Issue two
Spring 2015

Alzheimer's Society
Leading the fight against dementia

Careandcure

The Alzheimer's Society research magazine

An ideal match

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What's in this issue of Careandcure

Welcome back to a second helping of Care and cure. We had a fantastic response to the first issue and there has been no shortage of research news in the meantime to fill these pages.

We recently announced the launch of eight doctoral training centres around the country to bring 53 new PhD students into dementia research (page 10). In one fell swoop, this has doubled the number of PhD students that the Society has ever funded. We hope that this will help to counter the decades of underinvestment in dementia that has led to a lack of researchers in the field.

It can often be difficult to chart the progress of research, as each new answer gives rise to new questions. For example, previous research has produced conflicting results about whether cholesterol in the blood is linked to dementia. Now, as the article on page 3 describes, the connection may be more to do with how the body responds to cholesterol.

This raises even more questions: Will the results hold up in a larger study? Why are the changes seen in people with dementia? Are there any drugs that can prevent this process?

To be sure, this result will spur further research and further questions. That is nature of science. However it is only by having the brilliant minds to ask the right questions and the funding to find the answers that we can continue to make progress.

Ian Le Guillou
Editor
Careandcure

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Cholesterol by-products point to new Alzheimer's discovery

A lack of certain molecules that are formed from cholesterol and found in the blood could be linked to the development of Alzheimer's disease, according to new research.

The study, funded by Alzheimer's Society, looked at fatty molecules in blood samples from 124 people including 36 with Alzheimer's disease. The researchers identified 10 molecules in the samples that appeared to be reduced in people with Alzheimer's.

Six of the molecules are by-products, or metabolites, formed from the breakdown of cholesterol in the body, though the researchers found no overall link between cholesterol itself and Alzheimer's.

These metabolites had not been linked to Alzheimer's disease before, and the discovery highlights the potentially important role of how the body processes cholesterol. This insight could lead to new targets for future Alzheimer's drug treatments.

Dr Petroula Proitsi, Alzheimer's Society Research Fellow at King's College London and lead author of the study, said, 'The results are very interesting as the identified metabolites are biochemically related to metabolites previously shown to be associated with Alzheimer's.

'This interesting study could be another piece in the jigsaw of helping us understand the condition.'

Dr Brown

'It will be very interesting to see whether changes in these metabolites are also associated with disease initiation and progression. However we would like to stress that these findings need to be expanded and replicated in larger cohorts.'

Dr Doug Brown, Director of Research and Development at Alzheimer's Society, commented, 'Finding a way to detect Alzheimer's before the disease takes hold would provide a huge step forward in the way we carry out research into the condition.

'This interesting study identifies a number of molecules connected to cholesterol which weren't previously thought to be linked to Alzheimer's disease and could be another piece in the jigsaw of helping us understand the condition.'

Unclear link between common drugs and dementia

A large-scale study in the US has suggested a link between dementia and certain drugs, including some sleep aids and hay fever treatments.

The researchers studied more than 3,000 people aged 65 and over to follow their use of drugs known as anticholinergics. After following these people for seven years, the researchers found that people taking the drugs for three years or more were more likely to have developed dementia than those who didn't take the drugs.

As this was an observational study it is not possible to say whether the drugs themselves increased the likelihood of dementia, or whether they are linked indirectly. As all of the drugs were studied together, the researchers could not tell whether this effect is due to one drug in particular rather than the whole group.

Dr Doug Brown, Director of Research and Development at Alzheimer's Society, said, 'More robust research is needed to understand what the potential dangers are, and if some drugs are more likely to have this effect than others.

'We would encourage doctors and pharmacists to be aware of this potential link and would advise anyone concerned about this to speak to their GP before stopping any medication.'

Currently available treatments for Alzheimer's disease include cholinesterase inhibitors, which help to boost the levels of a chemical messenger called acetylcholine in the brain. The anticholinergic drugs found in some hay fever treatments or sleep aids work in an opposite function, which is why they have been scrutinised, though it is unclear whether there are long-term effects.

Rescuing immune system cells halts brain damage

Results from a study published in the Journal of Clinical Investigation suggest that dysfunction of a type of immune system cell could provide a target for future drugs for Alzheimer's disease.

Researchers from Stanford University studied cells known as microglia, which form part of the immune system and work to protect the brain.

Professor Katrin Andreasson, who led the study, said, 'The microglias are supposed to be, from the get-go, constantly clearing amyloid-beta, as well as keeping a lid on inflammation. If they lose their ability to function, things get out of control. Amyloid-beta builds up in the brain, inducing toxic inflammation.'

By studying mice with hallmarks of Alzheimer's disease, the researchers found that deleting the gene that produces a protein called EP2 restored the function of the microglia. This included clearance of amyloid-beta, suppression of toxic inflammation, and prevention of memory deficits and damage to synapses.

The researchers hope that future studies will lead to the development of treatments that can have the same effect in people and potentially prevent the development of Alzheimer's disease.

Pain missed in hospital patients with dementia

A new study has shown that pain in people with dementia when admitted to hospital is underreported, which leads to symptoms worsening.

Pain is commonly under-detected and under-treated in people with dementia, as they may not easily be able to indicate that they are in pain. To investigate the extent of this in a hospital setting, researchers followed 230 people with dementia during their stays in hospital.

The study, which was jointly funded by Alzheimer's Society and the BUPA Foundation, found that 39 per cent of the participants reported pain at least once during their hospital admission. By comparison, 57 per cent of the subjects were observed by the researchers to be in pain at some stage.

About half of the participants in the study could use the standard scale to describe their level of pain although this varied strongly, from 80 per cent of people with early-stage dementia to just 3 per cent of those with advanced dementia.

The researchers, led by Dr Elizabeth Sampson, reported, 'This illustrates how self-report may lead to underestimation of pain in people with dementia, and the importance of careful observation for pain.'

Underestimation of the prevalence of pain could mean that people with dementia are not receiving adequate pain relief.

The presence of pain was strongly associated with signs of behavioural and psychiatric symptoms of dementia (BPSD), such as aggression and apathy. This matches with what has been previously observed in care homes, but this is the first study to demonstrate the same in a hospital.

'Some BPSD in the acute hospital may be due to under-detected and under-managed pain. This then leads to a cycle whereby behavioural problems and rejection of care by the person with dementia can lead to dysfunctional coping in staff, increasing care burden and further alienating staff from the person with dementia,' said the researchers.

News in brief

A protein activated in response to cold may prevent the loss of connections between brain cells in neurodegenerative diseases. It was already known that reducing body temperature can protect the brain from damage but new research has identified the protein responsible, RBM3. Artificially boosting levels of RBM3 in the brain prevented further damage in mice with Alzheimer's disease.

A study of twins suggests that playing a musical instrument in later life reduces the risk of developing dementia. Swedish researchers surveyed the musical habits of 157 pairs of twins where just one twin in each pair had dementia. They found that people who had played an instrument were less likely to have developed dementia.

People remember more of complex information if they rest after learning than if they are given new information. The study, funded by Alzheimer's Society, gave healthy volunteers two routes to memorise. One route memorisation was followed by a 10-minute rest and the other by a 10-minute game. After seven days, memory recall was better for the route that had been followed by a rest.

An ideal match

With less than 5 per cent of people with dementia involved in research studies, we hear from researchers about how a new service is making it easier to find volunteers.

Over the past decade online dating has become a big business. Busy singles are unable to meet enough new people who are also single and meet long lists of desired characteristics. Matches can be made more easily and efficiently by computer algorithms searching through details of people looking for one another in a database. This idea has been so successful that it is now being used to help scientists find research volunteers.

The right people

Advances in technology allow researchers to study diseases like dementia in petri dishes, in animals and even in computers. These have increased our understanding but ultimately new discoveries need to be tested in humans.

Studies and trials involving people rely on potentially thousands of volunteers taking part, which could involve taking a new drug, changing lifestyle or being observed over time. However finding the right people in the right location with the right condition can be tricky.

In the past, participants have been recruited via memory clinics or by placing adverts in GP surgeries and the local press. Finding the right people is often a lengthy and time-consuming process.

'We first had to find people who matched our inclusion and exclusion criteria. Then we had to find out if those people were willing to take part and then check that they weren't too advanced in their disease to be able to give consent,' explains Dr Paul Edison from the Imperial College Memory Research Unit in London.

Edison's team is currently conducting a study known as ELAD, which tests whether a drug used to treat diabetes could also be effective for Alzheimer's disease (see box). This is one of the first studies to recruit participants through a new matchmaking service called Join Dementia Research (JDR), which aims to make the recruiting process much simpler.

'JDR has been very helpful because people are effectively pre-screened. Patients go on and register their details to see if they match any study's requirements – so you already know if they might be a good fit. It also provides us with people who are interested in research, so half the battle is over,' Edison says. 'It brings the ideal patients closer to the researchers.'

The power of information

Join Dementia Research has been developed by the National Institute for Health Research working in partnership with Alzheimer's Society and Alzheimer's Research UK. The service aims to make it easier for people to take part in research by having studies listed in one place and screening based on eligibility criteria.

Dr Melanie Dani, a research fellow in Edison's team, leads on recruitment to another study on inflammation in the brain. She explained the steps involved, 'We put our criteria into the JDR website and that finds people who only match our study information. We then screen them on the phone and send them further information if they are interested. Then we follow up and if they agree to take part, bring them into our system. It's a more direct route to patients, so a much faster process.'

Another advantage is that, once participants have been matched, researchers can access their details in one place, as Dani described, 'JDR contains all the information we need for enrolment to a study, people's NHS numbers, their GP details, their consultant at a memory clinic and results of medical tests – all the information that we sometimes struggle to obtain.

'For example, we're now looking for people with a particular range of scores on the memory tests used routinely in research. A person's score is usually included in their medical records, so we can find out straightaway if they are eligible on that basis.'

Overcoming challenges

Studies can often struggle to recruit enough patients, whether that is due to strict criteria or the difficulty of taking part.

Dani's study is recruiting people with mild cognitive impairment. 'These are the people who are a bit worried about their memory but otherwise are functioning very well. It's a tiny window. Not everyone seeks medical advice at that point, so it's not often officially diagnosed.'

> **'It's a more direct route to patients, so a much faster process.'**
>
> Dr Dani

The ELAD study also poses some challenges for recruitment. 'There's a lot involved in taking part, including 14 visits to local sites and two visits to London for brain scans. The new drug also has to be injected daily, like insulin. People tend to be more hesitant about that than taking a tablet,' says Edison.

Join Dementia Research has helped overcome these difficulties, providing willing and enthusiastic volunteers.

'It's an excellent source of volunteers,' Edison says. 'They also know about our studies and have expressed an interest in taking part.'

'The people who have already signed up are so well informed and interested in our research. They know our studies are extremely important to help us understand the disease,' Dani says.

'I've enrolled five people. Five more are booked to be enrolled and I'm in contact with dozens more. I get two or three new names every day,' she says after using the service for three months. 'It's been great!'

For more information about JDR visit **www.joindementiaresearch.org.uk**

Read about a participant's perspective of getting involved in research in March's **Living with dementia** magazine – visit **alzheimers.org.uk/magazine**

The Evaluation of Liraglutide in Alzheimer's Disease (ELAD) study

Alzheimer's disease and diabetes appear to be connected. Research has suggested that there is a common disease mechanism operating in both, probably linked to the hormone insulin.

Type 2 diabetes is caused by cells in the pancreas becoming resistant to insulin. A similar resistance is seen in the brain's nerve cells in people with Alzheimer's disease.

Treatments for Type 2 diabetes reduce the effects of insulin resistance and so this opens up the possibility that drugs used to treat diabetes might also help people with dementia.

Liraglutide is one of the drugs used to treat diabetes. Early tests in animals have already shown promising results. Liraglutide appears to decrease signs of Alzheimer's in the brain and increase the number of connections between nerve cells.

The question is whether it can do the same thing in people. If effective, it could be available for people with dementia in a couple of years.

The ELAD study will carry out a large number of brain scans on people with Alzheimer's disease who are taking liraglutide to see if it makes a difference to their brain structure and prevents the loss of nerve cells. Importantly the researchers will also assess whether the drug prevents memory loss and improves people's quality of life.

The view looking in

Dr Paul Edison is a clinical senior lecturer at Imperial College London and is being funded by Alzheimer's Society to run a clinical trial of a diabetes drug against Alzheimer's disease.

When Paul Edison was first training to be a doctor, dementia was a very poorly understood disease. 'I was attracted to dementia research by the lack of understanding about the disease. I have always been interested in finding novel methods of diagnosis and trying to understand what causes damage to the brain,' he explained.

Although we have yet to reach the day where we can understand and treat dementia, Edison has helped to bring us closer.

He heads a team of researchers who use brain-scanning techniques to explore the mechanisms of Alzheimer's disease. His team was one of the first to use scans to detect the build-up of amyloid protein in the brains of people with Alzheimer's. They thought their approach might prove to be the definitive diagnostic test. 'But we've since found it's not specific for Alzheimer's. Amyloid deposits are found in the brains of people with other types of dementia,' Edison says.

This disappointment led to another important observation – about 25 per cent of people around age 75 have high levels of amyloid in their brain, but don't have any symptoms of dementia. Edison thinks there

'I have always been interested in trying to understand what causes damage to the brain.'

Dr Edison

are different ways to explain this. 'Perhaps what we're seeing are people at the early stages, and perhaps in 15–20 years' time, they would have Alzheimer's. But the other interesting possibility is that amyloid is not the only problem. Something else might be causing the nerve damage.'

There are a number of possible causes of nerve damage, including brain inflammation and the build-up of another protein called tau. Edison's team are studying how these processes are linked.

'We want to find out if all these processes are abnormal at the same time, or does one lead to another? Which comes first and how do they interact? And importantly how does this all relate to brain function and symptoms of dementia? Understanding this might lead to a clearer diagnosis and more options for treatment.'

Another strand of Edison's research is directly testing a treatment, as he explains, 'There's a strong relationship between Alzheimer's disease and diabetes. People with Type 2 diabetes are more likely to develop dementia. It's not just a result of damage to blood vessels in the brain. We think there could be a common mechanism – resistance to insulin.'

Insulin not only affects blood sugar levels, it also acts as a signalling molecule between nerve cells. In Alzheimer's, the nerve cells appear to stop responding to insulin. Drugs used to treat diabetes restore the effects of insulin, which raises the possibility that they might also treat dementia.

Edison's team is conducting a study to test one such diabetes drug, liraglutide. 'If it's successful, if we see an improvement in memory, then we can take the drug to the clinic very quickly, because we already know it's safe for patients, because it's already used to treat people with diabetes. We just need to find out if it's effective.'

For more information about the liraglutide study, contact **memory@imperial.ac.uk** or **020 8383 3704.**

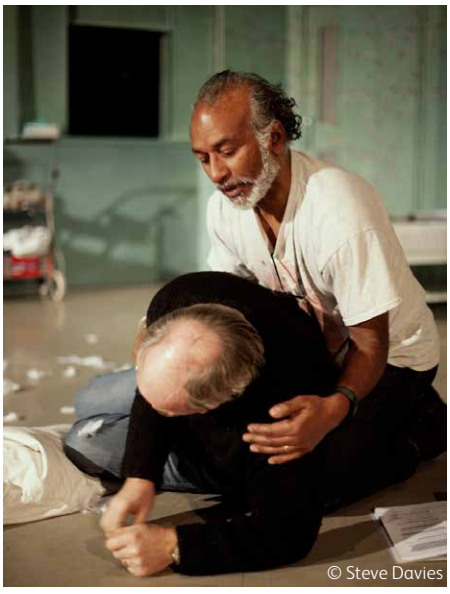
Putting on a show

When Justine Schneider was faced with 600,000 words of notes from observations in dementia wards, she knew that normal academic publications would not be enough.

In 2010, Justine Schneider, a professor of mental health and social care at University of Nottingham, was reading the notes from three of her researchers who had spent up to a year on dementia wards, following healthcare assistants at work.

Healthcare assistants, also known as nurses' aides, make up more than half of hands-on staff in the NHS. Despite their number, there has been little research into this group of staff.

Schneider's study aimed to explore the stresses, coping strategies and rewards of caring for people with advanced dementia. 'I didn't have any plans at the proposal stage to put out anything other than reports, journal articles and maybe conference talks,' says Schneider. 'But the researchers were very gifted and had an excellent ear for dialogue. Their field notes were extremely detailed and they came across most vividly.'



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'As a social researcher I've already been aware of the potential of drama to show research findings – it is in the research methods literature, but I've never before had the opportunity to do it. Academic writing is seldom able to portray the full nature of human experience in the same way that the arts can achieve.'

Schneider contacted Tanya Myers of Meeting Ground Theatre Company to see what she might be able to do with all of their observations. 'She was very sympathetic towards the situation and had cared for her own mother-in-law with dementia.'

> **'I think working with the arts has an enormous amount of potential.'**
>
> Professor Schneider

Myers wrote and directed a play, Inside out of mind, that featured many of the observations from Schneider's team. The play was initially performed to an audience of healthcare assistants and other health support workers, along with a workshop to discuss the issues that it raised. In total, over 1,100 healthcare assistants attended the show and over 90 per cent of them said that the play positively affected their work with people with dementia. 'I have been working in dementia for some time and today's play gave me more insight into dementia, quite inspiring… fantastic,' said one.

The many positive comments from the people whom the play was portraying are what Schneider thinks ensured the play's further success. 'It was the feedback from that show which helped us to win a grant from Arts Council England's Strategic Touring fund.'

This £187,000 grant has enabled Inside out of mind to go on tour until the end of March 2015 to Derby, Nottingham, Exeter, Warwick, Canterbury and Leicester.

The traditional gap between science and the arts is clearly one that Schneider is keen to bridge. 'I think working with the arts has an enormous amount of potential. We've just been awarded a doctoral training centre from Alzheimer's Society to look into the arts and dementia.'

Even Schneider has been surprised by the effect that the play has had. 'Our sound director in the production found himself some time later in A and E, and while he was waiting he discovered that the nurses were still talking about the show.'

'We like to say that we started a conversation with this production and it is carrying on.'

For more information about the play visit www.meetingground theatrecompany.co.uk

£5 million for new dementia researchers

The biggest ever commitment to early-career researchers in dementia in the UK has been announced by Alzheimer's Society. The funding will create a network of doctoral training centres at universities across the UK to encourage young scientists to study dementia.

The eight doctoral training centres will cover both biomedical and care research, recruiting 53 PhD students from a variety of academic and clinical backgrounds. Over £3.2 million of the investment was provided by Alzheimer's Society, with an additional £1.6 million awarded through matched commitments from universities.

Research at the centres include:

- At Newcastle University, researchers will collaborate to understand the distressing non-cognitive symptoms of dementia with Lewy bodies.
- Researchers at the University of Sussex will study a gene that increases the risk of Alzheimer's disease by up to 10 times.
- Scientists at four Scottish universities (Edinburgh, Aberdeen, St Andrews and Dundee) will look at how heart health and high-fat diets affect the risk of developing dementia.
- PhD students at the Universities of Nottingham and Worcester will explore the benefit of creative art activities for people with dementia and their carers.
- University of Bradford researchers will study how to improve the transitions experienced by people with dementia between different care settings to improve quality of life.
- Researchers at University of Southampton will explore how to enable people with dementia to take calculated risks in daily life, such as travelling on their own, in order to maximise control and independence.
- PhD students at University of Exeter will study dysfunctional brain networks in dementia using a range of approaches including mathematical modelling, brain scans and experiments with brain cells in a dish.
- PhD students co-ordinated by the University of Cambridge will build on the 20-year Cognitive Function and Ageing Studies to look at the impact of lifestyle and cognitive health on the risk of developing dementia.

Dr Doug Brown, Director of Research and Development at Alzheimer's Society, said, 'For too long dementia research has been underfunded and, as a result, we have significantly fewer scientists than other conditions, with six times more people working in cancer than dementia.

'That's why we're proud to be announcing the largest investment of its kind, which will see £5 million committed to create the next generation of dementia researchers. People with dementia deserve nothing less than an all-out fight back against the condition and our doctoral training centres will help us enlist the right people to lead it.'

For more information about the centres visit alzheimers.org.uk/nextgeneration

Drug discovery projects announced

Alzheimer's Society has announced funding for projects investigating the potential use of a Viagra-like drug and new two-in-one treatments inspired by diabetes research.

The two studies will be funded jointly with the Alzheimer's Drug Discovery Foundation, a US-based organisation that is matching up to $2 million (£1.3 million) of Alzheimer's Society funding into drug discovery research.

The first study will investigate a potential treatment for vascular dementia, which is the second most common form of dementia. There are no treatments currently available for vascular dementia but researchers hope that the erectile dysfunction drug tadalafil, a drug similar to Viagra, could improve blood flow to the brain.

This is a 'test-of-concept' study, where the researchers are looking for an increase in blood flow in people who have damaged blood vessels in the brain. The results from this will help to build evidence for a full-scale clinical trial to test if the drug can prevent or treat dementia.

The second project is testing new drugs that were developed from research into two hormones linked to diabetes, known as GLP-1 and GIP, which protect against neurodegenerative conditions such as Alzheimer's disease.

The researchers, led by Professor Christian Hölscher at Lancaster University, have developed a range of potential drugs that may recreate the effects of both GLP-1 and GIP at the same time. It is hoped that this two-pronged attack could offer an even better therapy than liraglutide (see page 6), which works by mimicking the effects of GLP-1 alone.

The researchers will study the effects of these new drugs in mice that show changes similar to Alzheimer's disease. If the drugs show an improvement in symptoms, then it will clear the way towards following liraglutide into clinical trials.

Trial for vascular dementia begins recuitment

A major new clinical trial of a blood pressure drug to treat vascular dementia has begun recruiting volunteers. Led by Professor Peter Passmore at Queen's University Belfast, the £2.25 million trial will recruit almost 600 people around the UK and will last for four years.

The trial, which is being funded by Alzheimer's Society and the British Heart Foundation (BHF), will recruit people with a particular type of vascular dementia called subcortical ischaemic vascular dementia. Trial participants will be given either a placebo or amlodipine, a drug that is commonly used to treat high blood pressure, to test whether it may be used to treat vascular dementia.

Dr Doug Brown, Director of Research and Development at Alzheimer's Society, said, 'By testing a drug that is already licensed for other uses, this trial could result in a treatment for people with dementia much faster than developing one from scratch.

'Through our Drug Discovery programme, Alzheimer's Society is committed to the concept of repurposing treatments used for other conditions to develop them as new treatments for different forms of dementia.'

Professor Peter Weissberg, Medical Director at the BHF, said, 'Since amlodipine is inexpensive and available for certain conditions, there's little incentive for a pharmaceutical company to fund a trial like this. It's therefore vital that the BHF and Alzheimer's Society, as charities, have joined forces to make this trial possible.'

For more information about this trial visit alzheimers.org.uk/vasculartrial

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About us

Alzheimer's Society is the leading support and research charity for people with dementia, their families and carers.

Since 1990, Alzheimer's Society has funded £30 million of cutting-edge dementia research. We aim to increase our investment in our research programme to around £10 million a year by 2017. This money funds important research that will help us to improve the quality of life of people with dementia, by tackling questions related to the causes of dementia, investigating good practice in care and treatment, and pursuing a cure.

Research Network

One distinctive feature of our ground-breaking research programme is the integral involvement of people with dementia and carers.

As part of our Research Network, volunteers with direct experience of living with dementia inform our research priorities.

If you have been a carer for someone with dementia or you have dementia and are interested in joining the Research Network, please contact Anna Grinbergs-Saull, Research Engagement Officer, for an application form or apply online at **alzheimers.org.uk/researchnetwork**

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