Busy brains may delay Alzheimer’s
Mental activity helps people with risk gene. Page 5

Social isolation
PhD project on social factors that affect risk of dementia. Page 8

£250m for institute
Largest ever investment into dementia research. Page 10

Finding mid-life changes linked to Alzheimer’s disease. Page 6

Early signs

Prevention is one of the main strands of research funded by Alzheimer’s Society, yet what do we mean by this term?

The word prevention implies that there is a way to completely avoid dementia, yet in reality we all have a risk of developing the condition. On an individual level it is more appropriate to talk about reducing that risk. If enough people reduce their risk, then fewer people develop dementia and we can talk about prevention on a population level.

We know from studies comparing people with different lifestyles that diet, exercise and not smoking are associated with a lower risk of dementia. Yet we still do not know for sure if, how or why these different factors affect the brain.

The PREVENT study, described on page 6, is trying to identify the earliest signs of dementia in people long before the symptoms may ever appear. By understanding what happens at this stage, researchers will be better able to see how lifestyle factors or new drugs might have an effect.

One day this might make it possible to treat the causes of dementia long before a diagnosis would be needed. Then we finally would be able to talk about prevention on an individual level.

Ian Le Guillou
Editor
Careandcure
The role of the immune system in Alzheimer’s disease is receiving more attention as researchers try to reduce the harmful inflammation that creates stress and damage for brain cells. New results in mice suggest that an injection of the protein IL-33 can stop the immune system from creating inflammation and instead begin clearing away the toxic amyloid plaques that are a hallmark of Alzheimer’s disease.

Inflammation is a natural response to damage or infection that helps the body to cope, however it can cause damage itself if it lasts for a long time. When the sticky amyloid plaques form in the brain, the immune system triggers inflammation which worsens the damage to the brain cells.

By injecting the protein IL-33 into mice with signs of Alzheimer’s disease, researchers in Hong Kong were able to reduce the amount of inflammation and switch the immune system to a more targeted approach to clear the plaques.

There are clinical trials currently ongoing that are testing existing drugs to reduce the level of inflammation in the brain, including the antibiotic minocycline and arthritis drug etanercept.

Dr James Pickett, Head of Research at Alzheimer’s Society, said, ‘We know that inflammation plays a key role in the development of dementia and some genetic studies have suggested a link between this protein and the development of Alzheimer’s disease. ’ It’s still early days for this line of research and we will need to see if similar mechanisms occur in people as in mice.

‘With an ageing population and no new dementia drugs in over a decade, the need to find treatments that can slow or stop the disease progression is greater than ever. There are already some clinical trials looking at inflammation – this latest finding adds to our understanding of why targeting inflammation may be a promising approach.’
Mice can recall ‘lost’ memories

Researchers in the US have used an innovative technique involving flashing lights to discover more about how Alzheimer’s disease can affect memory.

One of the earliest stages of Alzheimer’s disease involves problems with episodic memory, such as about where an event took place or who was there. One of the mysteries of the condition is whether this problem arises because the brain can no longer store new episodic memories, or if they are stored as normal but cannot be recalled.

The researchers used a technique called optogenetics to try and find an answer to this question. Optogenetics involves using cells that have been specially tagged in way that means they respond to a special blue light.

The researchers tagged brain cells in mice that are involved in the storage and retrieval of memories, meaning that they would respond to the special light. The mice also showed symptoms of Alzheimer’s, gradually losing certain memories over time. However, after using the special light to activate the brain cells, the researchers found that the mice were able to recall things that they had previously forgotten.

This research offers evidence that memories that are ‘lost’ due to Alzheimer’s disease remain stored in the brain and that memory problems occur due to a loss of the ability to recall them. While the use of optogenetic techniques would not be possible in people, this research gives us valuable insight into the mechanisms that may lie behind memory loss in Alzheimer’s.

Dr Doug Brown, Director of Research and Development at Alzheimer’s Society, said, ‘While interesting, the practicalities of this approach – using a special blue light to stimulate memory – means that we’re still many years away from knowing if it would be possible to restore lost memories in people.’

Gum disease link to faster decline

People in the early stages of Alzheimer’s disease appear to decline more quickly in their memory and thinking if they have gum disease.

Researchers assessed 59 people with mild to moderate Alzheimer’s disease for memory ability, levels of inflammation and dental health. The majority of participants were followed up at six months when all assessments were repeated.

People who had gum disease declined in memory ability six times faster than those who did not over the six-month follow-up period. The researchers concluded that gum disease is associated with an increase in cognitive decline in Alzheimer’s, possibly by mechanisms linked to the body’s inflammatory response.

Dr Doug Brown said, ‘It’s unclear, however, whether this is cause or effect – if the gum disease is triggering the faster decline of dementia, or vice versa.

‘This study adds evidence to the idea that gum disease could potentially be a contributing factor to Alzheimer’s, but we would need to see clinical trials to provide more solid evidence. If this is proven to be the case, better dental hygiene would offer a way to help slow the progression of dementia and enable people to remain independent for longer.

‘We know as dementia progresses, a person may lose the ability to clean their teeth, stop understanding that their teeth need to be kept clean, or lose interest in doing so. If this does happen then carers may need to help with this task – a dentist or hygienist can provide guidance and support on how to assist in cleaning another person’s teeth.’
The study followed 393 people aged over 70 who did not have dementia. They were asked questions about their education history and how mentally active they were in middle age. The researchers then looked for signs of Alzheimer’s, including amyloid protein in the brain.

They also took into account whether the participants had the APOE4 gene. This gene is the strongest known genetic risk factor for the most common form of Alzheimer’s disease. Having two copies of this gene (one from each parent) is thought to increase your risk of dementia by about 10 times.

The results showed that, for people with the APOE4 gene, having at least 14 years of education and keeping mentally active in mid-life was associated with lower levels of amyloid in the brain.

Dr Doug Brown, Director of Research and Development at Alzheimer’s Society, said, ‘Alzheimer’s disease is caused by a complex mix of genetics and lifestyle, and it could be that particular groups of people may benefit from making certain lifestyle changes to reduce their risk.

‘Although people with the APOE4 gene have a higher risk of dementia, there are things they, and indeed all of us, can do to cut that down. This might include staying fit and active, not smoking, and keeping the brain busy – this could be through reading or playing games and puzzles.’

People who regularly take anticholinergic drugs, such as some hayfever or sleeping medications, show differences in the structure and activity of their brains, according to a small study using a brain scan database. This research has not been able to say if the drugs themselves are causing the changes.

Research in worms has suggested that the cancer drug bexarotene could help to stop the formation of the hallmark amyloid plaques seen in Alzheimer’s disease. Although the drug previously failed to work in people, it is suggested that it may need to be given at an earlier stage in the disease.

A study comparing diagnosis rates of dementia between 1991 and 2011 has found that people are now at a lower risk of developing dementia. This change is mostly due to improvements in risk among men, potentially because of healthier lifestyles.
‘What’s my risk of getting dementia and what can I do about it?’

When asked this question by a middle-aged patient with a strong family history of dementia at his cognitive disorders clinic, Professor Craig Ritchie replied, ‘I don’t know and I don’t know. We don’t know for people like you in your 50s what your risk is and what works for you.’

When the patient responded, ‘Well, you’re going to have to do something about that,’ it prompted Professor Ritchie to set up the PREVENT study to answer these questions.

PREVENT is unusual for a dementia research project as it is studying people in their 40s and 50s, long before you would expect to see symptoms of dementia. However, this is crucial to understand what changes happen in the body at the very earliest stages of the condition.

Subtle changes
In recent years we have started to understand how long it can take for diseases like Alzheimer’s to develop. Previous research found subtle differences in memory tests up to 18 years before dementia is diagnosed. While the differences are far too small to be able to reliably identify who is at risk, we can see the effect when results from hundreds of people are studied together.

What this suggests is that if we want to prevent dementia then we need to act in mid-life, at the very earliest stages of the disease. The problem is that we do not know what these early stages actually look like, as by the time someone has a diagnosis it could be years later.

Finding these subtle, early changes is like looking for a needle in a haystack. Professor Ritchie is keen to make sure that they do not miss anything, so each person in the study is examined for their memory, genetics, lifestyle, diet, and physical and mental health. They also have brain scans and give samples of blood, saliva, urine and spinal fluid.

‘There have been other studies looking at this age group but they haven’t gone into this much detail,’ he says.

The study began at Imperial College London in 2013 with funding from Alzheimer’s Society. The study has since opened in Edinburgh and the Society is funding new recruitment sites in Oxford and Cambridge that will open this summer.

Reducing risk
What we know about risk factors for dementia has come from studies that have either followed a group of people for a long time or looked at health records for a population. One example is the Caerphilly study, which monitored a group of 2,500 men from...
the Welsh town since 1979 and found that those who had healthier lifestyles were less likely to develop dementia. From studies like this, we have evidence that eating a healthy diet, being physically active and not smoking are linked to having a lower risk of dementia. However, we cannot know this for sure without comparing one group who, for example, change diet to a similar group who keep the same lifestyle habits.

‘There are a lot of things that we propose may be helpful, but there’s nothing that we absolutely know. In this age group there’s lots of speculation that lifestyle factors are important in reducing your risk, but until we actually do specific trials I think it’s going to be very hard to prove that,’ says Professor Ritchie.

The problem with these kinds of trials is deciding what to measure to know whether you are seeing a real difference. The development of dementia is an obvious choice, but if you are studying middle-aged people then the trial might need to run for 20 or 30 years to see any benefit. In looking at the samples and scans of its participants, the PREVENT study is hoping to find biological differences or ‘biomarkers’ between those who are at high risk of dementia and those at low risk. These biomarkers can then be a way to monitor the risk of developing dementia in later life.

‘If you can affect these biomarkers then you have confidence that you’re actually changing the course of the illness,’ says Professor Ritchie. ‘There are parallels with heart disease where you’d intervene in mid-life and look for improvements in cholesterol, blood pressure and coronary artery blood flow, and you take that as an indicator that you’ve reduced your risk of having a heart attack.’

Secondary prevention
These biomarkers would be very useful in so-called ‘secondary prevention’ trials. This is where researchers try to stop or slow the progress of the disease in the brain before the outward symptoms of dementia appear.

The large gap between the development of the disease and the beginning of symptoms provides a large window of opportunity. Drugs that previously failed in trials with people with mild-to-moderate Alzheimer’s disease might have potential when given even earlier. These drugs are now being tested in people who have inherited genetic mutations that mean they are certain to develop young-onset dementia.

The ultimate aim for PREVENT would be to one day help inform prevention trials like this for healthy middle-aged people without that genetic certainty. To do this, we would need to understand what signs indicate that someone is at risk of Alzheimer’s and what to measure to check if a drug is helping.

The PREVENT participants have now been well studied before any signs of Alzheimer’s disease, making them very useful for taking part in such drug trials. The first of these participants has recently been approached to take part in a study as part of the European Prevention of Alzheimer’s Dementia consortium.

While this secondary prevention work will take many years to come to fruition, the PREVENT researchers are already working through the data they have collected and will publish their initial findings later this year. Preliminary results show differences in patterns of brain activity in a memory test for people at higher risk of Alzheimer’s. Once further tests, samples and participants are studied we may finally get a clearer picture of what Alzheimer’s disease looks like from the very beginning.

‘There have been other studies looking at this age group but they haven’t gone into this much detail.’

Professor Ritchie

‘It is kind of the equivalent of having an MOT carried out.’

Malcolm Weller, pictured right with his dad who has mixed dementia, describes his experience of taking part in the PREVENT study in the June/July issue of Living with dementia magazine. See alzheimers.org.uk/magazine

To sign up to the PREVENT project and to other studies, please visit www.joindementiaresearch.org.uk
I have always enjoyed learning about how the brain works, and what happens when it starts to work less well with age, or things go wrong due to illness or injury. My first experience of dementia was when one of my grandparents’ friends was diagnosed with Alzheimer’s. At the time, I didn’t really know much about dementia.

A few years later I began volunteering at a memory café. As people with dementia and their families shared their personal experiences with me, it became clear that there is still a lot of uncertainty surrounding the causes and prevention of dementia. This is what motivated me to join dementia research, to try and help make a difference to these people’s lives.

Prevention research aims to reduce the number of people who develop dementia. This is important, as there is currently nothing available to prevent or cure dementia. One approach to prevention research is to change aspects of an individual’s lifestyle that are thought to affect the risk of dementia, such as diet, leisure and physical activity, social participation and smoking.

Some of these lifestyle factors are thought to protect against cognitive decline by building cognitive reserve. Cognitive reserve refers to the idea that a combination of activities and experiences throughout life create a buffer against cognitive decline. This reserve may be in the form of a set of skills or strengthened communication pathways in the brain.

Increasing involvement in activities that protect against cognitive decline, and reducing risk factors, should enhance cognitive reserve and reduce the risk of cognitive decline and dementia. For example, being more mentally and physically active should increase cognitive reserve, while stopping smoking should reduce risk.

My research focuses on social isolation as a risk factor for cognitive decline. We hope that this research will establish whether social engagement enhances cognitive reserve and helps to maintain healthy cognition. Social isolation could potentially be reduced by developing interventions which, if effective, may help to prevent or delay cognitive decline.

My research will use data from the Cognitive Function and Ageing Study Wales (CFAS-Wales), involving 3,700 people over the age of 65 living in Wales. Participants in CFAS-Wales were interviewed when they joined the study and then again two years later. This large-scale database will allow me to examine whether social isolation is related to cognitive impairment, and whether people who are isolated have a higher risk of developing cognitive decline or dementia over the next two years.

Working within the field of cognitive health and dementia is really exciting as there is a lot of new research being completed, which suggests new directions and sometimes more questions that need answering. I am extremely grateful to Alzheimer’s Society for supporting my work. I am hopeful that my research will contribute to extending the available evidence about prevention and inform efforts to reduce the number of people living with dementia.

‘We hope that this research will establish whether social engagement enhances cognitive reserve and helps to maintain healthy cognition.’

Isobel Evans
Many people with dementia can find themselves withdrawing from activities and pastimes they once enjoyed. Problems with memory loss and cognitive abilities can also make it more difficult for people to carry out everyday tasks.

Cognitive rehabilitation, a form of therapy developed from those offered to people who have sustained a brain injury, is thought to help manage some of the difficulties faced by people with dementia.

‘With funding from Alzheimer’s Society, we were able to complete the first randomised controlled trial of cognitive rehabilitation – an approach whereby people with Alzheimer’s disease work with healthcare professionals to set personally relevant and meaningful goals and develop strategies to reach them,’ says Professor Linda Clare at the University of Exeter.

‘Our trial showed that cognitive rehabilitation therapy could improve the quality of life of both people with early-stage Alzheimer’s disease and close family members.’

All of the study participants set personal goals that ranged from resuming enjoyable activities such as reading, knitting or going on day trips to more practical things such as remembering details of jobs to be done around the house, learning to use a mobile phone or maintaining concentration when cooking.

A therapist worked with the study participants who were allocated to receive cognitive rehabilitation individually to plan how to address each goal, taking into account what the person was able to do and what was needed to achieve the goal. The plan included ways of using their abilities better, for example how best to remember important details, and ways of getting around a difficulty by doing things differently, for example having a set of written instructions to follow.

Professor Clare explains, ‘The idea is to take a problem-solving approach and build on the skills that people still have.’

The results showed that people who received cognitive rehabilitation therapy improved their ability to carry out activities related to their goals and were more satisfied with how they were managing. Brain scans showed an increase in activity in certain areas of the brain for these participants when carrying out a memory task.

‘This is difficult to interpret exactly, but we think it shows that the brains of people in this group were able to deal with the demands of the task more efficiently,’ says Professor Clare.

Professor Clare and her team are now running the GREAT trial, which is funded by £2.4 million from the National Institute for Health Research and recently featured on BBC’s Horizon, to provide robust evidence of the effects of cognitive rehabilitation and how it can be integrated in clinical practice. It is hoped that the results of the study, expected in 2017, will guide practice within the NHS and help develop the services provided by memory clinics.

Professor Clare says, ‘This approach is about finding ways of making things possible. Obviously you have to be realistic. You can’t take away someone’s memory problems, but you can try to address everyday challenges – to help people to remain engaged, and retain their confidence and self-respect.’
Alzheimer’s Society has pledged £50 million towards the work of the UK Dementia Research Institute, in the single biggest financial commitment to dementia research in the history of the charity.

The institute will bring together scientists and experts from across the globe to transform the landscape of dementia research and firmly secure the UK’s reputation as a world leader in research and development against the condition.

Set to be fully up and running by 2020, the institute will have a central UK hub with a network of regional centres and is expected to engage hundreds of scientists. This research will help to drive new approaches to diagnosis, treatment, care and ultimately prevention of the disease.

The creation of an institute was first announced by the Prime Minister last year with £150 million funding from government. This has since grown with an additional £50 million each from Alzheimer’s Society and Alzheimer’s Research UK.

As well as increasing the amount of fundamental biomedical research taking place in the institute, the funding from Alzheimer’s Society will broaden the vision and strategy of the UK Dementia Research Institute to include research in care, supportive technology and public health.

The direct experience of people with dementia and their carers will help to inform the work of the institute, which Alzheimer’s Society is uniquely placed to ensure. By enabling them to define what high-quality, evidence-based care and support means to them, we can reduce disability and distress, limit harmful practices and improve the inclusion of people with dementia in society.

Jeremy Hughes, Chief Executive Officer of Alzheimer’s Society, said, ‘The UK Dementia Research Institute heralds an exciting era for global dementia research, as it launches an unprecedented collaboration of world-leading dementia expertise and provides the largest single investment in dementia research to date.’

‘Alzheimer’s Society is working to create a better world for people living with dementia and their families, and this significant investment emphasises how important research is in achieving our ambitions. Today we offer people affected by dementia, and all of us, hope for a better future in much the same way that cancer research has transformed how we diagnose, treat and care for those living with cancer.’

Alzheimer’s Society has partnered with the Medical Research Council and Alzheimer’s Research UK to create the country’s first dedicated Dementia Research Institute.
Increased focus on care research

Alzheimer’s Society announces new calls for grants of up to £2 million to study important aspects of dementia care.

Alzheimer’s Society is dedicated to funding research into many aspects of dementia. This involves not only looking for the underlying biomedical causes of the condition and investigating potential treatments and cures, but also finding ways to better care for people living with the condition today.

With this in mind, we are increasing our focus on care research with new grants of up to £2 million that will help researchers to investigate important aspects of dementia care. In order to ensure that we are addressing real needs and tackling common issues within dementia care, we held a consultation among our staff, Research Network volunteers and service users to find out what mattered most to them.

The consultation provided four priority areas for our researchers to focus on – support after a diagnosis, how to remain independent at home for longer, care for advanced dementia and how to improve quality of life. Other considerations that the researchers can take into account include how to accommodate people who have other conditions alongside dementia, how to involve harder-to-reach communities and how the results of the research will be put into practice.

The funding will be available for a maximum of five years and the grants must have a strong focus on making a difference to the lives of people living with dementia. The successful projects will be announced in Spring 2017.

Focusing more on care research is a vital part of the work of Alzheimer’s Society, as we aim to improve the lives of people who are affected by dementia now or who may be in the future. Best practice in dementia care can only happen with high-quality, evidence-based research behind it, and grants such as these will ensure that we build on existing work in four key areas. The results will have the potential to address some of the major issues facing dementia care.

Sign up now at memorywalk.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 over £35 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.

Keep up to date

Care and cure is the research magazine of Alzheimer’s Society. To receive a copy of this magazine quarterly, please sign up to become a Friend of Research at alzheimers.org.uk/friendsofresearch.

For general enquiries, email info@alzheimers.org.uk

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