Review of the year

Professor Clive Ballard, Director of Research

It has been a mixed year of breakthroughs, disappointments and opportunities. Three new ‘risk genes’, which alter the risk of developing Alzheimer’s disease, have been discovered – the first new risk genes to be identified for more than 15 years. The size of the risk is modest with each of these genes, so they are probably not that important for individuals, but their discovery will help us identify new mechanisms that lead to the development of Alzheimer’s disease and this will help us to develop new and novel treatments.

It has however been a disappointing year for drug trials. One of the most promising treatments, Dimebon, which had very encouraging results in early clinical trials, failed to show any benefit in a larger final stage clinical trial. However, on average it takes ten clinical trials to lead to one successful treatment. There are still ongoing trials of Dimebon and several other drugs and vaccines targeting amyloid, the protein at the core of the plaques seen in people with Alzheimer’s disease, but this is not enough! We desperately need more investment in clinical trials and the development of new drug treatments for dementia to guarantee the emergence of effective new treatments.

It would be even better to prevent dementia from occurring in the first place. If we believe the ‘prevention by tabloid’ headlines that we see every week, we can prevent the development of dementia with anything from curry to Nintendo brain training games – but can we cut through the spin and find the truth? A couple of collaborations with the BBC have allowed us to take a few important steps forward. Firstly, we convened an expert panel with the BBC to review the available evidence, and concluded that there was convincing evidence that regular exercise and not being overweight can reduce the risk of developing dementia. Better treatment of medical problems such as high blood pressure and high cholesterol can also reduce risk. There is evidence that a Mediterranean diet, modest alcohol intake and an active social life can also be protective. There is no convincing evidence to suggest that vitamin tablets or fish oil are useful.

The second collaboration with the BBC, Brain Test Britain, was a massive trial involving more than 11,000 adults under the age of 60 which demonstrated that brain training games do not improve brain function – a disappointing but important finding.

Research supported by Alzheimer’s Society, and work from my own research at King’s College London, has contributed to our increasing understanding about the risks of sedative antipsychotic drugs. These treatments are widely used to treat behavioural symptoms in people with dementia, and although they do have a very small beneficial effect on symptoms such as aggression, they have...
Another exciting year has gone past in a flash and several events stand out as significant steps up on the way to understanding the diseases that cause dementia.

ICAD went annual
The organisers of the International Conference on Alzheimer’s Disease (ICAD) decided to make it an annual event. The conference in Vienna attracted 4,500 researchers from around the world. A clutch of Alzheimer’s Society funded researchers presented their data and met with others to discuss how best to progress in their fields. On the last day, three new Alzheimer’s genes were announced, generating great excitement because it pointed researchers towards new directions for investigation.

Dementia Research Summit
One of the outcomes from the National Dementia Strategy for England was a dementia research summit organised by Department of Health. The summit brought together a select group of senior researchers, policy makers, charities and users of research to discuss the barriers to dementia research and how to overcome them. Working groups have been established and will report later this year. The groups will play an important role in progressing dementia research and in helping to catch the attention of government offices and large research funding bodies.

Alzheimer’s Society Research Symposium
The Alzheimer’s Society Research team held a particularly successful conference with Professors Alistair Burns and Carol Brayne reporting on their research. Our research symposium is one of the highlights of my year as it presents the opportunity to meet so many of our hard-working volunteers.

Today programme with David Blunkett
The launch of the Brains for Dementia Research brain bank was very successful. I had the great pleasure of being on the BBC Today programme with David Blunkett, who has pledged to donate his brain to dementia research.

The biggest PhD studentship round yet
This year we received our largest number of PhD funding applications and awarded more studentships than ever before. Six newly funded students will start at the beginning of the academic year. Their research will mostly be laboratory based and ranges from continued work on a blood test that we funded in an earlier stage, to why chocolate may be good for you – I can’t wait to hear the results.

Review of the year continued
An increasing body of research, including the FITS (Focussed Intervention Training and Support) study funded by Alzheimer’s Society, shows that simple psychological therapies and training programmes for staff in care homes are effective and can improve behaviour while reducing the use of antipsychotic drugs. We now need to make sure that these treatments are available throughout the country. The Society is closely involved in a series of ministerial groups related to dementia research, one of which is directly addressing the implementation of effective research. This, together with ongoing programmes from the National Institute of Health Research, should provide the mechanism to implement these treatments and substantially improve the treatment and care of people with dementia.

numerous serious side-effects including an increased risk of stroke and death.

As a result of the research and some effective campaigning, the Department of Health has finally commissioned a report to look at ways of addressing this major problem. The key will be to make sure that effective alternatives to antipsychotics are available.
Brains for Dementia Research

Brains for Dementia Research (BDR) is a brain banking initiative for England and Wales that aims to improve brain donation services and raise awareness about the importance of brain donation.

BDR is jointly funded by Alzheimer’s Society and the Alzheimer’s Research Trust. There are five BDR centres across England and Wales that are now fully functioning and actively recruiting donors. BDR was officially launched in the press in October 2009 with MP David Blunkett pledging himself as a brain donor. The idea for a co-ordinated brain banking service originated with a group of QRD Network members who included Ted Freer and Chris West. Since its inception, QRD members have been involved throughout, some acting as monitors for one of the five centres. Angela Clayton-Turner has been particularly active in BDR. She has spoken at ethics training days and gave a presentation about the user/carer perspective on brain donation at the Alzheimer’s Disease International Conference last year. Angela was asked to write up her presentation and it was published in the journal Clinical Ethics.

QRD member Elizabeth Hughes wrote of her personal experience with BDR after they helped to manage her mother’s brain donation. ‘Myself and two colleagues from the QRD network had the opportunity to meet the research team who run the brain donation centre at Newcastle. We were impressed by the commitment and sensitivity of the research team, their openness and willingness to be questioned. I know that my mother would have been pleased that some good had come from her suffering and that she had made a significant contribution to research into brain disease processes.’

Summary of the year’s activities

From April 2009 to March 2010, the 173 volunteers in the QRD Network reviewed a total of 64 grant applications. Of those, 47 were approved by the Network, with ten going on to receive funding. This year has also seen a rise in the number of Friends of Research, with the total reaching 244 in April 2010 compared to 95 in April 2009.

Many Network members have contributed to ongoing projects as monitors, reporting to the Society on the progress of the projects and providing a link between researchers and users. Some Network members have also given talks at fundraising events and been active members of a variety of dementia-related committees.

QRD members have been involved in a number of events and forums this year. Shirley Nurock and U Hla Htay took part in a UK Clinical Research Collaboration workshop on involvement in research and Shirley Nurock and Francis Weiss attended the the 2009 Dementia and Neurodegenerative Diseases Research Network (DeNDRoN) conference. Jim Ellis was closely involved in a dementia awareness training project for nurses in Burton on Trent which resulted in a number of publications. QRD members also played an important role in the Dementia Research Summit in July 2009. Barbara Woodward-Carlton started proceedings with an excellent talk, whilst Victoria Morgan held the last question of the day. Her input struck a chord with Baroness Greengross who returned to it in her closing remarks. Our media star of the year is Angela Clayton-Turner for her appearance on Sky News during the launch of Brains for Dementia Research.
The role of Rab8 and Toll signalling in Fronto-temporal dementia related neurodegeneration
Dr Sean Sweeney, University of York

A cross-section of the head of a fruit fly used in Dr Sweeney’s research

Fronto-temporal dementia (FTD) affects the areas towards the front of the brain, which are responsible for behaviour, emotional responses and language. Very little is known about the biological basis of FTD and so treatments are very limited. Four genes have been linked to FTD and Dr Sweeney’s team have used one of these genes to create a model of FTD in fruit flies. The team have already used the model to observe that one protein, Rab8, is linked to FTD.

A PhD studentship has been awarded to Dr Sweeney to continue to develop this important genetic model in the hope of understanding the biological basis of FTD. The student will use a combination of genetic manipulation, biochemical techniques and high-powered microscopy to analyse the effect of the FTD gene on nerve cells.

This research will be extremely useful in both understanding the causes of FTD and in identifying new targets for treatments in the future.
Professor Young has been awarded a project grant to carry out the first research study into dementia in the Deaf community. Her team will work with 700 older Deaf people to assess cognitive abilities as the basis of a future diagnostic test for dementia.

The team will also hold in-depth interviews with ten Deaf people with dementia and their carers to learn about their experiences, as well as working closely with Deaf organisations to discover what Deaf people already know about dementia. This pioneering research will enable Professor Young to advise on the best ways to diagnose and care for Deaf people with dementia, enabling them to have access to the correct treatments that will improve their quality of life and enable them to remain independent for longer.

The research will also begin to provide the Deaf community with dementia information services, helping to sustain choice and decision-making for all those living with the condition.

Extraordinarily little is known about dementia in the signing Deaf community. It is thought that the majority of Deaf people with dementia do not receive a proper diagnosis. This is partly due to the difficulties associated with communication and also because the standard diagnostic tests for dementia cannot be applied. No research has ever been done into the experiences of Deaf people with dementia.

Overcoming obstacles to the early identification of dementia in the signing Deaf community
Prof Alys Young, University of Manchester

Functional genetic analysis: Mechanisms of dementia in people with Down’s syndrome
Dr Emma Jones, King’s College London

People with Down’s syndrome make up the second largest group of people with dementia under the age of 60. However, these people have been largely neglected by dementia research in the past.

Previous work has identified genes that are linked to the development of the toxic plaques and tangles that develop in Alzheimer’s disease. Some of these genes are located on chromosome 21. People with Down’s syndrome have an extra copy of this chromosome and they therefore present a fascinating opportunity for research into early onset dementia.

Dr Emma Jones has been awarded a fellowship grant to investigate the genetic basis of Alzheimer’s disease in relation to people with Down’s syndrome. She will focus on the gene for an enzyme which is closely involved in production of toxic amyloid plaques.

Using a groundbreaking new technology, Dr Jones will produce stem cells from skin cells taken from people with Down’s syndrome. She will then use these to produce nerve cells to study the genetic link between Down’s syndrome and Alzheimer’s disease.

This exciting project will shed light on the processes that take place during early onset dementia. It will improve our understanding of how genetics cause the changes that occur in the brain and why people with Down’s syndrome are so commonly affected. In the future this work could enable clinicians to identify people who are likely to develop dementia by examining their genetic make-up.
Dual-task impairment in Alzheimer disease: An investigation on specificity and development of a clinical tool
Prof Sergio Della Sala, University of Edinburgh
(See opposite for details)

A double blind, placebo-controlled trial of aromatherapy using melissa/lavender compared to Aricept for the treatment of significant agitation in people with severe dementia
Prof Alistair Burns, University of Manchester

Project grants
In vivo analysis of the Fe65L2 protein in health and Alzheimer’s disease
Dr Declan McLoughlin, King’s College London

Assessing fitness to drive in people with dementia
Prof Nadina Lincoln, University of Nottingham

Is the RER peptide a promising substance for treating Alzheimer’s disease-related learning and memory deficits?
Prof Karl Giese, King’s College London

Fellowship grants
Targeting amyloid-β precursor protein cleavage in Alzheimer’s disease
Dr Michael Perkinton and Dr Robert Williams, King’s College London

The structure and function of a novel apolipoprotein E-binding protein
Dr Paul Hopkins, King’s College London
(See opposite for details)

Dissemination grants
Deliurium is bad, what’s the confusion?
Dr Valerie Page, Watford General Hospital

Fundraising for research
In the financial year 2009/10 over £1.7 million was raised towards funding all areas of the Society’s research. Donations were secured from charitable trusts, companies, individuals, and from legacies.

In this year, grant-making trusts were particularly generous, giving a total of £686,207 towards research projects. Some of our key supporters include The Henry Smith Charity, the Robert Luff Foundation, the Eranda Foundation, the Hartley Charitable Trust and the Steel Charitable Trust. Other supporters include the Henry Lumley Charitable Trust, Rosetree Trust, Sir Samuel Scott of Yews Trust and The Edwin George Robinson Charitable Trust. Furthermore, over £40,000 was raised for the research programme through our charity of the year partnership with KPMG. We are particularly grateful to Mr Edwin Harry Lea and Rhoda Patricia Fraser, who between them contributed £500,000 towards research through gifts in their wills during the financial year, as well as to Miss Margaret Curtis, who gave a donation of £30,000 in memory of her friend, Mary Kathleen Bourhill, and to Dr Christopher Beels, who made a generous gift in memory of his mother. Thank you also to the Scott family who have contributed over £5,000 towards the Society’s research programme through the William Scott estate.

Without this support we would not be able to invest in so many high quality projects and researchers. We are extremely grateful to all the people and organisations who give so generously towards the Society’s research programme.

Summary of research income 2009/10
Investigating dual task impairment in Alzheimer’s disease
Prof Sergio Della Sala,
University of Edinburgh

The circles task – one of the tests for dual-tasking used in Professor Della Sala’s research

Talking to someone with Alzheimer’s disease (AD) whilst they are walking makes them more likely to stumble and fall. This is because walking and talking at the same time is a ‘dual task’, and the ability to dual task becomes impaired with the onset of AD.

In a project funded by Alzheimer’s Society, the team at the University of Edinburgh has been researching these difficulties. Several studies have suggested that dual tasking ability is unaffected by age, but is significantly impaired by AD. The first aim of this project was to determine if this dual task impairment is present only in AD, or also present in other disorders that can be confused for AD.

One such disorder is chronic depression, which can cause severe memory disorder in older people. Another is Mild Cognitive Impairment (MCI) which is often considered to be the stage before AD, but not all people with MCI progress to having AD. The researchers examined dual tasking ability in healthy older people, people with MCI, people with depression and people with AD. Tests showed that only people with AD had difficulty performing the dual task. However, some people in the MCI group had greater difficulty performing the dual task than others, and it is suspected that these people will be more likely to go on to develop AD. This has since been supported by research elsewhere.

This research suggests, therefore, that dual task impairment is specific to AD, and unlike memory loss, is not present in normal ageing, MCI or chronic depression. As this impairment is specific to AD, a quick measure of dual tasking ability may help determine if someone with an age-related memory disorder has AD or not.

The second major aim of this project was to develop a clinical tool that could be used to assess dual tasking ability in the clinic. The team has now developed a new paper-and-pencil version of the dual task assessment, which takes 20 minutes, is easy to use and is easily transportable. Doctors can use this test to classify dual task performance as average, borderline or impaired, in order to support a diagnosis of AD.

We hope this research will highlight how important it is to avoid asking people with AD to dual task, such as walking and talking, and also help improve the diagnostic process.

The structure and function of a novel apolipoprotein E-binding protein
Dr Paul Hopkins,
King’s College London

High-power microscopy image showing the optic nerve of a fruit fly

The single most common risk factor for Alzheimer’s disease is a gene called apoE4. One in six people carry apoE4, so it plays a role in many cases of Alzheimer’s disease. However, the biological processes by which apoE4 contributes to Alzheimer’s disease have not been found.

Dr Hopkins has identified a novel gene, which he has called dementin, which associates with apoE4 in a different way than with the more common form of apoE, called apoE3. This gene had, however, never been previously studied. During his fellowship, Dr Hopkins found that apoE4 is associated with lower levels of the protein dementin in human brain and that it directly alters the biology of other known risk factors in Alzheimer’s disease. Experimentally altering the dementin protein in Drosophila fruit flies leads to abnormal brain development, and separately to neurodegeneration in adults. It is therefore highly likely that dementin plays a significant role in Alzheimer’s disease and so these findings open up new avenues for the development of treatments.
Research in the press

2009–2010 was a big year for media coverage of dementia research. The press team distribute press releases and statements, train and brief spokespeople, pitch studies to journalists and arrange interviews to hit the headlines. Sixty-eight research statements were issued by the team last year. All the hard work paid off with a staggering 327 pieces of press and broadcast coverage mentioning Alzheimer’s Society, reaching an audience of over 254 million. Of these, over 200 were about non-Alzheimer’s Society research, demonstrating the extent to which we are seen as an authority on dementia research. Here are some of the year’s highlights.

**Systemic inflammation**
Research funded by Alzheimer’s Society and published in Neurology found that people with Alzheimer’s disease who develop an infection need to be treated as soon as possible to prevent it worsening their dementia. A link was observed between common infections and an increase in inflammation-like reactions in the brain, which led to an increased rate of cognitive decline. This research appeared in the Daily Mail, The Times, BBC News Online and Guardian.

**Early retirement may be a risk factor for dementia**
In research published in the International Journal of Geriatric Psychiatry, scientists found that men with dementia who retired later also developed dementia later. Dr Susanne Sorensen claimed there could be a number of reasons why later retirement is linked with later onset of dementia, including better health and the benefit of keeping active through work. Her comment was published in the Daily Telegraph, The Sun, Daily Mail, The Times and Daily Mirror.

**Genetic breakthrough could cut dementia cases by a fifth**
An exciting study published in Nature Genetics identified two potentially key genes, CLU and PICALM, linked to the development of Alzheimer’s disease. Dr Sorensen’s comment was picked up by media outlets including BBC News Online and Daily Mirror, and Neil Hunt, Alzheimer’s Society’s former Chief Executive, was on Channel 4 News.

**Brain training**
In association with the BBC, researchers followed 11,000 volunteers over six weeks to see the effects of playing brain training games designed by scientists supported by the Medical Research Council and Alzheimer’s Society. Whilst performance on the games improved, players’ reasoning, memory, planning and visuo-spatial abilities remained unchanged. This important longitudinal experiment was covered by BBC News Online, Daily Telegraph, Daily Mirror, Daily Mail, Daily Express and BBC Breakfast.

**Lifestyle and dementia**
A study published in Journal of Neurology, Neurosurgery and Psychiatry found that middle-aged smokers and those with high blood pressure and diabetes were at a much greater risk of developing dementia. Our comment featured in the Guardian, The Sun and The Times.