

## Alzheimer's Disease

such as Parkinson's, Motor Neuron and Huntington's diseases. Professor David Finkelstein is leading research investigating oxidative stress in these diseases and particularly in Parkinson's Disease.



Dr Susan Rossell  
Head of Clinical Research

In addition to this work Dr Susan Rossell, Head of Clinical Research at the Mental Health Research Institute, is leading cognitive studies that are investigating particular symptoms of the disease. As Alzheimer's Disease progresses, individuals may experience changes in personality and behaviour, such as anxiety, suspiciousness or agitation, as well as delusions. Delusions have recently been reported to be a common symptom in Alzheimer's Disease and are associated with greater aggression, caregiver stress and earlier institutionalisation or dependence for daily living activities. Dr Rossell and her team are studying the types of delusions experienced in the disease, their frequency of occurrence, and the demographic and cognitive risk factors. This research hopes to understand what role stage of organic disease plays on the presence of delusions, and to address the neurobiological changes involved in the generation of delusional beliefs in Alzheimer's Disease.

The Alzheimer's Disease Research Group continues to examine the underlying cause of Alzheimer's Disease and to investigate methods of early and accurate diagnosis of the illness. The latter is important as the earlier we can begin treating the illness the better the outcome for the patient. Our ultimate aim is to prevent Alzheimer's Disease and eventually to be able to cure it.

This work relies heavily upon donations. Your support for the search for a cure will be appreciated.



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The Mental Health Research Institute  
155 Oak St, Parkville Vic 3052  
Ph. 03 9388 1633  
**enquiries@mhri.edu.au**  
**www.mhri.edu.au**

## THE MENTAL HEALTH RESEARCH INSTITUTE

### ALZHEIMER'S DISEASE RESEARCH – THE SEARCH FOR A CURE

The impact of Alzheimer's Disease is well documented:

- The number of Australians with dementia, of which Alzheimer's Disease is the most common form, has passed 200,000, or 1% of the population
- The economic cost to the Australian community is in excess of \$7 billion annually

Alzheimer's Disease is named for Dr Alois Alzheimer, a German physician. In 1906, while conducting an autopsy of a woman who had died after what appeared to be a mental illness, he observed tangles of brain fibre surrounded by dense deposits (plaques). These tangles and plaques are now recognised as the hallmarks of the disease.

Professor Colin Masters, who heads the Alzheimer's Disease research team of scientists from the Mental Health Research Institute and University of Melbourne, was the first person to discover that overexpression of a brain protein, amyloid Beta A4 (A-beta protein), is the cause of the disease. This protein is toxic to nerve cells and forms plaques in the brain that interfere with normal brain function.



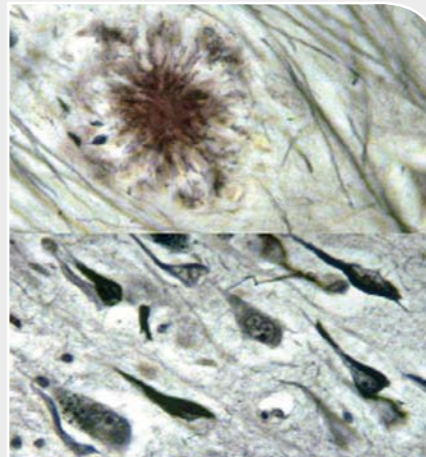
Professor Colin Masters  
Program Leader of the Alzheimer's Disease Research Group

## Alzheimer's Disease

There are competing theories as to the mechanisms that cause the plaques to form, but it is universally agreed that the A-beta protein aggregates to form these insoluble deposits which precede the appearance of the tangles in the course of the disease.



Mental Health Research Institute Oxidation Disorders Research Team



Alzheimer plaques (above) and tangles (below) as seen down the microscope.

Professor Ashley Bush  
Head of the Oxidation Disorders Laboratory



The Alzheimer's Disease research team of scientists from the Mental Health Research Institute and University of Melbourne, together with collaborators from the Harvard Medical School, is pursuing the theory that the abnormal accumulation of A-beta protein occurs as a result of an "inappropriate" interaction with trace metals that occur naturally in the brain and which are integral to normal brain function.

This work has led to the discovery by Professor Ashley Bush, Head of the Mental Health Research Institute Oxidation Disorders Laboratory, that the formation of

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A-beta protein brain plaques is due to the interaction of A-beta protein with trace metals, most notably copper, in the brain. This protein-copper interaction produces toxic molecules (oxidative free radicals mentioned above) that destroy neurons (nerve cells in the brain). With this understanding of the cause of the illness we finally had a target to focus on and turned our attention to methods of stopping the toxic protein-copper interaction.

These findings led to a Phase II clinical trial at the Mental Health Research Institute of the drug PBT1, designed to remove A-beta protein from brain. This drug reduced the rate of mental deterioration of patients with Alzheimer's Disease.

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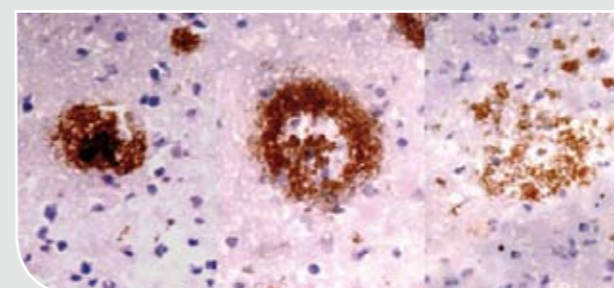
PBT2 was also shown to remove soluble A-beta protein (the most toxic form of the protein), and block the interaction between the protein and copper. Experimental mice that overexpress A-beta protein develop behavioural signs of cognitive deficits including loss of place or spatial memory, a hallmark of Alzheimer's Disease in the human. Remarkably, PBT2 reversed cognitive deficits in these mice. A safety trial (Phase I) of PBT2 in healthy humans has been completed, with satisfactory results, and a Phase II trial of PBT2 is now planned to begin in Sweden before 2006 year end. This trial will test the drug in people in the early stages of Alzheimer's Disease, primarily for safety and efficacy.

The Bush hypothesis of the adverse interaction between abnormal brain proteins and trace metals in the brain may also be relevant to other neurodegenerative diseases



Dr Robert Cherny  
Senior Research Fellow, Oxidation Disorders Laboratory

Three typical Alzheimer plaques as seen down the microscope



Brain scans showing normal brain (left) and brain affected by Alzheimer's Disease (right)

