Welcome to the ninth issue of Care and cure. I am pleased to introduce myself as the new editor, taking the helm from Dr Ian Le Guillou.

I hope to continue building on the strengths of this magazine to bring you informative and interesting updates on dementia research. From laboratory work revealing new treatment targets to studies into better social care, high quality research is essential to improve the lives of people affected by dementia, now and in the future.

In this issue, we take a look at new tests of cognition – thinking skills such as memory, language and reasoning. Understanding and measuring how dementia affects people’s thinking skills is critical to help them cope with these changes, and to test whether treatments and therapies are effective. However, compared to advances in our understanding of biology and genetics, cognition can sometimes get left behind.

Now cognitive scientists, such as assistant professor Dr Mario Parra (see page 6) and PhD student Katrina Dick (see page 8), are stepping up their game, bringing new insights and technology to make accurate tests for use around the world.

Tim Shakespeare
Editor
Careandcure
Researchers have developed a new treatment that could block the development of Alzheimer’s disease by using microscopic droplets of fat to carry drugs into the brain. This approach, used to target drugs to cancer cells, has been successfully applied to Alzheimer’s for the first time, restoring memory loss in mice.

The study was led by researchers at Lancaster University, funded by Alzheimer’s Society, and was published in the journal Nanomedicine: Nanotechnology, Biology and Medicine.

The treatment uses tiny droplets of fat, called nanoliposomes, which are coated in protein fragments. These fragments are able to stop amyloid protein accumulating into plaques, even at low concentrations. Amyloid plaques are the toxic clumps of protein that cause damage to cells in the brains of people with Alzheimer’s disease.

Lead researcher Professor David Allsop said, ‘Following results this summer, there is renewed optimism for antibody drugs – treatments that harness the body’s immune system to target amyloid plaques. However if these prove successful, treatments will have to be administered in a clinic by an IV drip and could have some potentially harmful side effects.’

Nanoliposomes are already used to better target toxic chemotherapy drugs to cancer cells. Recent studies have also shown that the fat droplets can pass directly into the brain through the nose, opening up the possibility of using a nasal spray to administer treatments for brain diseases, such as Alzheimer’s.

Professor Allsop said, ‘Using nanoliposomes offers an alternative way to inhibit the toxic build-up of amyloid plaques without activating an immune response in the brain.

Our hope is that this could one day be administered by something as simple and non-invasive as a nasal spray, which patients could use in the comfort of their own home.’

Mice that were genetically altered to develop Alzheimer’s disease were injected with the nanoliposomes for three weeks. Those which received the drug recovered their long-term memory and could recognise familiar objects after a 24-hour period. In comparison, mice that received a placebo injection had no memory of objects seen the day before.

Commenting on the need for innovative approaches to dementia treatments, Dr Doug Brown, Director of Research and Development at Alzheimer’s Society, said, ‘With no new dementia drugs in nearly 15 years, we’re at a critical time for dementia research. It’s absolutely vital that we continue to sniff out new approaches to getting drugs into the brain.

‘While we wait in anticipation for the results of ongoing clinical trials, Alzheimer’s Society will continue to fund innovative research to tackle dementia head on.’
We know that keeping active, along with a balanced diet, is one of the best ways to reduce your risk of developing dementia. A new study suggests that exercise may also benefit people who already have vascular dementia.

The study involved 70 people with vascular dementia, the second most common type of dementia. This causes problems with memory and thinking skills as a result of damage to large and small blood vessels in the brain.

Half of the people in the study took part in one-hour exercise classes three times a week for six months. The other half received information about vascular dementia and a healthy diet, but no information on physical activity.

All of the participants were tested on their overall thinking skills, executive function skills – such as planning and organising – and how well they could complete their daily activities. The people who exercised had a small improvement on the test of overall thinking skills compared to those who did not exercise. Six months after participants stopped the exercise programme, their scores were no different than those of people who did not exercise.

Dr Doug Brown, Director of Research and Development at Alzheimer’s Society, said, ‘Although this was a small study and the benefits of exercise didn’t help those involved with daily decision making or activities, it is promising to see researchers focusing on important issues around exercise.

‘We need to know more about who it can benefit, what kind of exercise works, and how to encourage people to take it up and keep it up.’

Blood supply boost

A small trial suggests that people with vascular dementia may benefit from regular exercise.

A better memory for words may make women more resilient to early Alzheimer’s.

Women typically have better verbal memory skills compared to men, and new research indicates that this could make them more resilient to damage caused to brain cells in the early stages of Alzheimer’s disease.

The research, conducted at Albert Einstein College of Medicine in New York, included 254 people with Alzheimer’s, 672 people with mild cognitive impairment and memory problems, and 390 people with no thinking or memory problems. The researchers measured how much glucose – a simple sugar that provides energy for the body’s cells – was used in the temporal lobe, an area of the brain that is important for memory. This gave a measure of how well brain cells were functioning, which was compared to verbal memory skills.

Women scored better on verbal memory tests than men, even when both groups had mild to moderate reductions in how much glucose was used, or metabolised, in the brain. Once people had more advanced metabolism reduction, there was no difference in the test scores between women and men.

This result adds weight to the ‘cognitive reserve’ theory, which suggests that the way people use their brains throughout life may help them to be more resilient to brain cell damage caused by Alzheimer’s disease.

Other aspects thought to increase cognitive reserve include having an intellectually challenging job and higher levels of education.
People with dementia may develop behavioural and psychological symptoms, including restlessness, aggression, delusions, hallucinations, depression and anxiety. These symptoms become more common as the disease progresses. They can be caused by an unmet need – for example, hunger, thirst or discomfort – or a health problem such as an infection.

People with these symptoms are often prescribed antipsychotic drugs inappropriately. These may reduce experiences such as delusions, but they are also linked to serious side effects, including increased risk of stroke and even death. After an initiative to reduce the prescribing of antipsychotics in England, an audit of GP practices in 2012 found that prescriptions had reduced by half between 2008 and 2011.

However, a recent study led by Professor Ala Szczepura at Coventry University suggested that prescriptions may not have decreased in the way we believed they had. The study examined prescribing in 600 care homes and found no decrease in prescription rates between 2009 and 2012. They also reported that antipsychotic drugs were often given for much longer than the recommended six weeks.

George McNamara, Head of Policy at Alzheimer’s Society, said, ‘This continued reliance on antipsychotics to manage behavioural symptoms of dementia is deeply worrying. With person-centred approaches and training programmes for care home staff, continued inappropriate prescribing is a step backward into the dark ages.’

Importantly, the risks of antipsychotic drugs aren’t the same for all people with dementia. Another recent study analysed data from six trials of an antipsychotic called risperidone, involving a total of 1,723 patients. The study, led by Professor Rob Howard and Dr Sergi Costafreda at Camden and Islington NHS Foundation Trust, found that patients who were experiencing delusions when the treatment started didn’t have a significantly higher risk of stroke. This may help to improve guidance about when medication is or is not appropriate.

The American Heart Association has issued a scientific statement reinforcing the link between high blood pressure, also known as hypertension, during midlife and an increased risk of developing Alzheimer’s or vascular dementia in later life. This effect is thought to be due to damage to blood vessels in the brain.

A gene delivered to the brain by a specially designed virus has been shown to reduce levels of amyloid protein in mice. This is an important target for Alzheimer’s disease treatments. Although gene therapy has shown promise in mice, it is not yet clear whether it will be suitable for people.

Researchers examining brain tissue from people who died with Alzheimer’s disease have identified microscopic particles from polluted air in the brain. Particles of a mineral called magnetite are thought to enter the brain through nerves in the nose, but it is not known whether this has any effect on brain health or conditions such as Alzheimer’s.
The last decade has seen remarkable innovations in tests for Alzheimer’s disease, revealing biological changes in people with the condition 10 to 20 years before symptoms develop. Precise scans can now accurately measure shrinkage of important brain areas, and measurements from spinal fluid can show changes in specific protein levels that indicate presence of the disease. Many of these innovations are now starting to make their way out of research centres, finding use in specialist clinical practice and drug trials.

Now researchers are keen for the field of cognitive assessment to catch up. The idea is to discover whether particular tasks can reveal subtle changes in thinking skills before clinical signs and symptoms emerge.

“We are looking for ways to tease apart the cognitive decline of people embarking on the journey of Alzheimer’s disease from the changes that are part of normal ageing,” says Dr Mario Parra, whose research focuses on how to improve cognitive assessment.

While revealing biological changes is incredibly informative, the critical test for any treatment is whether it improves thinking skills and daily function. Sensitive assessments of cognition – such as in memory, language and reasoning – are therefore essential for treatment trials. The recent trend in clinical trials for Alzheimer’s has been to give treatments at earlier stages of the disease. To establish whether these treatments are working, cognitive tasks that can monitor early changes are needed.

A task that could show who was experiencing normal ageing and who was in the very early stages of Alzheimer’s disease would also help with diagnosis. It could be given to people who are worried about their memory to find out whether they are likely to experience progressive symptoms that will require support and treatment.

A binding problem

At Heriot-Watt University in Edinburgh, Dr Parra is developing assessments to tackle this challenge. In collaboration with colleagues from the University of Edinburgh and overseas, the task he has created taps into a specific brain function – the ability to remember the combination of two features of an object.

Participants are shown a computer screen displaying objects of different colours and shapes. The screen goes blank and, after a delay of about a second, they’re shown objects that are either the same or different.

In one part of the task, only one feature can change between the original and second screens – for example, the shapes change but the same colours are used – and people with Alzheimer’s disease are usually
able to identify this change. In another part, when the objects are different in the second screen, they have the same shapes as in the original but the colours have switched. It is this part, where the combination of features changes, that people with Alzheimer’s disease tend to find very difficult.

‘This ability to store the combination of features over a short time period is called short-term memory binding,’ says Dr Parra. ‘It’s not memory in general that is affected very early in Alzheimer’s disease, it’s the ability to combine different parts.’

Studies have shown that this specific ability is affected in people who are worried about their memory, even when more traditional assessments don’t reveal any problems. They’ve also found that people who have a rare genetic mutation causing Alzheimer’s disease to develop at a young age have difficulty with the task before symptoms emerge.

**Ticking all the boxes**

Working with international collaborators, Dr Parra has shown that this ability is affected early in the disease. They have collected data from the UK, Colombia and Brazil to show that the task isn’t affected by age, education or culture. The team are now investigating the biological reasons why this task is affected at this stage of the disease’s development. They are also looking at how people’s performance on the task is related to biological markers for Alzheimer’s disease.

In addition, it’s important to establish whether the task can predict who will go on to develop further symptoms of Alzheimer’s disease and who will not. Data currently being collected with the same individuals over a number of years should reveal exactly that. ‘If we can tick all those boxes, we’ll have an Alzheimer’s disease-specific cognitive biomarker,’ says Dr Parra.

**Crucial collaborations**

So what does it take for research like this to succeed, and where will it go next?

Dr Parra says, ‘Important ingredients are collaborations and support. The international scientific community has become aware of this methodology, and people are now using it and replicating the findings which is very encouraging. It’s not just our lab, people in different settings are arriving at the same conclusions.

‘It’s not memory in general that is affected very early in Alzheimer’s disease, it’s the ability to combine different parts.’

Dr Parra

‘We’ll continue expanding our collaborating activity to make more people aware and invite them to use the tasks. The support we’ve had from Alzheimer’s Society enables us to continue expanding our network and refining the tasks into clinical tools.’

Not satisfied with detecting and monitoring memory changes in Alzheimer’s disease, Dr Parra is also setting up a team to use these insights to help people live well for longer. Studies such as the Alzheimer’s Society brain training trial have shown that cognitive training packages can help older people with daily activities.

Dr Parra wants to take a different approach, using computer science to create a virtual environment to simulate people’s own homes. In this environment, people with Alzheimer’s disease can practise everyday activities such as making a cup of tea or using the TV, and adjust the difficulty to meet their changing abilities while still posing enough challenges that can be overcome with practice. Having established a new Everyday Life Settings Lab at Heriot-Watt University, the team will trial a prototype next year.

**Associations between the brain and behaviour**

Dr Parra and his team use electroencephalography to record the brain’s electrical activity. This allows them to understand how changes in people’s ability to do tasks relates to changes in the brain.
I have studied and worked in the field of dementia for the past four years, first becoming interested in dementia while studying undergraduate psychology and working as an assistant psychologist. During this time, I administered widely used tests of memory and thinking skills to people with different diagnoses of dementia.

I now co-ordinate an international research project called GENFI – the Genetic Frontotemporal Dementia Initiative – looking at the rare genetic mutations that cause genetic frontotemporal dementia (FTD).

FTD is the second most common form of dementia in people aged under 65, and often causes problems with behaviour, planning and language skills. For many people with FTD the cause is not known, but around a third of people develop FTD due to a specific genetic problem.

We recruit participants who already have symptoms of FTD and also those who are likely to develop the disease. In genetic FTD, the risk of developing the disease is 50 per cent if your parent carries a problem mutation.

Our project is particularly exciting, as we know what is causing dementia in this group of people and can explore ways to prevent symptoms developing or stop them getting worse.

Using advanced brain scans, studies have revealed changes in the brain of at-risk participants up to 25 years before any obvious symptoms develop. This suggests the disease process starts many years earlier than expected, and the ideal time to treat people is likely to be when the disease is in its earliest stages.

At present, traditional tasks, such as recalling lists of words or naming pictures, are almost always performed at a research centre by a trained psychologist. These assessments are not sensitive enough to detect early changes. There is therefore a need for new tasks to detect earlier cognitive changes in people with genetic FTD. This will require a new set of assessments performed in new ways.

With the support of Alzheimer’s Society, my research is leading us to create assessments to reflect the subtle changes in the brain that we know exist years before symptoms develop.

These will be administered using a tablet computer, such as an iPad, so they can be performed at home without a psychologist present. They will also be more demanding than standard tasks in order to detect very subtle changes. The tasks will be short at 60–90 seconds each, and designed like enjoyable games to make them more stimulating.

Existing assessments often lack tasks that can pick up early FTD symptoms, which can be quite different to those of Alzheimer’s disease. Ours will include tasks relevant to FTD, such as flexibility of thinking, speed of processing and recognition of emotion.

The lack of detailed information about the earliest changes that occur in FTD is a major hurdle in the development of clinical drug trials. I am hopeful that the results of my research will be valuable in trials, to establish when treatments should be given and whether they are working. If such trials were to be successful, this may mean that the onset of symptoms could be delayed or even prevented.

‘My research is leading us to create assessments to reflect the subtle changes in the brain that we know exist years before symptoms develop.’

Katrina Dick
When we think about dementia we rarely think about eye health, but its importance is clear. Good vision is essential for so many everyday tasks and arguably even more so for people with dementia, who may rely on vision if abilities such as memory and planning are affected.

The Prevalence of Visual Impairment in People with Dementia, or PrOVIDe, study was developed as a collaboration between the College of Optometrists, Alzheimer’s Society and Thomas Pocklington Trust. The results revealed how common visual problems are, paving the way for improvements in eye care for people with dementia.

In the study, over 700 people with dementia had standard sight tests carried out by optometrists visiting homes and care homes. Of most interest to the researchers was the number of people with impaired vision, defined by low visual acuity (poor clarity of vision). When wearing their spectacles, one third of people with dementia had poor acuity. The researchers found that much of this could be improved with the right treatment. Almost half (44 per cent) could be remedied with new glasses and almost a quarter (22 per cent) was due to cataracts, which can often be operated on. The next leading cause was macular degeneration, which can sometimes be treated but not cured. In the study, people in care homes were significantly more likely to have impaired vision than those living in their own home.

James Pickett, Head of Research at Alzheimer’s Society, offered guidance from the start of the project, and Sue Maskell, a Research Network volunteer, assisted in a successful application for funding from the National Institute for Health Research.

The study was led by Michael Bowen, Director of Research at the College of Optometrists, who said, ‘The fact we had three charities as full co-applicants on the submission was a strength. Having Sue as a co-applicant from the outset was very helpful in avoiding problems with the design.’

The striking results from this study have spurred the College of Optometrists to take further action. The college has published proposals in its journal, Optometry in Practice, to address the need for more dementia-friendly optometry practices and the creation of a dementia eye care pathway.

This care pathway could provide people with dementia and carers with better information about the services available to them. For example, it’s not well known that sight tests at home, known as domiciliary visits, should be available to people who are unable to attend a practice unaccompanied. It could also provide additional subsidies for spectacles and improved access to eye care services.

With the problems clearly outlined and potential solutions in the pipeline, it’s hoped that these insights will translate into better eye health for people with dementia in future years.
Earlier this year, Alzheimer’s Society announced our involvement as a founding partner in the £250 million Dementia Research Institute, in collaboration with the Medical Research Council and Alzheimer’s Research UK.

This institute will support large programmes of research across the UK, funding research into dementia care and public health as well as biomedical research.

A major aspect of the Society’s involvement in the Dementia Research Institute is to make sure that the voices of people affected by dementia shape its work throughout.

Over the past six months, we have been developing plans to involve people in meaningful ways, and in September 2016 we held our first activity – recruiting the institute’s Director.

To ensure that people affected by dementia had their say, we set up a ‘lay’ interview panel of six people with dementia and carers. This panel met shortlisted candidates to hear about their plans for the institute and ask them questions.

Before the first interview, the lay panel decided to focus its questions on:

- The candidates’ views on what should be the priority in dementia research.
- The use and sharing of patient data.
- How to encourage more diversity in research participation.
- The role of patient and public involvement in the institute.
- The candidates’ approach to communication.

Candidates gave a short presentation at the start of their interview by the lay panel, and the panel’s questions inspired fascinating and varied conversations.

The lay panel fed back on each candidate and its chair, Research Network volunteer Sara Gregson, presented a report to the broader recruitment panel.

Sara said, ‘It was an honour to be asked to chair the lay interview panel and to hear and speak to the potential candidates – all of whom had significant backgrounds and experience in dementia research.

‘At the end of the day, it was my job to present our advisory findings to the recruitment panel. I had five minutes to summarise what we had done and the highlights from each candidate, ending up with our conclusions of who might be the best person for the job from our perspective. They reacted warmly to our conclusions!’

A fantastic candidate has been selected to lead the UK’s first dedicated Dementia Research Institute. We hope to be able to announce the new Director before Christmas, and tell you more about them in the next issue of Care and cure.
James Pickett, Head of Research at Alzheimer’s Society, discusses how the arts can help people living with dementia.

Art and culture holds a unique place in our lives. Whether it’s singing, poetry, museums or dance, the arts enrich our lives and bring pleasure to everybody at some point.

This is no different for people with dementia, as the popularity of Singing for the Brain shows. Researchers have therefore begun to develop an increasing interest in the arts, aiming to find evidence as to how and why they may be able to help people with dementia.

The arts and dementia research
In 2015, Alzheimer’s Society funded eight doctoral training centres around the UK to train the next generation of dementia researchers. One of these centres is shared between the universities of Nottingham and Worcester, and is known as Tandem – short for ‘the arts and dementia’. It will train eight new PhD students in understanding the role of the creative arts in dementia care. As part of the work of the centre, these bright and energetic students were charged with organising a conference to bring together academics, arts practitioners and people affected by dementia. It was described as the first conference of this kind in the UK on this topic, and I was lucky to be invited as a speaker.

Along with interactive dance and poetry sessions, there was a lot of discussion about the role that research has in the arts. After all, if the arts are pleasant and enjoyed by people with dementia, why do we need to measure this effect? Who are we trying to convince? Lots of discussion focused on how research in relation to the arts. Another project that Alzheimer’s Society is involved in, called the Hub, started in October. Based at the Wellcome Collection in London, this offers a large area for exhibitions and performances where researchers, people affected by dementia and arts practitioners can mingle and work together. It is open for two years and we have some interesting ideas about how we will work with them – watch this space.

‘Shall I compare thee to a dose of donepezil?’ is a tongue-in-cheek line – one written by an actual poet – but it asks an important question about whether using the creative arts could be comparable to the therapeutic effect of drug treatments.

Thankfully, people with dementia should not have to choose. They should all be prescribed any appropriate medication, and also be provided with rich opportunities to take part in activities that don’t rely on drugs, such as the arts.
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 over £40 million of cutting-edge dementia research. We aim to increase our investment in our research programme to £100 million over the next decade.

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 Manager, for an application form or apply online at alzheimers.org.uk/researchnetwork.