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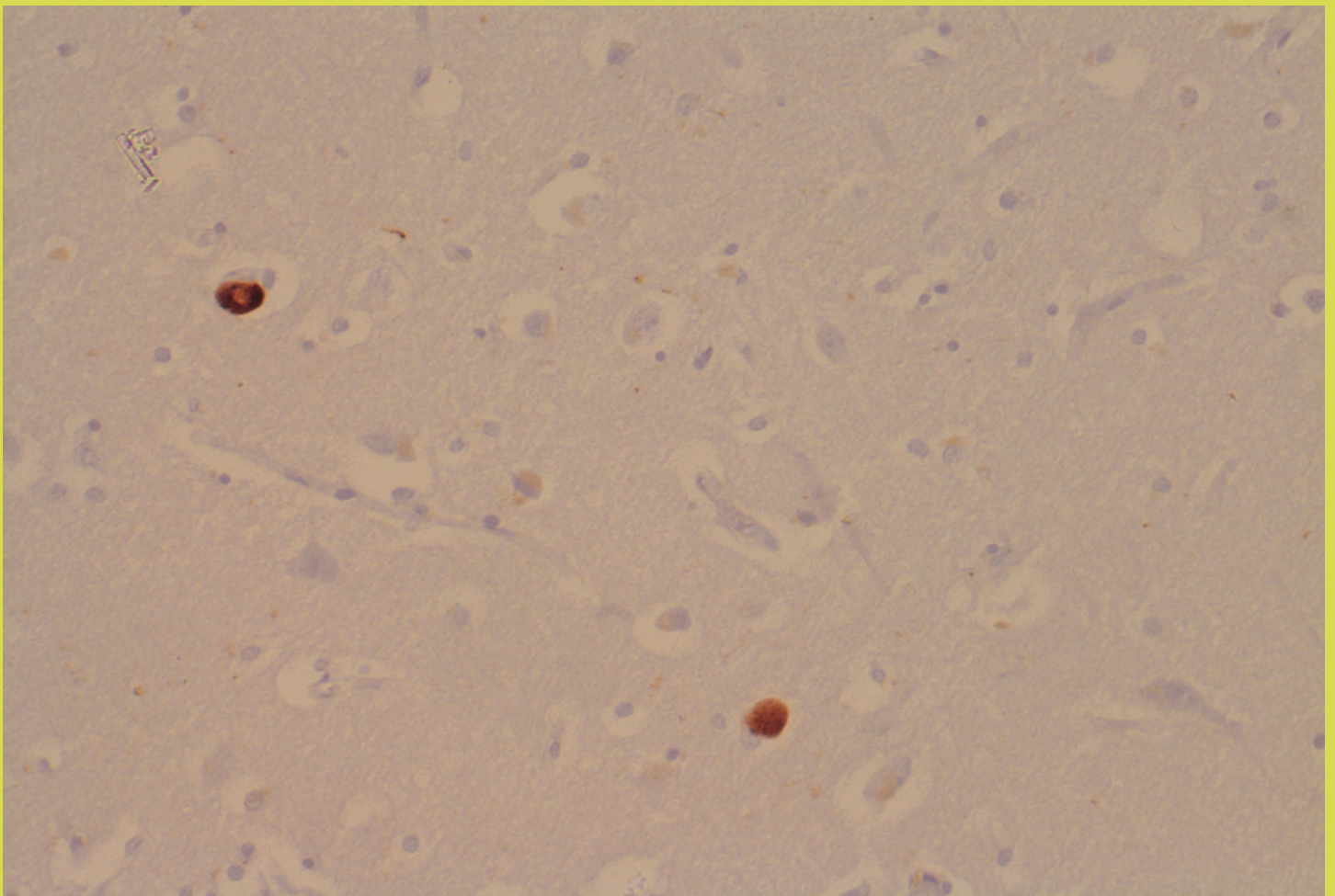
**Alzheimer's
Society** | Leading the
fight against
dementia

Research newsletter

Quality Research in Dementia

August 2012
Issue 120

Research into Lewy body dementias | AAIC conference report



Notes from the editor

Jess Smith, Research Communications Officer



One of our priorities for the Research programme at Alzheimer's Society is to increase the 'capacity' of dementia research; this means attracting the best young researchers into dementia research early on in their careers. Funding PhD studentships and research fellowships at good laboratories is an excellent way to support young researchers entering into or staying in dementia research.

Last month, the American Alzheimer's Association's International Conference (AAIC) took place in Vancouver, Canada. AAIC is the biggest dementia research conference in the world, and attracts the best dementia researchers from around the globe to present their research and talk about their latest findings. As usual, some very exciting results were revealed, including some preliminary results from early stages of clinical trials into new drug treatments for Alzheimer's disease.

In this edition of the newsletter we also focus on one of our PhD students' work. David Whitfield is a student in Professor Paul Francis' laboratory at King's College London and is conducting research into Lewy body dementia, a rarer form of dementia. David has written about his research, as well as completing a '60 seconds' interview.

At the end of July, we sadly said goodbye to Dr Anne Corbett, our Research Communications Manager. Anne has been an invaluable asset to the Research team during her time at Alzheimer's Society, having been the driving force behind many ambitions and developments. Anne has left to take up a position as lecturer in dementia communications at King's College London, a role that will involve leading her own research. We are sad to see her leave but wish her luck in her new role, and we're very pleased that she has not left the world of dementia research.

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On the cover

An image through a microscope of brain tissue containing Lewy bodies (in brown). Lewy bodies are made up of a protein called alpha synuclein. They are found in Dementia with Lewy bodies and also in Parkinson's disease dementia (see pages 7 and 8 for more information about our research into Lewy body dementias). Image courtesy of Professor Francis' laboratory.

Research in the press



An overview of research stories that have made the national press in the last month and how Alzheimer's Society commented on them.

Researchers in Iceland have identified a mutation in the APP gene – a gene usually associated with the development of Alzheimer's – that actually protects against the disease.

According to the study published in *Nature*, this particular mutation (A673T) disrupts the production of amyloid-beta protein, a hallmark of Alzheimer's disease. During Alzheimer's disease, amyloid-beta 'clumps together' to form plaques within the brain. Reducing the amount of amyloid-beta produced reduces the amount of amyloid-beta that is available to form plaques. The researchers also found that, among people living in care homes, those with this genetic mutation were less likely to develop cognitive decline, including Alzheimer's disease.

Dr Anne Corbett, Research Communications Manager, commented, 'We know that the development of Alzheimer's can be linked to a combination of

genetic and lifestyle factors. We still have a lot to learn about what happens in the brain but this research offers new insight into a gene we already know is linked to the disease.'

An Alzheimer's Society funded project received a lot of coverage in the press when it was launched this month. Professor Clive Holmes at the University of Southampton is conducting a project to understand how stress may contribute to a cognitive decline from mild cognitive impairment to Alzheimer's disease.

The study will follow people over age 70 with mild cognitive impairment for 18 months. The researchers will measure the participants' biological reactions to stress (measuring proteins in blood and saliva), as well as recording stressful events in their lives and asking them about the ways that they cope psychologically with stress.

It is impossible to avoid stressful events in life but this study aims to discover if there are better ways to cope with stress, both biologically and psychologically. This could help people to better cope with stressful events or lead us towards effective treatments, and so reduce the worsening of any cognitive decline.

Dr Corbett explained, 'The study will look at the role chronic stress plays in the progression from mild thinking and memory problems – mild cognitive impairment – to Alzheimer's disease.'

'We feel this is a really important area of research that needs more attention. The results could offer clues to new treatments or better ways of managing the condition.'

'It will also be valuable to understand how different ways of coping with stressful life events could influence the risk of developing Alzheimer's disease.'

Scientists investigating members of families who possess rare genes that lead to Alzheimer's disease have identified a variety of biological markers, which appear before symptoms are apparent. This work was conducted as part of an international research partnership, the Dominantly Inherited Alzheimer's Network (DIAN).

Using medical histories of the subjects' parents to estimate the age that symptoms would begin in the subject, the scientists assembled a timeline of changes in the brain leading to the memory loss and cognitive decline that characterises Alzheimer's disease. The earliest of these changes, a drop in levels of amyloid in the spinal fluid, can be detected 25 years before the anticipated age of onset.

Professor Clive Ballard, Director of Research, said, 'This important research highlights that key changes in the brain, linked to the inherited form of Alzheimer's disease, happen decades before symptoms show, which may have major implications for diagnosis and treatment in the future.'

AAIC dementia conference, Vancouver, Canada

Every summer, the Alzheimer's Association of the United States hosts their annual dementia conference, the Alzheimer's Association International Conference (AAIC). Dementia researchers from all over the world attend this conference and present their work. It is the largest and most eminent dementia conference in the world and presents the cutting edge of dementia research and new findings. Here, we outline a few of the key themes and studies that featured at this year's conference in Vancouver.

Reports from clinical trials

One of the big stories at AAIC was the report from an early stage of a clinical trial using an immunotherapy called IVIG as a potential treatment for Alzheimer's disease.

Researchers were reporting on phase 2b of the trial; at this stage of the clinical trial process, a small number of participants take part to test the safety of the trial drug and researchers begin to look at the effects that it may have. This particular study, where injections of a drug currently used as a treatment for people with conditions related to

deficiency in their immune system, showed positive results – the participants who were on the trial drug for the whole three years of the study saw no decline in measures of symptoms for the three years of this trial phase. This drug is now going through phase 3 trials, with a much larger number of participants. The results will tell us whether the findings from the previous phase are consistent in a much larger number of people with Alzheimer's disease.

Results from phase 2 trials on another new drug were presented,

showing that it may have benefits for people with Alzheimer's disease. This drug works in a similar way to current drugs such as donepezil (Aricept), but may provide additional benefits or be helpful to people with Alzheimer's disease who cannot tolerate the drugs that are currently available.

Lifestyle links tell us more about the causes of dementia

There is a growing amount of evidence related to risk factors for dementia, and what people can do to reduce their risk. This information helps us to understand more about the causes of dementia and the changes that occur within the brain, which can help us to develop better treatments. Studies presented at AAIC

included research that related to the amount of alcohol that people consumed. One study found that people over the age of 65 who participated in binge drinking were more likely to develop cognitive decline, and another that found that people who drank a moderate or large amount of alcohol in later life, or started drinking when they didn't before,

were more likely to develop cognitive decline. Other studies linked either too much or too little sleep with increased risk of mild cognitive impairment.

New techniques to help scientists investigate dementia

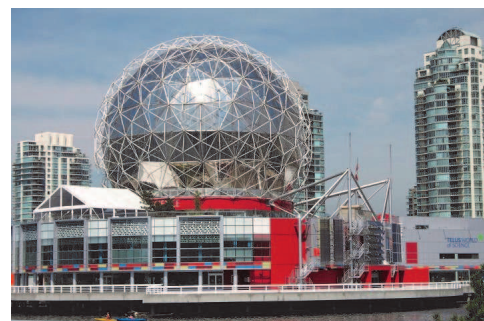
Scientists at the conference presented information about new techniques that will help other scientists to conduct better dementia research. A new model has been developed that allows researchers to use stem cells from people with inherited forms of Alzheimer's disease. Skin cells were taken from people with genes that will cause Alzheimer's disease, and the scientists were able to 'rewind' the cells back to stem cells (which can then go on to become any form of cell within the body), and then develop them into neurones. It is hoped that these neurones will behave in the same way as the neurones in people that develop this hereditary form of Alzheimer's disease, including the production of amyloid

plaques and tau tangles, the hallmarks of Alzheimer's disease. Scientists will be able to test conditions or drugs on these cells to see whether they have any affects at this basic level.

A separate group of scientists described a technique that they have produced for more accurately measuring the hippocampus, an area of the brain involved in memory and learning and often affected in Alzheimer's disease. By using a standard model of analysing the volume of this area in brain scans, researchers will be able to compare the results from many different studies, and so better understand changes and the effects of drug treatments.



This year's AAIC was held in Vancouver, Canada.



Science World, above, in Vancouver forms part of the city's strong science base. Dementia scientists from all over the world went to the conference.

Jargon buster: Dementia with Lewy bodies

(see page 6 for a summary of an Alzheimer's Society project in this area)

Dementia with Lewy bodies (DLB) is a form of dementia that shares characteristics with both Alzheimer's and Parkinson's diseases. It accounts for around 10 per cent of all cases of dementia in older people and tends to be under-diagnosed.

Lewy bodies are tiny, spherical protein deposits found in nerve cells. Their presence in the brain disrupts the brain's normal functioning.

A person with DLB will usually have some of the symptoms of Alzheimer's and Parkinson's diseases. They may experience problems with attention and alertness, often have spatial disorientation and experience difficulty with 'executive function', which includes difficulty in planning ahead and co-ordinating mental activities. Although memory is often affected, it is typically less so than in Alzheimer's disease.

They may also develop the symptoms of Parkinson's disease, including slowness, muscle stiffness, trembling of the limbs, a tendency to shuffle when walking, loss of facial expression, and changes in the strength and tone of the voice. To find out more about dementia with Lewy bodies, see factsheet 403

Understanding Lewy body dementias

David Whitfield, PhD student

David Whitfield is approaching the end of his PhD in Professor Paul Francis' lab. His research has been focusing on understanding more about Lewy body dementias, which include dementia with Lewy bodies and Parkinson's disease dementia.

I have spent my PhD investigating the relationships between synaptic biochemistry, pathology and symptoms in a large cohort of post mortem brain tissue from people who had a Lewy body dementia (either dementia with Lewy bodies (DLB) or Parkinson's disease dementia (PDD)), Alzheimer's disease or no dementia (healthy controls). Lewy body dementias remain poorly understood compared to Alzheimer's disease.

The group of cases with Lewy body dementias that I am working on is one of the largest assembled and has an invaluable depth of clinical data collated during the patients' lifetimes by psychiatrists from the various UK centres of Alzheimer's Society's co-funded Brains for Dementia Research brain banking programme. This data includes measurements of thinking and memory and key changes in behaviour such as hallucinations and agitation, which can be a major cause of carer burden and people requiring a nursing home.

Our lab and collaborators have assessed the extent to which three main types of protein deposits are present in the brains: Lewy bodies, amyloid plaques and tau tangles (the latter two are hallmarks of Alzheimer's disease). I have been measuring the levels of key proteins in three brain regions. It is known that these proteins are vital for healthy synapses.

Synapses are the junctions between nerve cells (neurones), which allow the brain to form complex connective networks throughout the brain. Any decrease in the amounts of these proteins equates to some degree of loss of function at the synapse, referred to as synaptic dysfunction.

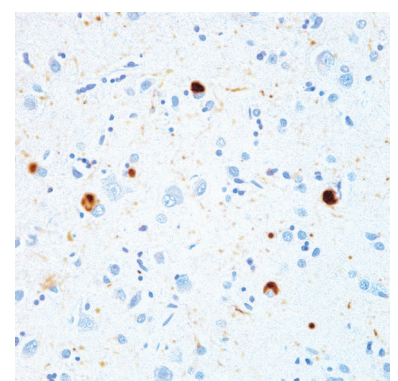
So far I have found substantial reductions of these proteins in two brain regions, the prefrontal cortex and the parietal cortex, which are different depending on diagnosis. For example, the levels of the protein synaptophysin are much lower in the prefrontal cortex of Parkinson's disease dementia patients than the other types of cases, but in the parietal cortex of Parkinson's disease dementia patients synaptophysin levels are no different to people without dementia. When taking into account the degree of pathology it appears that it is the Alzheimer's type pathology (plaques and tangles) that is related to the synaptic dysfunction in the parietal cortex and Lewy body pathology that is related to the synaptic dysfunction occurring in the prefrontal cortex.

I have also found that some proteins are decreased in one part of the brain in people with only moderate thinking and memory impairment whilst other proteins remain at more 'normal' levels until cognitive impairment is severe.

One of the proteins I have studied, ZnT3, is vital for zinc regulation and release at the synapse and I have found ZnT3 to be decreased in most brain regions and cases. This change may have an important consequence for the ability of nerve cells to communicate with each other.

These cognitive and pathology related changes in synaptic proteins could allow better distinction between dementia with Lewy bodies and Parkinson's disease dementia, as well as opening up the possibility of predicting disease progression based upon cognitive performance. For now I feel it has been useful to have been able to contribute to some of the gaps in understanding of the basic mechanisms of these complex and devastating dementias.

To find out more about the regions of the brain, and the cognitive functions these regions are responsible for, view our Brain tour at alzheimers.org.uk/braintour



Lewy bodies can be seen in the above image, stained in brown.

60 seconds with...David Whitfield

David Whitfield's project into Lewy body dementias has progressed well - see the article opposite. He is approaching the end of his PhD project in Professor Paul Francis' laboratory at King's College London.

What did you study at university?
Biochemistry and neuroscience at Surrey University.

What led you into dementia research and why?

I wanted to do research in any area of neuroscience but was aware that dementia was a growing problem attracting increasing funding for research, so it seemed like a good field to be in.

What has been the most exciting moment of your career so far?

My poster showing my data was selected for discussion and presentation at the European Congress of Neuropathology in Edinburgh recently. It was completely unexpected so I was not very well prepared but the experience of speaking at an international conference was invaluable!

What do you feel has been the biggest recent development in dementia research?

There have been many but one that comes to mind is the advances in brain imaging to differentiate between Lewy body dementias (see page 6) and Alzheimer's disease.

What is the best part of being a scientist?

I really enjoy the independence you have over your day-to-day work, also being able to spend so much time reading research articles to maintain a general knowledge of the wider field of neurodegeneration and neuroscience.

What would you be doing if you weren't a dementia scientist?

I can't really imagine doing anything outside of neuroscience but I enjoyed geography and biology at school and did think about trying to combine them working for an environmental charity like WWF or Greenpeace!

What is most misunderstood about dementia?

Surprisingly, I think a lot of people are still under the impression dementia is an inevitable and natural part of ageing rather than a disease. Also when telling someone I research dementia with Lewy bodies, or even just dementia, I often get a blank look and have to say Alzheimer's disease instead. I think the other dementias are still not widely known about despite their increasing prevalence.

What is your favourite brain function?

Memory – without it you would lose all the experiences of your life, all the people you have known and all the places you have been.

What book are you reading right now?

I am reading Bernard Cornwell, Redcoat, a great book about the American War of Independence.

I really like his writing, very gritty and realistic.

Which fictional character would you like to be and why?

Gandalf because of his combination of wisdom and mischievous humour...oh and the magic!

Name one new place you'd like to travel to?

I would really like to visit Australia as I have a lot of family there and so I would hopefully get something more than the average tourist's experience!

How do you relax outside of work?

I play squash and cycle around London to keep fit and read quite a lot. When I get the chance I try to go travelling or join my parents on their canal boat.

If you could only take one album to a desert island, what would it be?

This is a very hard question, I really love music and have about 8,000 songs on my iPod...all of which I know and listen to! Perhaps Fleetwood Mac, Rumours, just because it is so uplifting.

What did you want to be when you grew up?

I had many ideas. I always had a very vivid imagination when I was a child, so I think it was always something different, a writer, a policeman, etc. Although for a long time I wanted to be a doctor to follow after my grandfather.

The Research Network

People with dementia and their carers are integral to our grants programme. We believe that they make a unique and valuable contribution to our work. Their knowledge and passion ensures our research funding is allocated to projects that address the real needs and concerns of people with dementia and their carers.

Research Network volunteers:

- set our research priorities
- prioritise and comment on grant applications
- sit on grant selection panels
- monitor ongoing projects funded by Alzheimer's Society
- tell others about the results of research.

If you are a current carer, have been a carer for someone with dementia, or you have dementia and are interested in joining the Research Network, please contact Matt Murray, the Research Network Volunteer Coordinator and request an application form, or go online at alzheimers.org.uk/researchnetwork

If you are not a carer or a person with dementia, but you would like to learn more about our research and keep up to date, you are welcome to become a **Friend of Research**. Just fill in the form on the website (above) and you'll receive a monthly copy of the Research newsletter and information on all our research events.



Sunrise Senior Living is generously sponsoring the Research Network. Alzheimer's Society maintains editorial independence over this content.

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