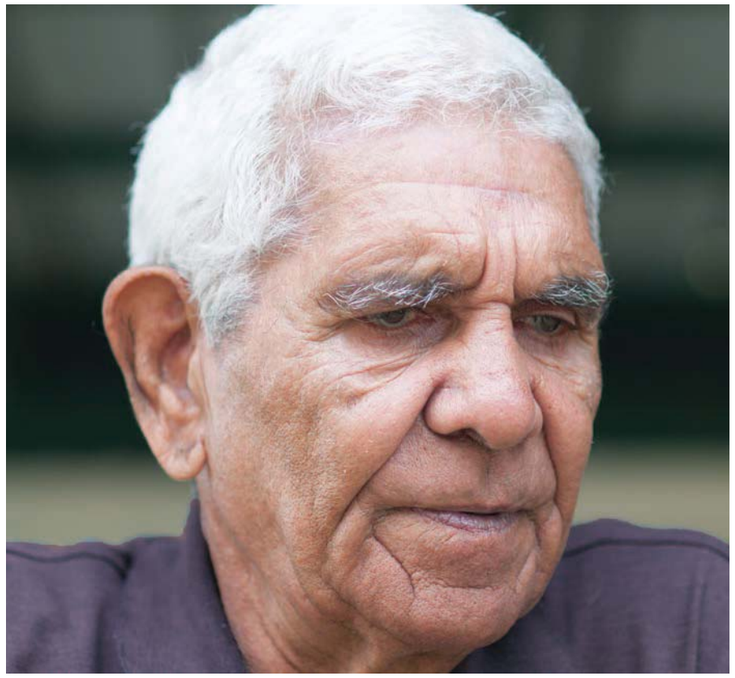
We are identifying the causes of these disorders and are working towards developing better diagnostic methods and improved treatments. As part of this research, we are also examining what happens to the brain as we age.

Our new facilities include expanded laboratories and state of the art clinical consultation and interview rooms. These spaces will speed up our work on Alzheimer's disease, frontotemporal dementia, Parkinson's disease, motor neurone disease and healthy ageing.

Diseases of the body are often diseases of the mind

Motor neurone disease (MND) is not a disease of pure motor symptoms, but can also affect one's ability to perform complex judgement and behaviour.
We have been at the forefront of describing these changes in people with MND and calling for more attention and treatment. Our work shows that almost half of carers of people with MND report high levels of carer burden and that non-motor symptoms are the major cause of this strain.
Our work has highlighted a significant gap in what happens to the families of people with MND. Non-motor symptoms such as changes in thinking, memory and behaviour are not accounted for in current diagnostic criteria.
Until these symptoms are included in diagnostic criteria, leading to an accurate diagnosis, carers will not know that these changes are common symptoms, rather than actions personally directed towards them by their loved one with MND.

Clockwise from top left:
Dr Eneida Mioshi investigates the burden on family carers of those affected by neurological disorders; a participant in the Koori Growing Old Well study; people with semantic dementia forget the names of common items; PhD student Kirsten Coupland.



Understanding disparity between Aboriginal and non-Indigenous communities

NeuRA research determined that the rate of dementia in urban and regional Aboriginal Australians is more than twice that of non-Indigenous Australians. The Koori Growing Old Well Study, conducted between 2009 and 2012, had 336 Indigenous participants from five urban communities, around Sydney and the Mid North Coast of NSW.
This information is now being used to develop education and aged health care services on the Mid North Coast and in La Perouse, through the Koori Dementia Care Project and through collaborations between NeuRA researchers and other organisations.

Treating dementia by bringing back forgotten words

A simple training program has been found to restore key words in people with semantic dementia – a disease that attacks language and our memory for words. The program pairs images of household objects, such as food, appliances and clothing, with their names, both written and spoken. After just three weeks of training, participants' ability to recall the names of the items improved.
Semantic dementia is a younger-onset dementia and, by relearning some of these everyday words, conversation becomes less frustrating with overall benefits for the whole family.

> *"After just three weeks of training, participants' ability to recall the names of items improved."*

Opposite: (top) Prof Peter Schofield in the new laboratories; (middle) architectural feature in the new building reflects NeuRA's vision; (bottom) DIAN study participant Chontell Johnson and study clinician Dr Bill Brooks.

No drug has proven effective at slowing or halting Alzheimer's disease. Is this because people have been trying to intervene when it is already too late?

In a critical research paper that sent waves of excitement around the world, NeuRA researchers and their international collaborators discovered that changes in spinal fluid and the brain can be observed up to 25 years before people with a genetic predisposition for Alzheimer's disease show clinical signs of this devastating disease.

The study is an international collaboration called the Dominantly Inherited Alzheimer Network, or DIAN. As part of this network, NeuRA and other study sites around the world are monitoring people who have a parent with one of the rare genetic mutations that cause Alzheimer's disease in middle age, usually between 30 and 60. These people have a 50% chance of having inherited the gene from their affected parent.

This network is the first chance we have had to look for changes related to Alzheimer's disease in living people who we know will develop the disease, with their brothers and sisters without the gene providing an ideal comparison group. There is currently no cure for Alzheimer's disease and available treatments target symptoms only. By looking at changes in people before they show memory loss, the hope is to develop more targeted treatments and identify the best window in which we may be able to prevent this disease altogether.

The landmark paper published in the *New England Journal of Medicine* in 2012 identified a number of major milestones in the way Alzheimer's disease progresses.

Around 20-25 years before Alzheimer's disease symptoms are expected, levels of a protein called beta amyloid decline in cerebrospinal fluid. And 10-15 years before the onset of Alzheimer's disease, accumulations of the beta amyloid protein is detected by imaging the brain and nerve cells begin to deteriorate. Patients start to experience memory problems five years later, and show the range of symptoms needed to diagnose Alzheimer's disease just three years after that.

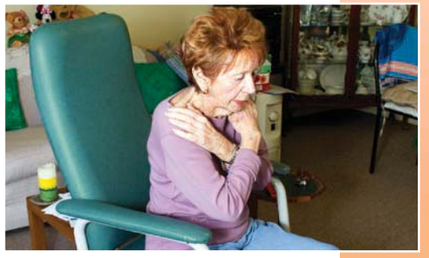
If you cannot measure the changes caused by a disease, how can you begin treating the disease, let alone cure it? Trying to alter the disease process before it takes hold is the best hope we have of winning the fight against this devastating disease.

Excitingly, using the biomarkers discovered through DIAN, clinical trials of new preventative medicines have now begun in the lead DIAN site in the USA. We hope they will be extended to the international DIAN sites including NeuRA within the next year.

Below: Staircase in the new building provides a colourful feature.

your body

The human body is an amazing machine that relies on a delicate interplay between our senses, our balance, our muscles and our brain.



Main image: Researching the sensory system.

Inset: (top) Balance and strength exercises in the home (bottom) Dr Jasmine Menant with a participant in the dizziness trial.

> *"Often we take the basic functions of our body – breathing, sleeping, walking, balancing and grasping objects – for granted until something goes wrong."*

Take a moment to look down and appreciate your hand – it's an extraordinary sensory and motor organ: you use it to explore the world using your sense of touch and perception. At the same time it is so sophisticated an instrument that you can also use it to manipulate objects and change the environment around you. Your ability to do this is a remarkable neurological feat – you control more than 20 hand muscles simultaneously!

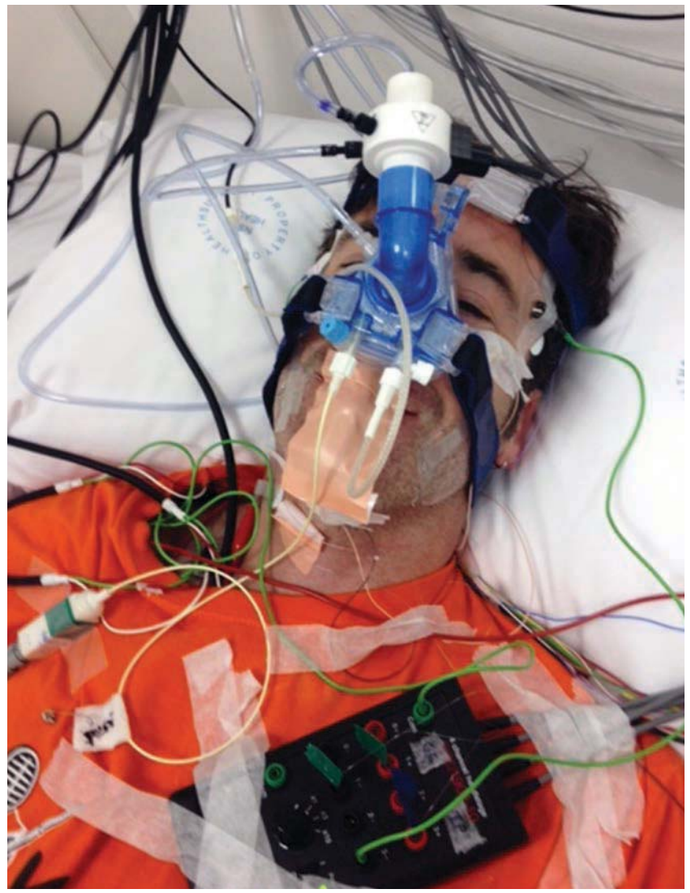
NeuRA scientists are examining how the sensory system works, how it affects the motor output from the brain, and how it gives us an accurate 'sensory' map of the external world, allowing us to make accurate movements.

Often we take the functions of our body – breathing, sleeping, walking, balancing and grasping objects – for granted until something goes wrong. This robs us of our innate abilities, through diseases such as multiple sclerosis, disorders such as strokes, or through ageing. Vertigo, dizziness, falling over, muscle fatigue and weakness, muscle contractures and impaired movement are debilitating outcomes of these diseases and disorders.

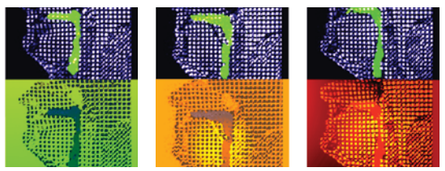
We are studying how these fundamental systems work, including the physiological, biomechanical and neurological aspects, as well as what happens when they go wrong. For many of these disorders, we also have to establish their prevalence and incidence, which we can do through our clinical work.

The effects of sleeping pills on sleep apnoea

Obstructive sleep apnoea affects at least 5-10% of the Australian adult population, and is characterised by repetitive narrowing or closure of the airway between the back of the nose and throat, which interrupts sleep. If untreated, sleep apnoea can cause daytime sleepiness, hypertension, and is associated with increased risk of stroke and cardiovascular disease. The main treatment, called CPAP therapy, involves wearing a mask during sleep that blows air into the nose to keep the airway open. It is very effective, but over 50% of patients cannot tolerate the therapy. Several studies are being conducted at NeuRA to determine the causes of sleep apnoea, and the effect of common sleeping pills on sleep and breathing. Certain pills may help some patients with sleep apnoea, but worsen outcomes in others.



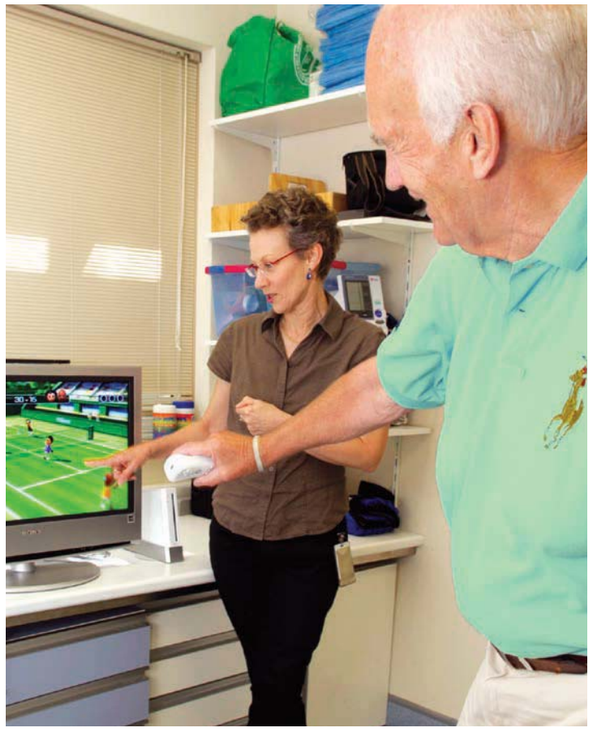
"Several studies are being conducted at NeuRA to determine the causes of sleep apnoea."

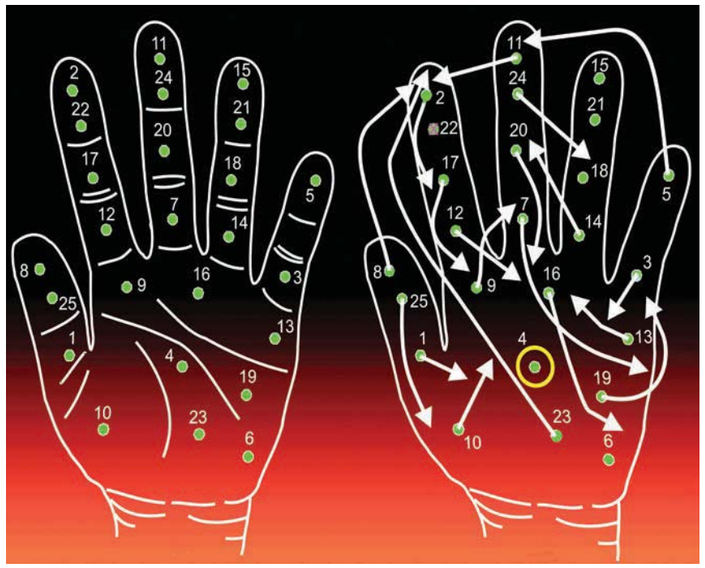


Broadband delivery of rehabilitation

Opened in October 2012, the Broadband Smart Home in Armidale demonstrates many of the real-world applications of faster broadband. Researchers at NeuRA took part in developing some of these applications, including a new stroke rehabilitation therapy utilising the Nintendo Wii. Already, our research has shown that an intensive, two-week Wii-based Movement Therapy can significantly improve the way stroke patients are able to use their limbs, even if they had a stroke many years ago. It was previously thought that the movement and function stroke patients had at 5-24 months post-stroke was the only recovery they would make. This therapy can be delivered online, and is set to be trialed shortly.

For more information on all research projects, visit ***neura.edu.au***

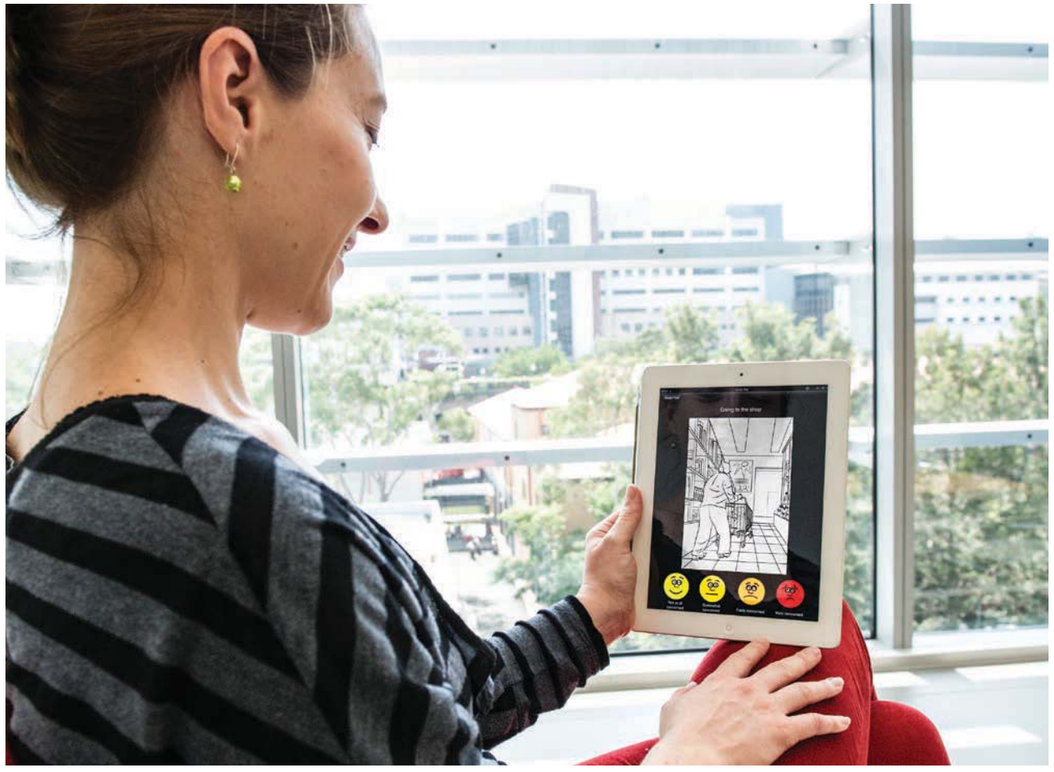




Clockwise from top left: A research volunteer tests a CPAP mask; Dr Penelope McNulty works with a post-stroke patient on Wii-based Movement Therapy; Mapping inaccurate touch points on the hand after stroke; Imaging the throats of people with (far left) no sleep apnoea, mild sleep apnoea and (far right) severe sleep apnoea.

Stroke alters the brain's view of the hand

Researchers have uncovered a new effect of stroke, where the brain develops an inaccurate map of the hand. They examined a stroke patient's hand using a fine-scale method of non-painful touch.
Of the 25 locations tested, the patient correctly identified only one spot where they were being touched. Instead, when a finger was touched the patient sometimes felt the touch in the palm, adjacent fingers, or a different spot on the same finger.
We are now testing for the same effect in more stroke survivors, and this research may affect rehabilitation strategies. Currently, rehabilitation focusses on regaining movement in order to recover hand and arm function. But this new research shows how sensory dysfunction could be one of the key factors to determine poor recovery of hand dexterity after stroke.



Opposite: (top left) Karl Hillebrand uses a balance exercise program, developed by NeuRA's research physiotherapists, to be used at home; (top right) Marje Donohoe rests after undertaking balance and strength exercises in her home; (bottom) Dr Kim Delbaere tests the iconFES iPad app.

We believe every Australian should be able to age independently, ideally in their home environment.

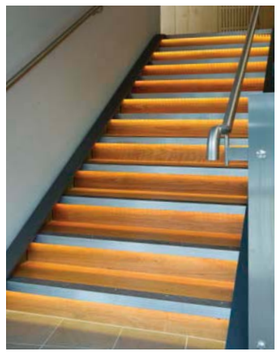
Falls are a major age-related health challenge, with about one third of older people falling at least once a year. Falls can significantly impact quality of life and can also incur major costs for health and social care. Over the last year, NeuRA researchers have developed iPad apps that help GPs and clinicians assess whether their patients are at risk of falling. So far, these apps look at two methods of assessing risk of falls: fear of falling and postural sway.

Fear of falling is very common in older adults, and is associated with higher rates of falls. While there are several instruments already available to measure fear of falling in older adults, the iPad app developed at NeuRA, called iconFES, is the first one to use pictures to gauge the level of concern people have about falling in daily situations. For example, the iconFES app asks a user how comfortable they feel walking on a slippery surface while showing them a picture of a person walking on a wet floor. The user then indicates how concerned they are about falling in that situation on a four-point scale using icons of smiley faces.

The iconFES app allows a GP or clinician to perform a fear of falling assessment quickly and reliably, which can then be shared with the patient immediately. The data collected via the iconFES app can also be used to create fall prevention strategies. Trials of the app indicate that people find it both simple and fun.

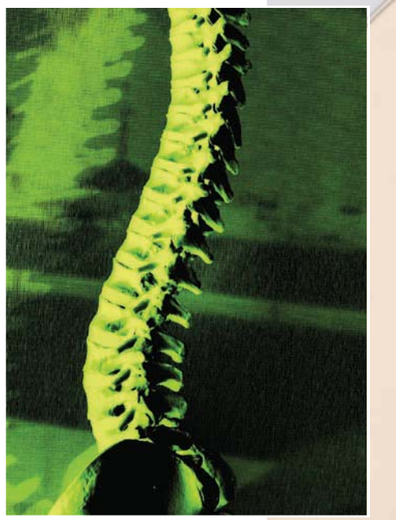
Physical activity levels often reduce as people age, which is associated with a reduced quality of life and independence. Our researchers have developed another app, called IPEQ, that assesses weekly physical activity levels in older adults on two levels – planned activities, which focusses on exercise and walks that were arranged in advance, and incidental activities, which focusses on casual, day-to-day activities. The IPEQ app gives clinicians the opportunity to assess physical activity levels more regularly in their older patients and ascertain whether their patients have taken up exercise. The IPEQ app can also identify activities that need a stronger focus as part of a falls prevention program to reduce fall risk in older adults.

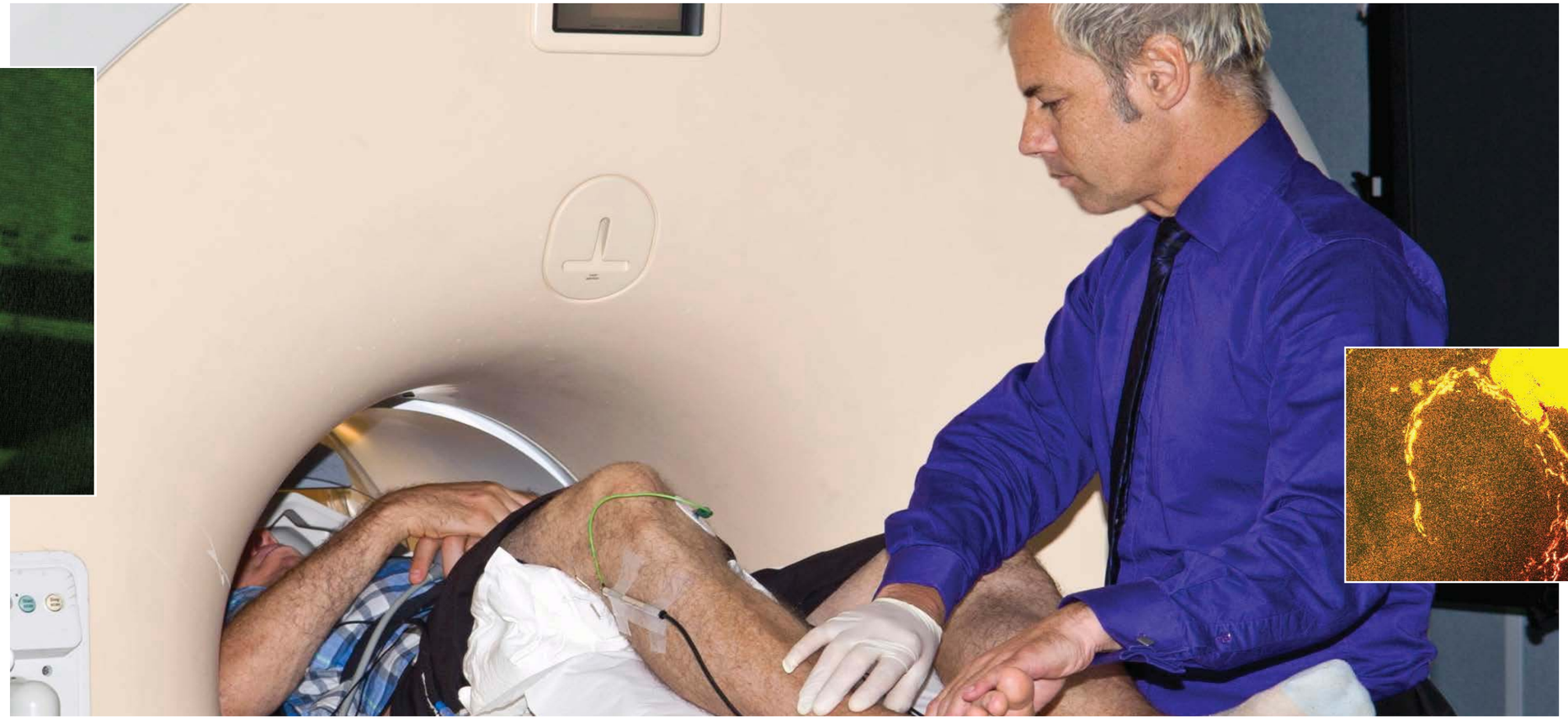
There are plans to release a series of apps that will measure other factors known to be associated with falling, such as response time, balance and cognitive performance.



your nervous system

Injury is the leading cause of death for people under 45 years of age.





Main image: Prof Vaughan Macefield recording nerve activity in a patient who is also having a brain scan.

Inset: (above) A human spine; (opposite) A neuron with an axon forming a perineuronal basket around a neighbouring cell.

"Our goal is to increase the ability of people with an injury to look after themselves."

Injuries to the nervous system, such as brain and spinal cord injuries, are particularly devastating, often leading to lifelong disability.

At NeuRA, we research the basic mechanisms of spinal injury: how do the tissues of the human nervous system respond to mechanical forces? And what can we do to minimise the impact?

Using leading techniques, our researchers also measure how individual nerves operate, both in health and in disease. We research the complex changes in nerve and muscle excitability that occur over time or after spinal injury, including the mechanisms underlying nerve dysfunction. We are developing tools to the help recovery of voluntary movement after injury.

Our goal is to increase the ability of people with an injury to look after themselves. We also focus on the actions of immune cells at sites remote from the injury and the consequences for other nerve pathways. Whether the immune cells are beneficial or detrimental is not known, but we are currently testing the link between immune cell activation and the progressive death of injured nerve cells.

At the other end of the spectrum, we work with policy makers and community organisations to translate our research into preventative strategies for car and motorcycle accidents – including better vehicle restraints and protective clothing. These are practical outcomes that lead to lives being saved and injuries averted.

Reducing the risk of injury among motorcyclists

Motorcyclists are in a high-risk road user group. Currently 22% of serious injury and 16% of fatal injury in road crashes involve motorcyclists, despite the fact that motorcycle usage accounts for only 1% of vehicle kilometres driven.
Our investigations into motorcycle crashes are aimed at improving current understanding around what factors increase risk of crash involvement and risk of serious injury. In 2012, researchers talked to more than 500 motorcyclists across NSW to develop a profile of motorcyclists' characteristics. This will help put the risk factors we identify in our crash studies into context.
We are also studying the qualities of protective clothing for motorcyclists, and the potential role of fatigue in motorcycle crashes.

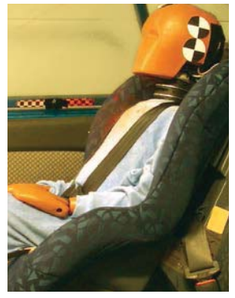
Clockwise from top left: Dr Liz deRome (right) discusses protective clothing with research physiotherapist and motorcyclist Betty Ramsay; Dr Daina Sturnieks uses correct restraints for Luca and Elsie; Dr Bonne Lee works with international partners on mapping spinal injuries; A test dummy used in NeuRA's crash lab.

Vehicle restraint use and early childhood education intervention

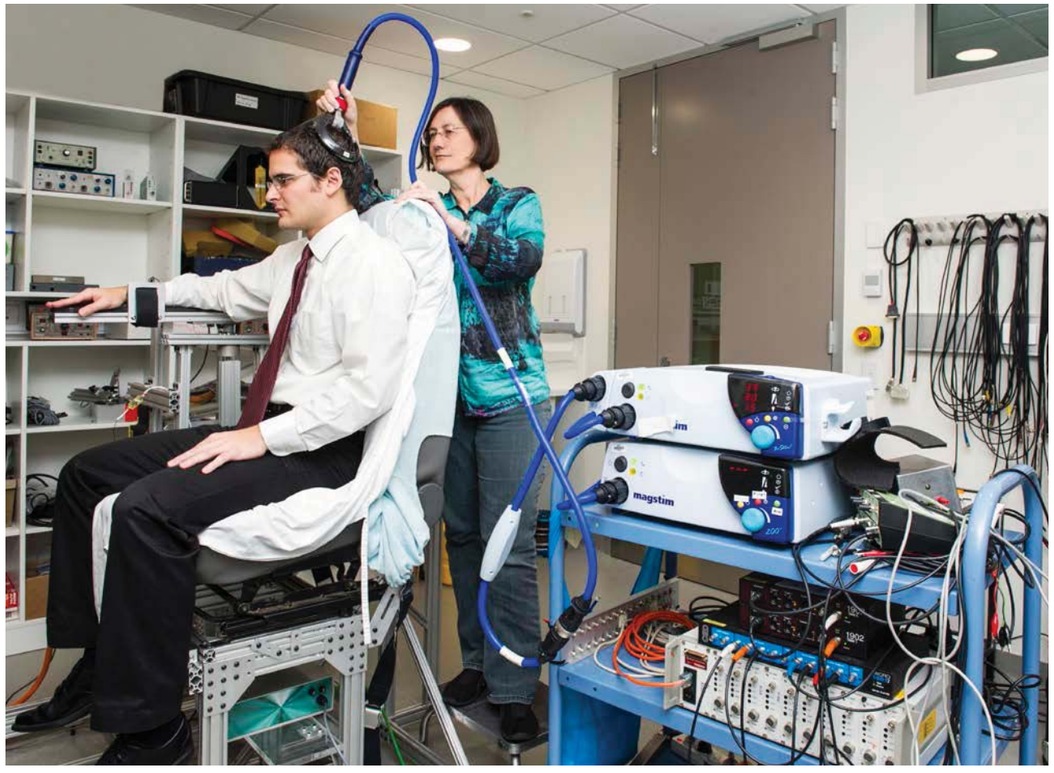
Injury in car crashes is a major source of death and disability in children.
As a direct result of NeuRA's research, Australian legislation was changed in 2009 requiring use of child restraint systems up to age seven. But education programs are essential to achieve widespread best practice. Our researchers have developed and evaluated an early education intervention program which teaches children aged three to five years, their parents, and their carers, how to correctly use the best restraints for their size. This year, some of this material has been incorporated into NSW Transport's Road Safety Education Program.

Global maps of spinal cord injury

Our scientists have collaborated with international partners to update an epidemiological map of traumatic spinal cord injury, and have produced the first estimate of a global incidence rate, at 23 cases per million people. They have also assisted with the release of the first global map for non-traumatic spinal cord injury. This will allow the international community to more easily access information reflecting patterns of injury and possible collaborations to help prevent these injuries from occurring. It is particularly important, as the regions of the world where the number of spinal cord injuries are on the rise are the same regions that have the highest mortality, and where the health systems are least able to cope with the complexity of treatment.



"Researchers have developed and evaluated an early education intervention program on the use of child restraints."



The control of muscles by the nervous system underlies all of our actions

To produce any voluntary movements, like reaching, grasping, standing or walking, requires a chain of events. Signals from the brain activate motor neurons in the spinal cord and these in turn activate muscle fibres to make them contract.

Moreover, the neurons in the brain and spinal cord must keep firing to keep the muscle working. As soon as they stop, the muscle relaxes. Therefore, during exercise, not only the muscles are working but so too is the nervous system.

Muscle fatigue with exercise is a common experience in healthy people. It is also a prominent symptom in people with many kinds of illnesses. Although processes in the muscle cause some of the weakness of fatigue, processes in the nervous system also contribute. Past research at NeuRA has shown that when people make repeated or sustained muscle contractions, the brain becomes less able to drive the motor neurons to drive the muscles. In some kinds of exercise, the failure of the brain is just as important as the failure of the muscles.

Recent NeuRA research shows that the behaviour of neurons in the spinal cord may also play a part in fatigue. When motor neurons have to fire repeatedly during deliberate, voluntary activity, they become less responsive to input.

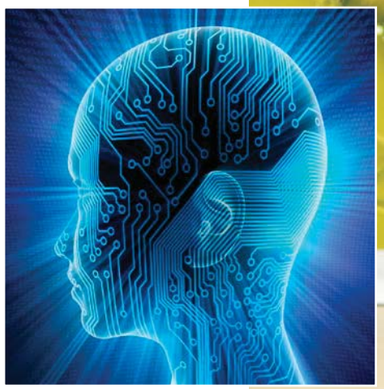
This may mean that the brain's task during exercise is made harder because extra drive from the brain is required to keep the motor neurons firing and the muscles contracting. For the person, the exercise will take more effort.

It is important to understand fatigue in healthy people as it influences the performance of tasks in work, sport and everyday life. Understanding its mechanisms will also allow better management of this symptom in illness.

Opposite: (top) PhD student David Kennedy performs a strong voluntary contraction of the elbow flexor muscles to measure force output; (bottom) Assoc Prof Janet Taylor and PhD student Jim Nuzzo use transcranial magnetic stimulation to measure how well the brain drives the muscles.

your mental health

Mental illness is responsible for one of the largest disease burdens in Australia.



Main image: Dr Leonora Long studies causes of schizophrenia.

Inset: (above) Mental illnesses are sometimes conceptualised as disorders of brain circuits; (opposite) Dr Dipesh Joshi looks at genetic sequences.

"Our best hope of combating mental illness effectively is to develop prevention and intervention strategies."

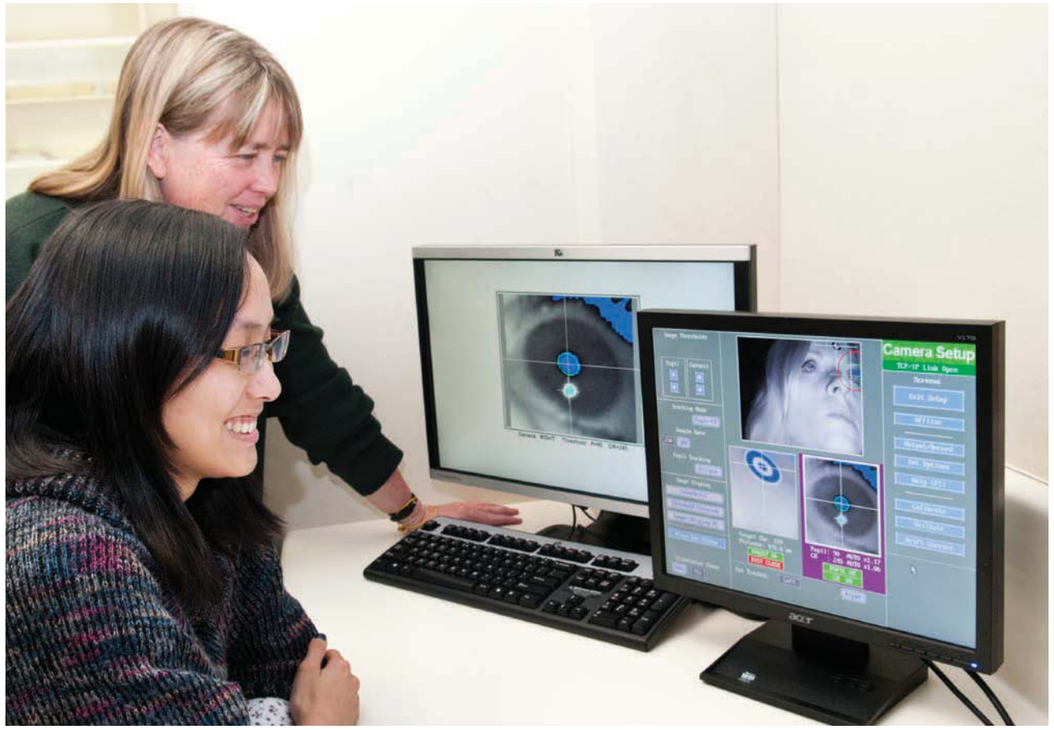
The statistics for mental illness are striking: every year some form of mental disorder affects around one in five adults; and the major psychiatric disorders, schizophrenia and bipolar disorder, each affect about 1% of the population.

When facing such large numbers, our best hope at combating mental illnesses effectively is to develop prevention and intervention strategies. For some of these disorders, early warning signs can be found in childhood or adolescence, and researchers are looking at early intervention strategies.

Our experts in brain imaging and genetics are researching biological features, such as those in the brain or in our genes, of schizophrenia, bipolar, conduct disorder and autism. Establishing knowledge of the early warning signs by neuro-imaging or by changes in gene expression will help develop tests to identify those at high risk of developing these debilitating mental illnesses.

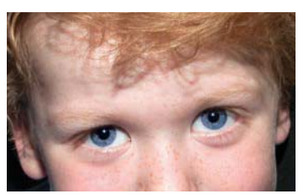
Research into biological features will also identify the sub-types of the illnesses. The root cause is not always the same. Patients may respond differently to signals such as sex hormones, inflammation, or adrenalin. We need to understand these different cases in order to tailor treatments to individuals. And we go one step further, to trial new intervention therapies and existing medications. Some therapies can even result in underlying changes in neural function, reversing the cognitive impairments in those with these mental illnesses.

The two faces of conduct disorder



Conduct disorder in early childhood, such as systematic aggression, lying and stealing, is the single biggest risk factor for mental disorders in adulthood. And yet, nearly 40% of children do not respond to existing interventions. This may be because a little-studied subtype of conduct disorder exists, in which children have an impaired recognition of fear in facial expressions and thus develop callous and unemotional traits. The neurological basis for these subtypes is being researched at NeuRA, as well as a possible intervention where children learn to intentionally direct their attention toward others' eyes, using eye tracking during MRI.

"Conduct disorder in early childhood, such as systematic aggression, lying and stealing, is the single biggest risk factor for mental disorders in adulthood."



Identifying those at high risk of bipolar disorder

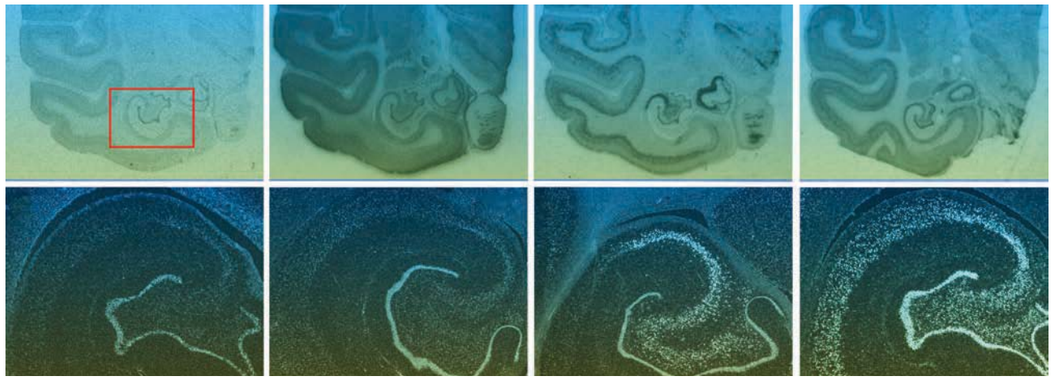
Bipolar disorder is a severe and complex mood disorder affecting more than 350,000 Australians. Children of individuals with bipolar disorder are at increased risk of mental illness, but tools to predict which of these genetically at-risk young people will eventually develop the disorder are very imprecise. Our scientists are using genetic information, plus brain imaging, to detect structural changes that may predict which 'at-risk' individuals are likely to become ill. This study will help elucidate early clinical and biological markers of bipolar disorder.

Cannabis and the teenage brain

Research has found that the brain network responsible for mediating the effects of cannabis, the endocannabinoid system, undergoes high levels of change during adolescence, making it more vulnerable to the drug during this time. Understanding this is important because cannabis use is common among teens, and adolescence is a time when adult behaviours and decision-making are being developed. Our discovery that the adolescent brain may be more vulnerable to the effects of cannabis is significant for the onset of schizophrenia.

For more information on all research projects, visit ***neura.edu.au***

Clockwise from top left: Prof Rhoshel Lenroot studies eye tracking with PhD student Pui Ka Yeung; Dr Jan Fullerton in the genetics lab; Cannabis use is being investigated for its role in schizophrenia and dementia; children with conduct disorder learn to direct their attention to others' eyes.



Opposite: (top) Brain sections showing areas of the hippocampus revealing the expression of schizophrenia risk genes; (bottom) Prof Cyndi Shannon Weickert is head of the Schizophrenia Research Laboratory.*

This year, NeuRA has made two significant breakthroughs in schizophrenia that are causing a paradigm shift in how we view the schizophrenic brain.

Schizophrenia is a devastating mental illness that ranks among the top 10 causes of disability in developed countries worldwide. It first manifests during adolescence, causing profound withdrawal from family and friends, a decrease in intellectual abilities, hallucinations and delusions.

In 2012, in a major breakthrough, our researchers found that the schizophrenic brain shows neuroinflammation, or signs of damage, in the dorsolateral prefrontal cortex, a frontal region of the brain involved in regulating emotional and social behaviour. This significant research provides the strongest evidence to date of a link between immune function and schizophrenia.

Using new genetic tools, the researchers were able to measure immune activity in the brains of people with schizophrenia and healthy people without the disease. From the types of immune markers measured, it's like the brain is on 'red alert', and this increased inflammation was found in 40% of patients.

With multiple biological causes of schizophrenia, the fact that inflammation occurs in 40% of cases now opens up a whole new range of treatment possibilities. Future therapies for schizophrenia aimed at immune suppression are now being investigated.

Another major study focussed on white matter tracts found deeper in the brain. While grey matter is found in the outer regions of the brain and consists primarily of neurons, white matter tissue consists primarily of the nerve fibers in their fatty, protective sheaths. In the brains of people with schizophrenia, the white matter has a higher density of neurons than in healthy brains.

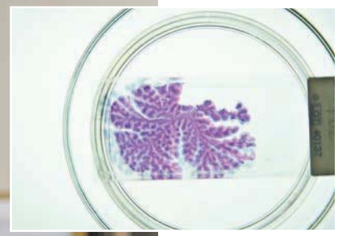
It had been thought that these neurons were simply forgotten by the brain, embryonic remnants that somehow didn't die off as they should during development. However, NeuRA research has shown how these neurons may be derived from the part of the brain that produces new neurons, and that they may be in the process of moving towards the grey matter regions. It appears that the schizophrenic brain is attempting to repair itself, that the neurons may be moving towards the surface of the brain, the area most affected by schizophrenia.

*The Schizophrenia Research Laboratory is a joint initiative of Neuroscience Research Australia, the University of New South Wales, Schizophrenia Research Institute and the Macquarie Group Foundation. It is supported by the NSW Ministry of Health.

Below: District views of Randwick

your brain

Understanding the human brain is one of the greatest challenges of 21st century science.



Main image: Dr Claire Shepherd, Manager, Sydney Brain Bank.

Inset: (above) Staining slides of brain tissue; (opposite) a selection of brain tissue slides.

"There's never been a more exciting time in neuroscience."

The brain is the last of the human organs to give up its secrets. Every other organ has had its structure and chemical composition identified. But the brain is so intrinsically bound up with the person to whom it belongs that the study of the organ in isolation can be problematic.

To date, medical research has identified more than 500 brain diseases. But it is only symptoms and syndromes that identify many of these diseases, which make it difficult to diagnose the diseases let alone pinpoint the underlying cause.

Here we perform fundamental neuroscience, researching the brain's structure and function, and our researchers are renowned world experts in brain mapping.

We also house the Sydney Brain Bank, which comprises more than 800 donated brains. The bank collects, characterises and distributes human brain tissue for research purposes. Uniquely, our researchers establish a relationship with a person for years before receiving their brain, collecting full medical and background information, including obtaining brain scans during life. The knowledge of this history can then be matched with what is observed of their brain tissue, post mortem.

New, non-invasive imaging technology also allows us to study the brain in situ. Our researchers can see live changes in brain activity and blood flow, and determine brain chemistry and structure. There's never been a more exciting time in neuroscience.

Stimulating the brain

Transcranial direct current stimulation, in which low currents are applied through electrodes on the scalp, is an emerging treatment for psychiatric conditions as well as neurological disorders. The treatment is safe, and has potential to translate into clinical practice, but how it works and what changes occur in the brain as a result are not well understood.
NeuRA researchers studying depression have shown how the brain responds to the treatment by decreasing acidity and by synthesis of major high-energy molecules. This may provide a way to identify those most likely to respond to a course of brain stimulation treatment, as well as a way to optimise depression treatments.

Clockwise from top left: PhD student Marshall Dalton; Dr Sharpley Hsieh (right) with volunteer Bob Bryans; Dr William Huynh studies the arm of a stroke patient; A stained slide of the human medulla oblongata, the lower portion of the brainstem.

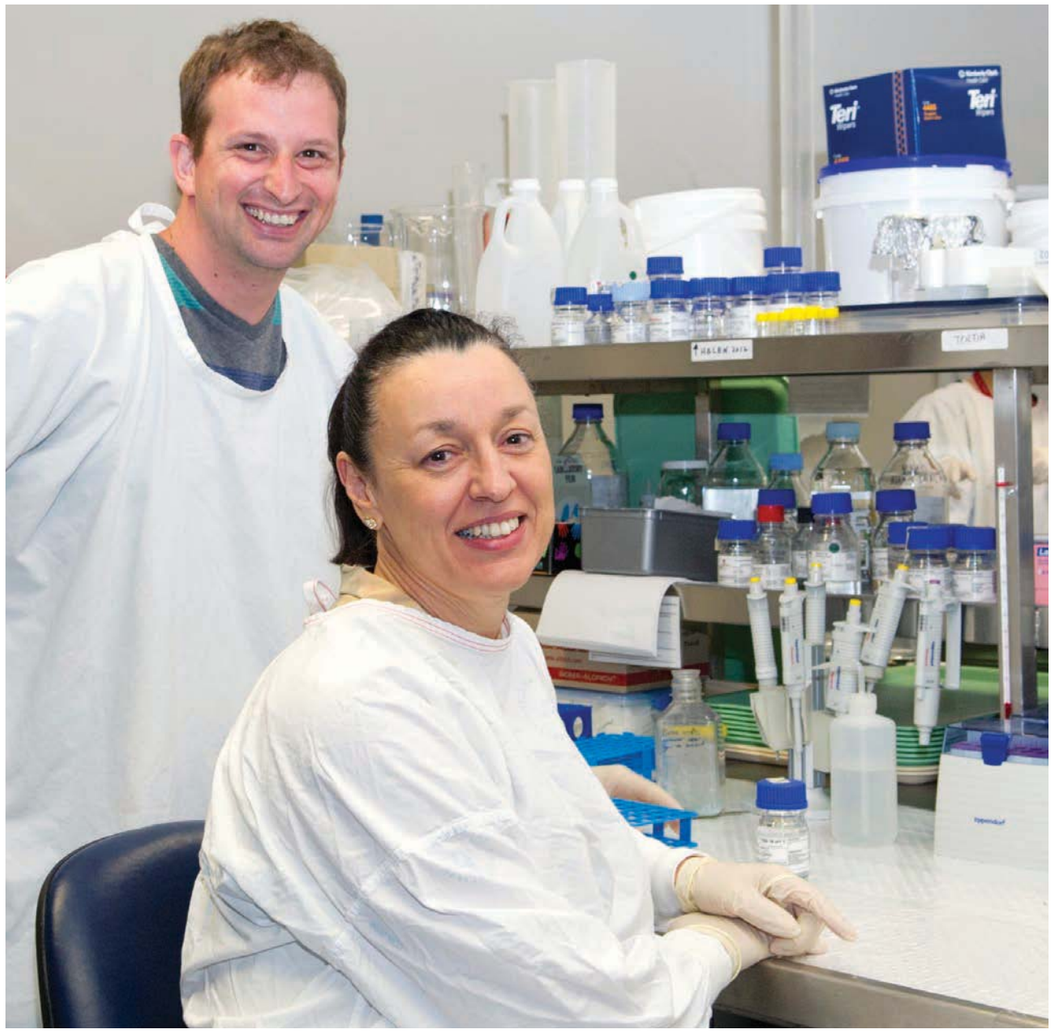
How does the brain process emotion?

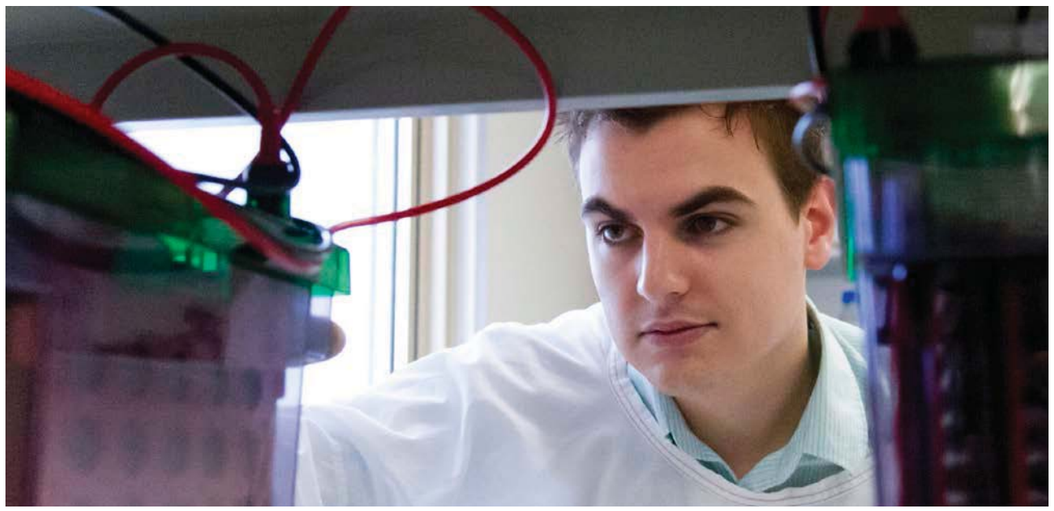
Melodies in music carry an inherent emotion that can be identified by almost everyone, regardless of their culture, as positive or negative, uplifting or depressing. NeuRA researchers found that people suffering from semantic dementia, a rare type of dementia affecting factual knowledge of words and objects, were more impaired at recognising emotions in music than those with Alzheimer's disease.
They discovered that recognition of the emotional content in a tune draws on some of the same brain regions involved in language and verbal skills. With this finding, our researchers are challenging the current understanding of how the brain processes emotions.

Botox helps restore electrical activity in the brain

Botox (botulinum toxin) may be most commonly associated with frown lines and wrinkles, but it is also an important treatment for rigid and stiff arm muscles following a stroke.
NeuRA researchers found that when botulinum toxin is injected into these arm muscles it not only improves movement, but also restores electrical activity in the cortex – the brain region responsible for movement, memory, learning and thinking. Restoring normal activity in the brain may assist with long-term recovery in stroke patients.

"NeuRA researchers are challenging the current understanding of how the brain processes emotion."





A major research initiative is underway at NeuRA, and the goal of this initiative is as ambitious as it is clear: to make Parkinson's disease history.

Parkinson's disease is the second most common neuro-degenerative disorder worldwide, and in Australia alone, 30 new cases are diagnosed each day.

Despite Nobel Prize-winning research surrounding the discovery of levodopa, a drug now used to manage the early motor symptoms of the disease, causes and cures have remained elusive in the 200 years since James Parkinson's first description of the disease in 1817.

Our research is looking into a protein called leucine-rich repeat kinase 2, or LRRK2. Mutations in the gene that codes for the LRRK2 protein are a leading cause of genetic Parkinson's disease. LRRK2 is a key research priority area internationally and, with the help of the Michael J Fox Foundation, NeuRA has joined a consortium of research institutions that work together across nine countries.

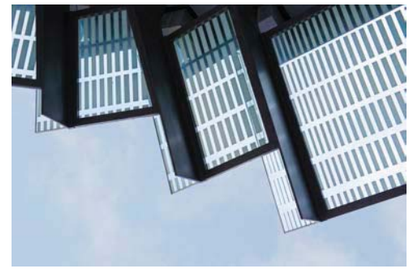
The latest findings from the team at NeuRA suggest that LRRK2 may be part of the signalling pathway that regulates the body's inflammatory immune response. That is, the body's response to viral or bacterial infection.

Increased inflammation in Parkinson's disease is not a new concept. In fact, many markers of inflammation are increased in patients. However, how inflammation, which everyone normally experiences during their lifetime, goes on to cause Parkinson's disease in only some people remains largely unknown.

Our scientists are determining whether LRRK2 affects the body's first line of defence – the innate immune system – and whether the function of LRRK2 is changed only in people with Parkinson's disease. If it is, this protein could be a potential new target for treating the disease.

Opposite: (top) Dr Nic Dzamko and Prof Glenda Halliday research possible causes of Parkinson's disease; (bottom) Honours student Pascal Segalin.

Below: Details of our architectural exterior



our clinics & facilities

A number of clinics and facilities, which form an integral part of the research matrix, are located at NeuRA.

Main image: Steve Turner, Facility Manager, Genetic Repositories Australia.

Inset: (above) Hilary Carter, Mechanical Workshop Manager; (opposite) MRI machine used by researchers in the NeuRA Imaging Centre.

NeuRA has for several years operated a major research clinic, Frontier, with the aim of better diagnosing and understanding frontotemporal dementia (FTD) and translating this research into better clinical practice. This clinic not only provides diagnosis and support for patient treatment but also underpins our research efforts to better understand the causes and progression of the illness.

There are several facilities at NeuRA to support the research environment and the wider medical community. These include the Genetic Repositories Australia, the NeuRA Imaging Centre, and the Sydney Brain Bank.

Genetic Repositories Australia (GRA) provides researchers, nationally and internationally, with a central facility for the processing, long-term secure storage and distribution of human genetic samples. This service forms an essential function for all genetic and epidemiological studies that aim to deliver new knowledge and improved health care.

The Falls and Balance Research Group has a long history of research into the assessment and prevention of falls in older people. As a result of the group's research, we have developed FallScreen®, a full detailed assessment tool for use in hospitals and long-term care institutions, and QuickScreen®, a falls risk calculator designed as a screening instrument for use in GPs' surgeries. Both tools are distributed globally.

Also supporting research are NeuRA's electrical and mechanical workshops. The unique nature of some of our work means that essential equipment required for experiments cannot be bought 'off the shelf'. Skilled technicians collaborate with scientists to design, prototype, and manufacture the equipment ranging from large-scale frames to small tissue baths, which can record electrical signals from individual nerve cells.

our boards

01

02

03

04

05

01 **Prof Peter R Schofield, BScAgr (Hons) PhD DSc**
Executive Director and Chief Executive Officer, 2004 – present

John Grill, BSc BE (Hons) Hon DEng
Independent Director, 2010 – present

02 **Dr Jennifer Alexander, MCom MB BS MHP FRACMA FAFPHM (RACP) FAICD FAIM FACHSM**
Director 2013 – present (Nominee of the University of New South Wales)

Prof Mike Calford, BSc (Hons) PhD
Director, 2009 – present (Nominee of the National Health and Medical Research Council)

03 **Barry Shepherd, PSM GradDipPSM**
Independent Director, 2005 – present

Assoc Prof Richard Matthews, AM MB BS
Director 2011 – present (Nominee of the South Eastern Sydney Local Health District)

Paul Brassil, BEc LLB FCA FTIA CTA
Independent Director, 1997 – present
Chairman of the Board, 2004 – present

04 **Lisa Pettigrew, BA (Hons-Econ)**
Director, 2011 – present (Nominee of the NSW Minister for Health and for Medical Research)

Prof Peter Smith, RFD MD FRACP FRCPA FAICD
Director, 2005 – present (Nominee of the University of New South Wales)

05 **Andrew Bernard, BSc MPH**
Director 2008 – present (Nominee of the South Eastern Sydney Local Health District)

Not shown
Michael Quigley, BSc BE
Independent Director, 2008 – present

foundation

Back row: Prof Peter Schofield, Ian Kennedy OAM, Sally Manion, Ian Harris

Front row: Paul Brassil, David Karpin AM, Graeme Bradshaw

your contribution

During 2012, more than 2,000 people and organisations from every state and territory supported NeuRA, and we have 44 living Australians making a gift in their will. Together we are building a healthier and safer community.

Laurie Cowled, of Queensland, started donating to NeuRA in 2005, and has supported Australian female PhD students, such as Rachel McBrain, to study Alzheimer's and other brain diseases for five years. Laurie has left a bequest to fund her Cowled Foundation, which in turn will foster the career of our most talented female researchers for years to come.

"I am keen to nurture these young women scientists, who will go on to become researchers of brain disorders that currently affect large sections of the community."

Reg Ryan, of Waverley, has pledged to donate his brain to the Sydney Brain Bank, and has been a financial donor since 2006.

"I can see the problems in medical science of getting proper samples and getting people to volunteer to participate in trials and that sort of thing. So I'm quite happy to support it and encourage it."

In 2012, The Coopers Brewery Foundation, of Adelaide, supported NeuRA by contributing to the costs of MRI scans involved in our early detection of Parkinson's disease research.

"We are happy to be involved in this study which aims to develop an early objective test, so that other people don't have to go through what Jeff did to get diagnosed."

Cheryl and Jeff Taylor, seen here with Assoc Prof Kay Double.

Doug Mitchell, Joan Heaney and John Muddle attend events of the Phyllis Luker Society, our bequest program, in Sydney. Each has decided to leave a bequest to NeuRA. Doug and John's wives and Joan's brother died of neurodegenerative disorders.

"It is only through medical research that answers to these diseases could be found. I don't want to see this happen to anyone else!"
John Muddle

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