Care and cure
The Alzheimer’s Society research magazine

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Science is built on a foundation of sharing ideas and knowledge. The greatest scientists have relied on using what others had found to develop new ideas – ‘If I have seen further, it is by standing on the shoulders of giants,’ as Isaac Newton said.

Back in Newton’s time, scientists recognised the need for an easier way to share their knowledge and so in 1665 the world’s first scientific journal, Philosophical Transactions, was published by the Royal Society.

There are now over 28,000 different scientific journals, but sharing information can still be deceptively difficult. As we discuss in this issue (page 6), although sharing data is far less constrained than it used to be, there are still ethical issues when it comes to study participants’ personal information.

New efforts, such as the Dementias Platform UK, are working to help this process and it is important that they succeed. Combining and comparing data from different studies is a hugely valuable opportunity and it would be reprehensible to not make the most of it.

However sharing isn’t just between researchers; information and ideas need to reach the outside world and feed back into the research community. Our Research Network volunteers are experts in dementia through their experiences and we hear from researchers about the impact that the network has had on their work and themselves (page 9).

Ian Le Guillou
Editor
Careandcure
Increasing evidence suggests that the immune system plays an important role in Alzheimer’s. This study, involving mice that showed symptoms of the disease, discovered that specialised immune cells in their brains broke down arginine, an essential nutrient.

A reduction in arginine levels can lead to brain cell death, the cause of Alzheimer’s disease symptoms. A lack of arginine has previously been reported in the brains of people with Alzheimer’s, and this research is the first to show a role for the immune system in this process.

When the researchers used a cancer drug called DFMO to block the mechanism that breaks down arginine, they found that the mice performed better in memory tests. This discovery could identify new areas to investigate in developing potential treatments for Alzheimer’s disease, including further research into how DFMO may work in people. The researchers stress that increasing the amount of dietary arginine may not be of benefit as a treatment, as it is unclear whether it can then reach the brain.

‘This study in animals joins some of the dots in our incomplete understanding of the processes that cause Alzheimer’s disease, in particular around the role played by the immune system,’ says Dr James Pickett, Head of Research at Alzheimer’s Society.

‘Importantly, these new findings reflect earlier observations that arginine is reduced in the brains of people with Alzheimer’s disease. The next step would be to show that targeting arginine metabolism in the brain can reduce the death of brain cells, as this was not shown in the current study.’
New toolkit to help dementia care for south Asian people

Several studies have shown that knowledge of the causes, symptoms and consequences of dementia can be more limited among south Asian people in the UK. This can lead to problems in making a diagnosis of dementia and delivering the right treatment.

To help understand why this is the case, researchers adapted a checklist that had been previously designed to gather perceptions of mental illness from people with different cultural backgrounds.

Through a review of previous work with south Asian communities and interviews with 25 people, the team developed a new tool which takes into account cultural sensitivities that can act as barriers to effective diagnosis and treatment.

Professor David Challis, from the University of Manchester who led the research, said, ‘South Asian people are, broadly, less likely to seek help for a mental health problem than members of other communities.

‘Using this toolkit could be a way of providing more evidence-based training for health workers and developing resources, such as leaflets that are attuned to this community’s particular needs.’

The toolkit is delivered as an interview with a participant who may have dementia. As the interview progresses, the researchers tick items off a checklist to give data about that person’s perceptions of symptoms, causes, the consequences of illness and preferred treatment methods.

Defence mechanism against toxic protein build-up discovered

In Alzheimer’s disease, amyloid protein gathers into small groups called oligomers, which then group further into large, sticky clumps known as plaques. Some scientists believe that it is oligomers that are responsible for the toxic effects of amyloid protein in Alzheimer’s.

Previous findings suggest that the plaques can speed up the production of amyloid oligomers, creating a feedback loop of ever more toxic protein. The scientists discovered that a protein called BRICHOS, which is naturally found in the body, can prevent the plaques from creating these oligomers.

This discovery shows a possible way in which the growth of amyloid clumps could be slowed and also helps to better understand how they function in Alzheimer’s disease.

Dr Doug Brown, Director of Research and Development at Alzheimer’s Society, said, ‘While most current research attempts to break up these clumps or reduce their impact on brain cells, this new discovery identifies a molecule that reduces their rapid accumulation. This revelation is exciting as it gives scientists a whole new way of looking at the problem, opening the doors to possible new treatments.’
Insight into early stages of frontotemporal dementia

A study in fruit flies has revealed a way in which brain cells may die in a common form of early-onset dementia.

Researchers at the University of York studied the protein CHMP2B, which is known to be altered in frontotemporal dementia. By studying the connections between brain cells in fruit flies, they uncovered mechanisms that control the way that CHMP2B functions. Changes to these mechanisms can cause the cell connections to overgrow, which has been shown to lead to brain cell death in the flies.

Frontotemporal dementia, also known as Pick’s disease, is one of the more common forms of early-onset dementia and it typically starts in individuals during their 50s. It can affect language abilities as well as a loss of inhibition. This is caused by the loss of neurons in the frontal and temporal lobes of the brain.

‘These findings shed light on the events occurring in neurons as dementia takes hold. The more we know about the steps that occur in disease progression, the more opportunities we have to intervene with potential therapies,’ said Dr Sean Sweeney, the study’s senior author.

Dr Ryan West, who carried out this work for his PhD funded by Alzheimer’s Society, said, ‘We hope that this work helps to tease apart complex molecular processes occurring in neurons and identify how these can go wrong in neurodegenerative diseases, such as frontotemporal dementia.’

Dr Clare Walton, Research Communications Manager at the Society, said, ‘We know less about the underlying causes of frontotemporal dementia than some other kinds of dementia, so research like this is a vital step towards developing treatments for this condition.’

News in brief

A large clinical trial in Finland has shown that offering detailed health guidance to people in later life improves brain function. Participants were split into two groups, with half receiving simple health advice and the other receiving in-depth guidance. After two years, the group that had received the personalised advice did significantly better on a range of tests, including reasoning and speed of brain processing.

The amount of money spent on dementia research in the UK is still too low when compared with its economic impact, according to a new study. Researchers tallied the cost of dementia in 2012 and other leading causes of death and disability. They found that for every £10 that was spent on dementia, just 8p went on funding research into the condition.

An analysis of almost 2 million UK health records suggests that being underweight in mid-to-late life is associated with a higher risk of dementia, and being overweight with a lower risk. This is in contrast to current thinking among scientists and previous research, which suggests that being overweight increases the risk of dementia.
We live in an age of information. Not only is it easier to create more information, it is also getting easier to tap into the sum knowledge of humanity.

Research is continuing to produce increasing amounts of data. One obvious source of this is in genetics studies – the entire sequence of the human genome would take 100 books to print out. However the use of data goes far beyond genetics; researchers are also gathering vast amounts of data from health records and long-term group studies.

Gathering this kind of data can be expensive – the original Human Genome Project cost roughly £2 billion and phase III clinical trials regularly cost hundreds of millions of pounds – and it’s important that we can make as much use of it as possible.

**Pooling data**

Dr Graciela Muniz-Terrera from University College London is being funded by Alzheimer’s Society to look at past studies into the relationship between education and the decline of brain function in dementia.

‘I’m trying to see whether there are common patterns across the different datasets. I understand that this is the only way we can make sure that a result we find is not just a fluke of the data. This involves the analysis of different datasets, trying to minimise the differences in results that may emerge from using different statistical methods.’

This kind of study is known as a co-ordinated analysis, where a researcher analyses data from several sources in a consistent way to reduce differences from the various approaches used. By pooling together data from several studies, new results can appear that wouldn’t have been possible to see in any one study.

This kind of research isn’t the only way that sharing data can help. Additional information may also help to build connections between fields of expertise. As Dr Petroula Proitsi explains (page 8), access to large datasets from other researchers can help to build a better understanding of the bigger picture.

However pooling data is not always straightforward. ‘In analysis of cognition, that is not an easy thing to do. Say if I want to measure verbal fluency, one study may have one measure of verbal fluency and another one will have another measure,’ says Dr Muniz-Terrera.

‘So we cannot bring together these datasets, because even though they

With the availability of new technologies and access to detailed information about public health, researchers are producing more data than ever before. To make the most of this information, new efforts are making it easier to share widely among researchers.
measure the same cognitive function, the tests used are different and may have different degrees of difficulty. So although these methods of pooling data from multiple studies may work in other research areas, in our area it is more difficult.

In confidence
Another difficulty involves the ethical concerns of sharing people’s personal information. When participants sign up to take part in a study it is based on an understanding of how their data is going to be used and protected. So when sharing their data, researchers have to ensure that they abide by the participants’ wishes.

‘I think that with development of technology, somehow we will be able to access data in such a way that the data does not need to leave researchers’ facilities,’ says Dr Muniz-Terrera.

‘There are ethical concerns, like identifiability of patients and so on, and people are concerned about where copies of their data are stored and I understand that. You can’t break participants’ confidence and trust.’

She adds that there is a need for an initiative that reassures the researchers and the study participants that their data is safe, but at the same time that doesn’t make the use of the data more difficult for researchers.

One way that researchers are tackling these difficulties is through the creation of the Dementias Platform UK, a multimillion pound public-private partnership. This will bring together 22 existing studies with a total of 2 million participants to create the world’s largest population study for dementia.

‘The challenge is overcoming the very real technical and ethical challenges of data sharing, so that the scientific advantages may be realised rapidly and cost effectively,’ says Dr John Gallacher, director of the platform.

‘The Dementias Platform UK aims to do this by developing a “one-stop shop” for scientists in which the technical and ethical challenges have been addressed centrally, releasing scientists to get on with what they do best: the science.’

Ways of sharing
Although the Dementias Platform UK includes an impressive number of participants, there are still hundreds of smaller studies that are not included, which might look at more niche areas of study. Dr Muniz-Terrera has been experimenting with ways of making the most of these smaller studies, without the researchers having to distribute their data.

‘I produce a script for statistical analysis and I send it to different people involved in the studies. They run the analysis and send me back the results. However that takes a long time, because it involves the other person having time to do the analysis and then I get the results back, but there is always some information missing so it takes many, many iterations.’

As well as this approach, she has also found that a more direct method is to do this in person. ‘We have organised workshops and invited researchers associated with different studies to come to our workshops, where we don’t access their data. Each of them comes with their own datasets and we guide the analysis and then we produce a common paper with summary results.’

Dr Muniz-Terrera is ‘really hopeful’ for the future of the Dementias Platform UK and other efforts to aid data sharing, but cautions that it won’t be easy. ‘We are in relatively early days in terms of using multiple datasets and we still have to convince people that it is worth the effort.’
As an undergraduate student I was fascinated by the release of the first draft of the Human Genome Project and the possibilities it opened up for the investigation and treatment of complex genetic disorders. After 11 years studying Alzheimer’s disease, I am still motivated by this fascination, and the desire to help make a difference in tackling this devastating illness.

My PhD started in the lab, where I learned a range of genetics techniques by looking for genes that increase the risk of specific symptoms frequently experienced by people with Alzheimer’s disease, such as depression, psychosis and aggression.

What captured my imagination and interest was how the problem was so complex and multidimensional. I had a database with thousands of patients, each experiencing a different degree of behavioural symptoms, each with different histories as well as genetic profiles. It was obvious that making sense of this complexity would need a new approach, and my PhD began to move from the lab to the computer as I started using new techniques to tackle huge amounts of complex biological data.

In the decade that I have been working on Alzheimer’s disease I have witnessed rapid technological advances. These have led to massive international studies that provide unprecedented levels of biological detail. As someone with lab-based skills as well as statistical expertise I have been able to help my colleagues in different projects, leading to interesting collaborations.

The advent of large-scale studies and increasing collaboration has provided us with study groups that are rich with clinical and biological information. These have led to the discovery of many biological and environmental factors associated with Alzheimer’s disease. However these advances have highlighted the complexity of this condition and the fact that information about many aspects of the disease is still missing.

This inspired my current Alzheimer’s Society fellowship, where I am trying to identify differences in molecules in the blood between people with Alzheimer’s disease and people who do not have the condition.

Experiments to measure the contents of blood have identified more than 4,000 different molecules, many of which are very similar. It is therefore very challenging to summarise all this information and to identify a combination of molecules that can predict if an individual has or will have Alzheimer’s disease.

Associating these molecules with other types of biological information is even more challenging. Large-scale genetic studies, for example, provide information on more than 9 million changes in DNA. Such analyses require well-designed programs and very powerful computers.

These large studies also require collaborations between scientists who work on different biological aspects of the same data, and independent datasets for us to replicate our findings.

Finally, they also require patience, systematic analysis and strong vision. We know that this data contains a large amount of information and we have to make sense of it by asking the right questions.

This is a very exciting project at a very important moment in Alzheimer’s disease research, as we have new tools to help to defeat it. I am thrilled that I have the opportunity to contribute to this cause and to be able to conduct exciting, ground-breaking science.
Alzheimer’s Society has long been a pioneer of involving people affected by a condition in research about it. A key part of this is the monitoring of research projects by our Research Network volunteers, people who have all cared for someone with dementia or have dementia themselves. Monitors meet every six months with researchers to get an update on how the work is progressing and to offer their expertise.

This provides many benefits to researchers. The most obvious example is to remind them of what their research is for.

Frank, a Research Network volunteer, says, “The main benefit I have found is that it has emphasised to researchers the critical importance of the work they are undertaking to society as a whole. This happens as a result of sharing a little bit about my own story in the first meeting at the start of the project, and linking it in some way to the work involved.”

Dr Sean Sweeney, a researcher from the University of York, says, “I feel it gives us focus and brings us back to the critical questions, rather than (as academics tend to) getting distracted with interesting areas of biology. The meetings also remind us very clearly why we are doing this work.”

Dr Gayle Doherty from the University of St Andrews summarised this by comparing the experiences of the monitors to the disease-causing proteins that she studies. “The monitors give an articulate voice to the patients and help us remember that Alzheimer’s disease is more than just amyloid beta and tau.”

As well as telling their story, monitors can also provide a fresh pair of eyes for research projects and insight into recruiting volunteers for studies. “An example of this was pointing out the potential difficulties of repeated visits and travel costs and difficulties for the person with dementia. This led to a rethink,” says Julia, another member of the Research Network.

One researcher said that monitors ‘have been really helpful in providing real context to questions we have had about certain practicalities in how to deliver studies, and what would be viable and what might be found more challenging for potential participants.’

The monitors’ exposure to several different areas of research puts them in a unique position. “I have been often impressed by the level of knowledge and clear understanding of network members about key topics in the field, including my own research,” says Dr Mario Parra from the University of Edinburgh.

Monitors can also provide support to researchers in their career path. One monitor received a letter from a PhD student saying, “I really appreciate meeting you and all of your input on my project; it really helped me decide that a PhD in dementia research was the way forward for me.”

‘The interactions with our network members are rich, both from a social and a scientific perspective. I have become more confident in sharing my results and doubts, and more skilful in taking suggestions from and conveying key messages to lay audiences,’ says Dr Parra.

Input from the public can help researchers to place their work in context, take a fresh look at their approach and develop their career. Involving people with a lived experience of dementia is not only about doing the right research, but making sure research is done in the right ways.
Our programme to build up the number of people conducting research into dementia has resulted in a record number of new fellows being funded. The initiative has also been shortlisted for a prestigious charity award.

In January 2014, we launched our Dementia Research Leaders programme to better support early career researchers with skills and training, more research funding and opportunities that will help them to become leaders in dementia research.

There are currently six times as many researchers working in cancer as in dementia. To make progress in our understanding of dementia, we need to make sure that more researchers are supported to work on the condition, that they are the best, and that the best stay in the field.

In our latest round of grant applications we have funded 10 new fellowships, more than ever before. Among these is Dr Claire Garwood from the University of Sheffield, who has been awarded a junior fellowship to study the effect of insulin on brain cells known as astrocytes. Dr Garwood is a good example of our commitment to supporting researchers through their early careers, as we previously funded her as a PhD student.

‘For me the funding provided by Alzheimer’s Society has been invaluable; the first step of my research career, my PhD, was funded by the Society. This enabled me to develop a research project that revealed some significant insights into the involvement of astrocytes in the disease, an area in which I have continued to work since gaining my PhD,’ said Dr Garwood.

‘The next key step for a junior researcher like me is to secure their own funding so that we can develop an independent research career in our specialised research area. The junior fellowship awarded to me by the Alzheimer’s Society means that I am now able to do this.

‘I can continue to use and develop the expertise and knowledge I have already gained to work towards my aim of developing my own research group. It also means that my expertise is retained within this important research area.’

The Dementia Research Leaders programme has been shortlisted in this year’s Charity Awards. Organised by Civil Society Media, these awards recognise excellence within the charity sector across 10 categories and winners will be announced on 18 June.

‘We’re delighted that our Dementia Research Leaders programme has been shortlisted to receive a prestigious Charity Award. Supporting talented individuals to develop a career in dementia research is a core priority for Alzheimer’s Society, bringing us a step closer to achieving our vision of a world without dementia,’ said Dr Doug.
UK living with dementia, there is a collective agreement that more needs to be done, that research plays an important part in that progress and that the public are willing to donate their time to come together to make it happen,’ said Professor Martin Rossor, from the National Institute for Health Research.

‘We need to maintain momentum to reach our aspiration for 100,000 people to sign up to Join Dementia Research. We still have a long way to go to spread the word about Join Dementia Research to people with dementia and their families living in towns and cities in every corner of the UK and make sure everyone knows that the opportunity is available to them.’

Hilary Doxford, who has dementia and is one of Alzheimer’s Society’s Research Network volunteers, said, ‘The involvement of people with dementia today will hopefully help not just us but so many in the future. I really would encourage anyone who has, or knows someone with, dementia to have a discussion about research and consider signing up.’

Great response to Join Dementia Research launch

After its national launch in the spring, Join Dementia Research has signed up over 6,000 people to register their interest in volunteering for dementia research. Over 1,000 of them have now been enrolled in research studies.

Alzheimer’s Society is urging more people to consider signing up to Join Dementia Research, especially people with early memory problems. There are now 39 studies looking for volunteers, many of which are looking for people in the early stages of dementia, or those with mild cognitive impairment who are experiencing memory and thinking problems that are not severe enough to be diagnosed as dementia.

‘The fantastic response we’ve seen to Join Dementia Research so far is indicative of the importance of dementia and research to the wider public. With 850,000 people in the UK living with dementia, there is a collective agreement that more needs to be done, that research plays an important part in that progress and that the public are willing to donate their time to come together to make it happen,’ said Professor Martin Rossor, from the National Institute for Health Research.

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For more information visit www.joindementiaresearch.org.uk
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-Saul, Research Engagement Officer, for an application form or apply online at alzheimers.org.uk/researchnetwork

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