

The BRAIN

THE BRAIN SERIES
IS BROUGHT TO YOU
BY THE **QUEENSLAND
BRAIN INSTITUTE**

Issue Three

DEMENTIA

Why we need to talk
about dementia

Can dementia be cured?

What is dementia?

Can dementia be
avoided?



QBI
Queensland Brain Institute



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A MESSAGE FROM
Professor Pankaj Sah

DIRECTOR OF THE QUEENSLAND
BRAIN INSTITUTE AT THE UNIVERSITY
OF QUEENSLAND



Dementia is one of society's most pressing health problems. It affects almost one in 10 people over the age of 65 and is the second leading cause of death in Australia. With life expectancy projected to increase in coming decades, more than one million Australians will be living with dementia by 2050 if no effective treatment is found.

But dementia is more than just numbers. Its tendrils reach far and wide: nearly all of us know somebody affected by the condition, whether it be a family member, friend or colleague. People with dementia experience devastating changes to their lives, gradually losing their independence, intelligence, personality, and ultimately, their identity. Families experience the terrible burden

of watching their loved ones suffer and disappear before their eyes.

Managing the impact of dementia is focused on three vital issues: care, treatment and prevention. With economic and personal costs of care rising, the need to delay the onset and progression of dementia, and to find cheap, effective and easily available treatments also grows. This is particularly important in a country such as Australia, with its vast population spread, which often results in great distances between specialist medical centres.

The only way forward is through research. In 2013, the Australian Government committed to boosting dementia funding to more than \$60 million per year and established the NHMRC National Institute of Dementia Research to

coordinate priority research. That same year, the Queensland Brain Institute at UQ, with help from the Queensland Government, established the Clem Jones Centre for Ageing Dementia Research (CJCADR), Australia's first dedicated dementia research centre, now home to more than 90 exceptional researchers. These scientists are united by the deep desire to understand the fundamentals of dementia: how and why dementia starts, how to stop its progression, and how to develop effective treatments.

These aren't easy questions to answer, but with bold ideas, bright people and hard work, we are determined to defeat this disease.

The Brain: Dementia reveals compelling progress towards understanding and treating this devastating condition.



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Queensland Brain Institute



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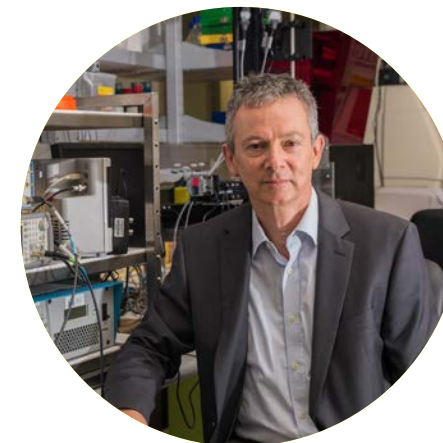
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CHAPTER 1. We need to talk about dementia



ISTOCK

Dementia is a complex health problem, both because of the sheer number of underlying conditions that can cause it (more than 50) and because of its direct and indirect impact on people and the health system.

We currently have no cure for any form of dementia. With an ageing population, people are living longer and

the social and economic costs continue to rise. More than 400,000 Australians are currently living with dementia; 244 people are newly diagnosed every day (and increasing); and the number of cases is expected to nearly triple by 2056.

Those numbers belie a more important cost: the personal toll that dementia takes on individuals and

families. This heartbreaking condition robs people of their partners. It robs children of their parents. It robs grandchildren of their grandparents.

People with dementia are more likely to be hospitalised, and once there, are twice as likely to develop complications, such as infections. Hundreds of thousands of carers are needed to assist dementia patients with basic daily activities, and almost half of these are partners, relatives or friends. Concerningly, 65% of informal carers are over the age of 65, and 46% have a disability themselves.

For the two in five people with dementia who live in regional or remote areas, the situation is even more difficult. With medical centres far away, these Australians share more of the burden of care, have greater distances to travel for medical assistance, and have limited options for treatment.



DEFINITION

Dementia is not a single disease, but an umbrella term describing a collection of symptoms stemming from a range of conditions that cause the brain to progressively deteriorate. What distinguishes dementia from normal cognitive decline in ageing is that distinct brain areas are affected and this severely impacts the ability to carry out normal daily activities.



ISTOCK

THE GROWING ECONOMIC BURDEN

The cost of dementia to the health system and the economy is significant. In 2017, direct costs (mainly medical and aged care) and indirect costs (lost income and productivity) of dementia are estimated to be over \$14b. Without effective treatments for dementia, those costs are predicted to skyrocket to almost \$37 billion by 2056.

The Queensland Government and the

Australian Government have recognised the urgency of the issue and have directed resources towards ageing and dementia research. This includes the creation of the NHMRC National Institute for Dementia Research, part of a \$200 million commitment to the World Dementia Council's priority of achieving a five-year delay in dementia onset by 2025. It's hoped this commitment spans beyond its expiration in 2018.

Dementia by the numbers

Each day 244 people are diagnosed with dementia

AUSTRALIANS WITH DEMENTIA:

1.1 million
2056*

760,000
2036*

413,000
2017

* if no cure is found

26,000

Australians have younger-onset dementia (2017)

2/5

people with dementia live in regional or remote areas

44% MALE

56% FEMALE

Indigenous Australians are

3-5x

more likely to develop dementia than non-Indigenous people

1/5

people with dementia have culturally and linguistically diverse backgrounds

CARERS:

291,000+

33% in aged-care settings
67% in the community

74% female



65%
older than 65

46%
also have a disability

DEMENTIA AFFECTS:

1/10

Australians over 65



3/10

Australians over 85



COST OF DEMENTIA TO THE ECONOMY

2056
(estimated)

2017

Direct: **\$9.1 billion**
Indirect: **\$5.6 billion**

Direct: **\$24.1 billion**
Indirect: **\$12.8 billion**

Dementia is expected to cost: **\$1 trillion** over the next 40 years

Direct: mainly medical and aged care
Indirect: lost income and productivity

PROFILE

ITA BUTTROSE

DEMENTIA AUSTRALIA AMBASSADOR ITA BUTTROSE HAS EXPERIENCED FIRST-HAND THE JOURNEY OF CARING FOR A LOVED ONE WITH DEMENTIA.

Media legend Ita Buttrose AO, OBE, might never have pursued a career in journalism if it hadn't been for her father, Charles Oswald Buttrose. Charles was a giant of journalism, a former war correspondent and at the time of his retirement, assistant general manager of the ABC.

When Charles was diagnosed with vascular dementia in his early 80s, it came as a shock to the family. "I now know there were signs that we just put down to him getting older," says Ita. "We didn't really think it was anything out of the ordinary."

Although her son was still living at home at the time, Ita didn't hesitate to become her father's primary carer. "Your parent is your parent," she says. "I never really thought I shouldn't be looking after him."

"He wanted to stay in his own home. That was something he was very passionate about and my brothers and I did manage to do that for him."

"I was the principal carer and we had other carers who came in to help out on the times when I wasn't there," she says. "What I did –

"...everybody's dementia is different, and it doesn't mean that they can't engage and enjoy social interaction with friends."

although I didn't realise this at the time – was to create a dementia-friendly community in the neighbourhood where

Dad lived." This is now one of Dementia Australia's principal goals.

Ita spoke to the chemist down the street where her father was a customer, and the manager at his local bank, who would calm him down if he became agitated. "I put steps in motion so that people kept an eye on Dad, enabling him to still have his independence."

Social isolation is a big issue both for people living with dementia and their carers, Ita says. "People don't quite know how to react to someone with dementia and when they hear a friend has dementia, they often stop calling," she says. "I think it's important for people to realise that even though a person has dementia, everybody's dementia is different, and it doesn't mean that they



can't engage and enjoy social interaction with friends."

Ita remembers visits with her children and family dog. "Dad enjoyed having us over and he was always more relaxed when I was there with the kids. He would join in our conversations to the best of his ability, he would go swimming and he loved it when my dog would jump in the pool and swim with him."

There were some challenging, but also humorous moments.

"The laughter is part of the dementia experience," she says. "You have to laugh, because if you don't laugh, you'd be in tears all the time."

The advice Ita has for carers is to be kind to yourself. "Carers often feel very guilty about taking time out for themselves but it's essential that they do, because caring is a 24/7 job and it's important to take some breathing space now and again. It's what you need to do in order to be an effective carer."



MORE INFORMATION

National Dementia Helpline: 1800 100 500

CHAPTER 2. What is dementia



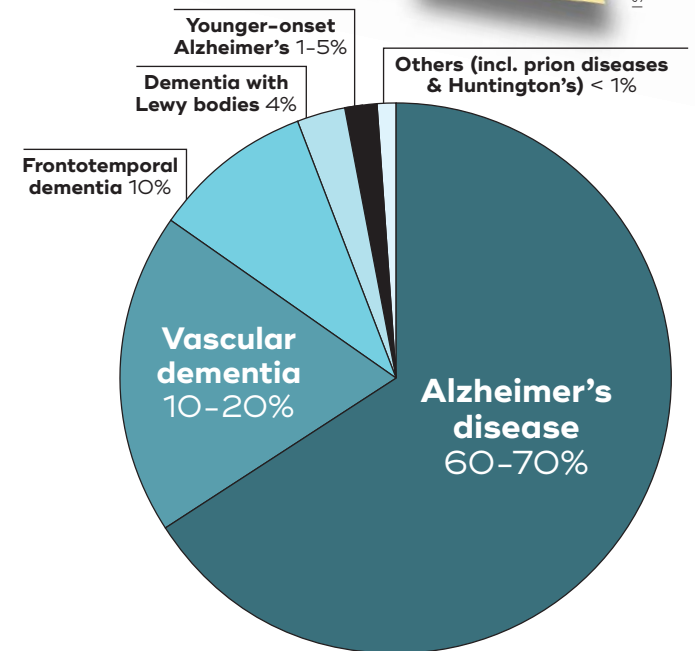
Dementia is not a single disease, but an umbrella term describing a collection of symptoms from a range of conditions that cause parts of the brain to deteriorate progressively. Dementia affects functions such as memory, perception, behaviour, language, and personality.

There are more than 50 conditions known to cause the symptoms of dementia. Alzheimer's disease is the most common, accounting for about 60-70% of cases. Other common types are vascular dementia, frontotemporal dementia, and dementia with Lewy bodies. Huntington's disease, and prion diseases like mad cow, as well as

stroke, head injuries and disorders of excessive alcohol consumption can also cause dementia.

The story is further complicated by the fact that about a third of people with dementia have more than one underlying cause. As age increases, having combined forms or 'mixed dementia' becomes more common.

Common types of dementia





ISTOCK

TYPES OF DEMENTIA

THESE ARE THE MOST COMMON FORMS OF DEMENTIA

ALZHEIMER'S DISEASE

Alzheimer's disease is the most common form of dementia. Named after the German psychiatrist Alois Alzheimer, the disease is characterised by cognitive decline and memory loss. Two hallmarks of Alzheimer's are seen in the brain: amyloid- β **plaques** and tau **tangles**, which are caused by the build-up of **toxic deposits** (see page 9).

Alzheimer's is divided into late-onset (age 65+) and younger-onset (under

65). Most cases of late-onset Alzheimer's have no known cause, and are referred to as sporadic.

Apolipoprotein E (ApoE) is a key gene associated with Alzheimer's. One of its three common forms, ApoE 4, increases the risk of developing Alzheimer's. Studies have identified about a dozen other genes that may also increase the risk (see page 19).

Alzheimer's affects women slightly more than men, but the reasons are unknown.

YOUNGER-ONSET ALZHEIMER'S

Up to 5% of Alzheimer's cases are classified as younger-onset, which typically affects people in their 40s and 50s, and even as young as 30. This form has a strong genetic basis, with most cases known to be inherited, and caused by single mutations in three genes: *APP*, *PSEN1* or *PSEN2* (see page 19). Each of these mutations causes excessive accumulation of toxic deposits in the brain. This leads to the death of brain cells (neurons) and causes

brain tissue to deteriorate. People with these mutated genes are said to have 'familial Alzheimer's disease' (FAD), and multiple family members are usually affected.

VASCULAR DEMENTIA

Vascular dementia is thought to cause about 10-20% of all dementia cases, making it the second most common type. In this condition, changes in the brain's blood vessels restrict the amount of blood and oxygen reaching particular areas of the brain, resulting in the death of brain cells. A major cause of vascular dementia is stroke, when blockages or haemorrhages cut off blood flow to parts of the brain. The underlying causes are atherosclerosis – the build-up of cholesterol and fat deposits in blood vessels – and arteriosclerosis, the hardening and loss of elasticity in artery walls. Unlike other forms of dementia, vascular dementia is not characterised by aggregations of abnormal proteins.

FRONTOTEMPORAL DEMENTIA

Frontotemporal dementia accounts for about 10% of dementia cases. It is a collection of rare and diverse dementias that mainly affect the frontal and temporal lobes of the brain. These areas are associated with high-order functions such as problem-solving, emotion, motivation, attention and language. The first signs, therefore, are often changes in personality and social behaviour, rather than the memory impairment seen in Alzheimer's. Frontotemporal dementia often emerges in the earlier stages of life, affecting people aged in their 40s and 50s.

As with Alzheimer's and many other dementias, the brains of people with this form have unusual deposits of proteins. About one-third of people with frontotemporal dementia have a family history of dementia and half of those seem to have an identifiable genetic basis.

DEMENTIA WITH LEWY BODIES

Cases of dementia with Lewy bodies make up around 4% of dementias. This form gained notoriety in 2014 following the death of comedian and actor Robin Williams, when a post-mortem examination of his brain revealed signs of the disease. Lewy bodies are abnormal deposits within neurons, made up of a protein known as α -synuclein. When these deposits occur in the brain they cause the cognitive loss typical of dementia. But they can also impair neurons that produce dopamine, a chemical that affects your emotions, response to pleasure and pain, and muscle control. The symptoms can therefore be similar to those of Parkinson's disease. In addition to having trouble with muscle control, people who have dementia with Lewy bodies can have problems with attention and executive function

(e.g. memory, planning, decision-making). These symptoms can also be seen in some people with frontotemporal dementia.

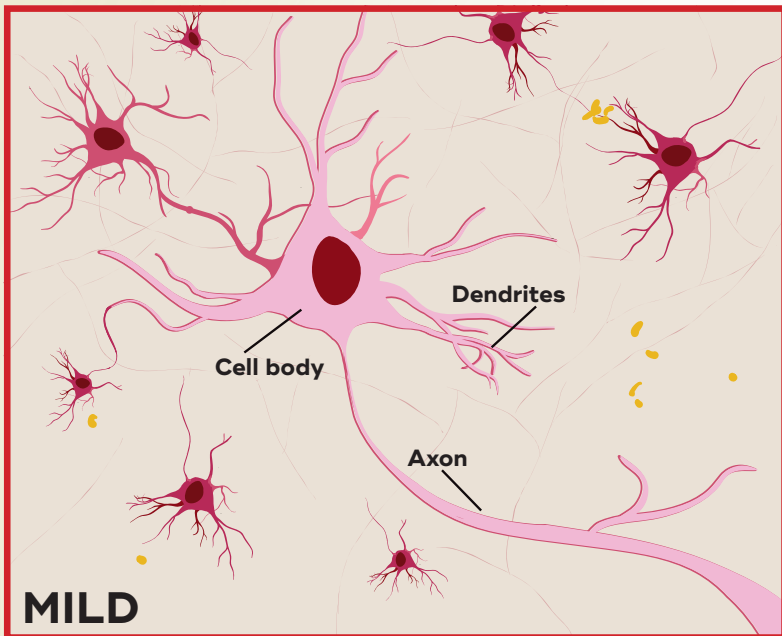


PARKINSON'S DISEASE AND DEMENTIA

Parkinson's disease is best known as a movement disorder, with patients suffering from tremor, muscle rigidity, slow movements, and problems with their gait (walking). As the disease progresses, cognitive symptoms such as memory loss and attention difficulties become apparent. As with other dementias, Parkinson's is characterised by the accumulation of toxic deposits in the brain. In this case, it is α -synuclein – the same protein that clumps to form Lewy bodies. Ultimately, there is a loss of dopamine-producing neurons, which are essential for control of normal movement.



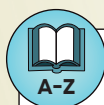
THE BIOLOGY OF ALZHEIMER'S



MILD: Amyloid- β (yellow) starts to accumulate near neurons. Tau starts to accumulate inside neurons.

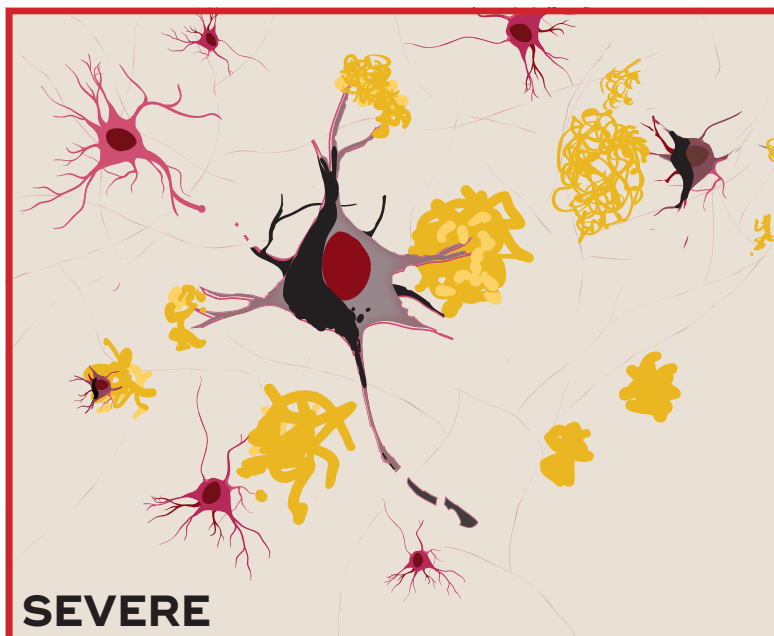
MODERATE: Amyloid- β plaques increase. Tau (black) begins to deposit inside the neuron, causing damage.

SEVERE: Death of neurons occurs, severing connections with other neurons.

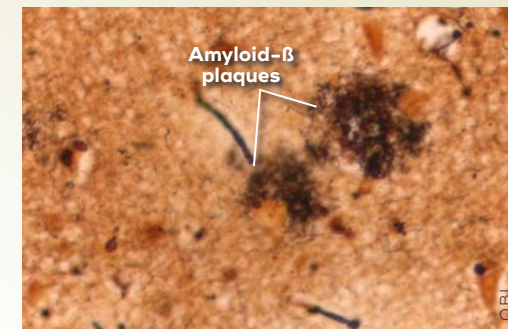


DEFINITION

Peptides and proteins Peptides and proteins are made of amino acids, the basic building blocks of the body. Amino acids form chains known as peptides, which bond to form polypeptides and fold into proteins. Peptides are smaller, with fewer than 50 amino acid chains, and proteins have more than 50.



RICHARD CAMPBELL



A PROBLEM CALLED AMYLOID- β

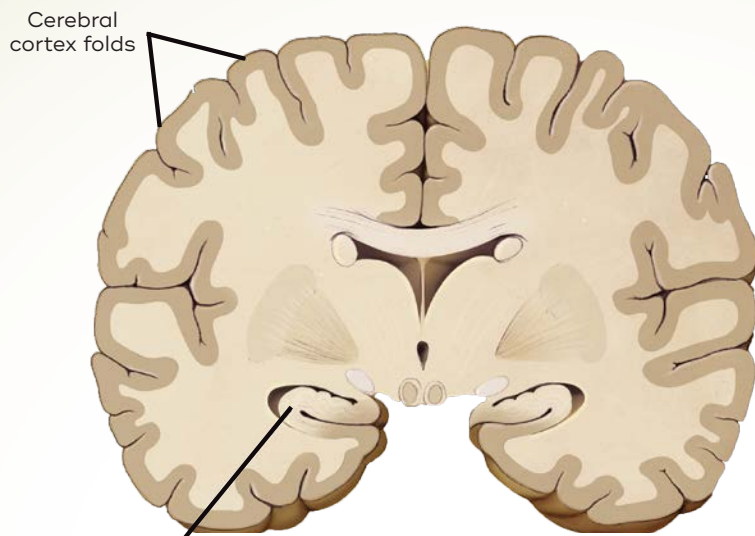
The main component of the hallmark plaques seen as lesions in the brains of Alzheimer's patients (above) is formed by a peptide called amyloid- β (beta). Certain neurons, particularly in the cortex and hippocampus, create amyloid- β .

Its function isn't well understood, but it has a role in neurogenesis (the creation of neurons), memory, and the normal operation of message transfer between neurons. When too much is made, or too little cleared, clumps of amyloid- β build up around and between neurons. As these plaques grow in size, they envelop and destroy the dendrites (branches) of neurons, interfering with their ability to communicate.

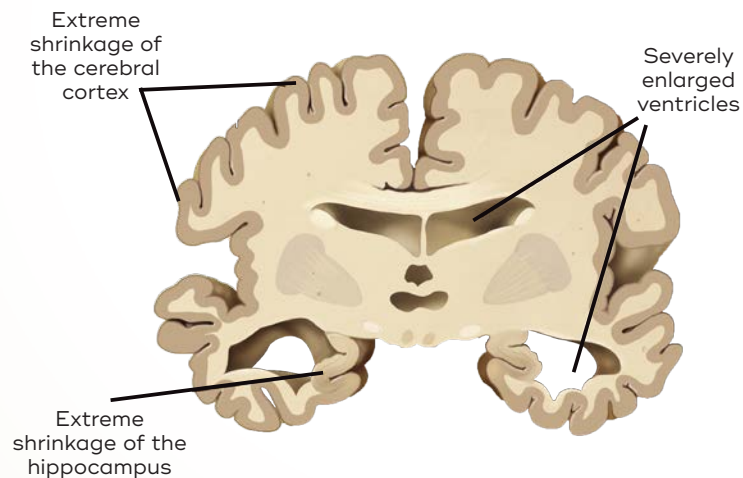
THE BIOLOGY OF ALZHEIMER'S

LOSS OF BRAIN TISSUE

Dementia is caused by neurodegeneration – the damage and death of the brain's neurons. Depending on the types of neurons and brain regions affected, the form of dementia differs. For instance, frontotemporal dementia mainly affects the frontal and temporal lobes, whereas Lewy body dementia affects part of the frontal lobe and the motor cortex. In the brains of patients with advanced Alzheimer's, there is widespread degeneration, and damage to the hippocampus – a part of the brain essential to memory formation, and which produces new neurons. The loss of brain tissue results in a shrunken brain, enlarged ventricles and more space between the folds.



NORMAL

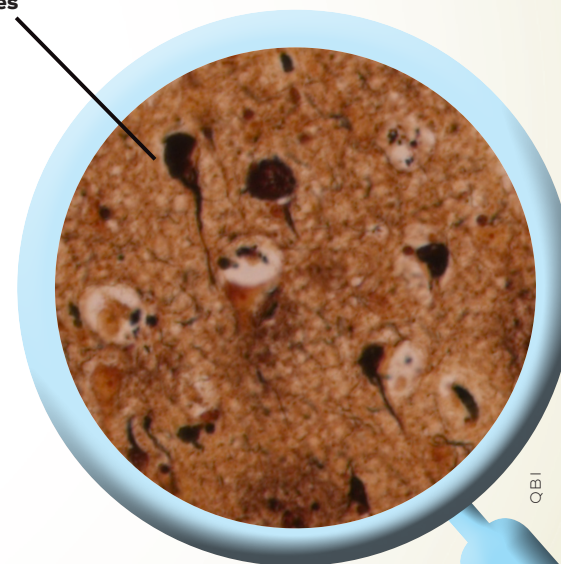


SEVERE ALZHEIMER'S

THE ROLE OF TAU

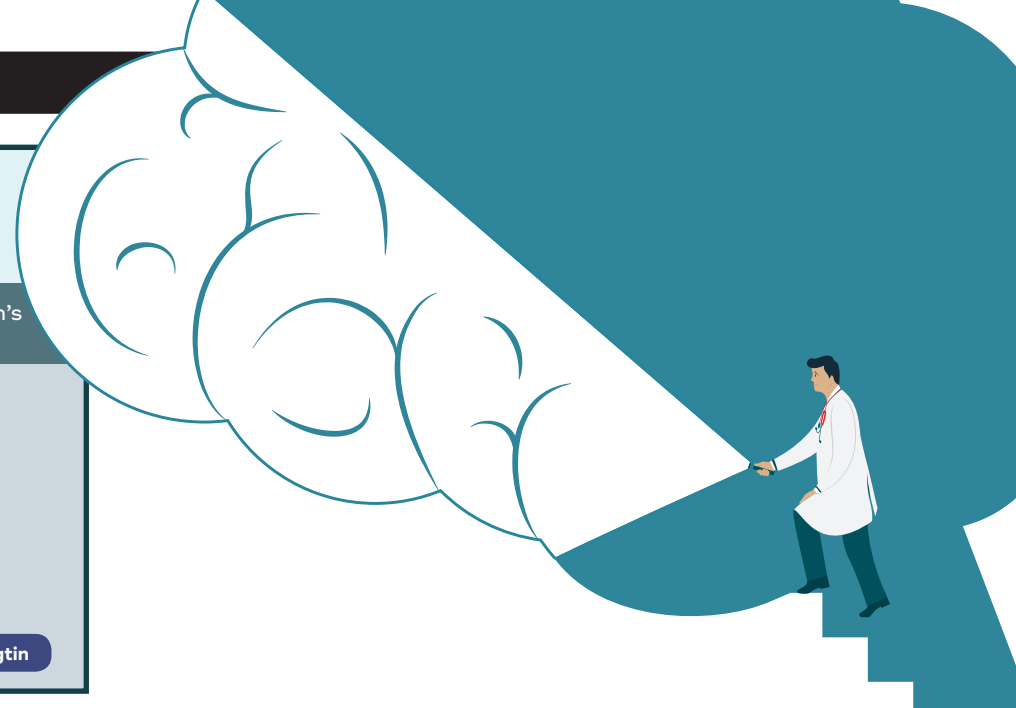
Tau is a protein that normally has an important role in maintaining the structure of a neuron's axon (the long cable that transmits signals). In dementias such as Alzheimer's and frontotemporal dementia, more tau is made, eventually accumulating in the cell body and dendrites. Here, it forms large deposits known as 'neurofibrillary tangles' – clumps that build up and gradually interfere with the neuron's function and eventually kill it.

Tau tangles



Key proteins and peptides in dementia diseases

Chronic traumatic encephalopathy (CTE)	Frontotemporal dementia (some forms)	Alzheimer's disease	Dementia with Lewy bodies	Parkinson's disease	Huntington's disease
tau	tau	tau			
		amyloid-β	amyloid-β		
			α-synuclein	α-synuclein	
TDP-43	TDP-43				
	FUS				
					huntingtin



WHAT CAUSES DEMENTIA?

TOXIC AGGREGATES

In most dementias, build-up of toxic proteins is a key part of brain degeneration.

This causes a loss of the contact points between neurons (known as synapses) as well as a loss of the neurons themselves. What sparks this neurodegeneration remains unknown, but for dementias other than vascular dementia, a build-up of toxic proteins and the loss of their normal function are defining characteristics.

Proteins can naturally aggregate as the body's

systems for clearing them start to decline, which occurs increasingly as we age. In neurodegenerative disease, these toxic clumps, known as aggregates, can damage or kill neurons.

In Alzheimer's disease, two key players called **amyloid-β** (a peptide that forms plaques around neurons) and **tau** (a protein that forms 'tangles' inside neurons) are at play. In dementia with Lewy bodies (which also forms amyloid-β deposits) and Parkinson's disease, the major

aggregates are formed by the protein α-synuclein. In frontotemporal dementias, deposits of TDP-43, tau or FUS protein are found. Each type of protein aggregate eventually leads to the death of affected neurons

LOOKING FOR ANSWERS

Researchers want to know why these protein aggregates form in the first place, how they distribute in the brain, how their signalling works, and how they and their precursors

cause neurodegeneration.

A range of theories have been put forward to explain what kickstarts damaging protein aggregation. In the case of Alzheimer's, this includes problems with the way oxygen is metabolised in brain cells and the movement of internal cell contents. The brain's response to inflammation (see page 12), and its systems for clearing waste could also play a role.

One main theory is that once amyloid-β begins to accumulate, it then promotes the build-up of tau. But the

relationship is not simple, because tau also has a role in influencing the toxic effects of amyloid-β.

Although some genetic risk factors for dementias have been identified, particularly for Alzheimer's disease (see page 19), we still don't know how these act to influence protein aggregation and cause degeneration. This is a key area of research focus, and knowing the answers to these questions is crucial to the prevention and treatment of dementia.

THE INFLAMMATION FACTOR



ISTOCK



ISTOCK

Inflammation has long been thought to be a side effect of dementias such as Alzheimer's, as the body ramps up its immune system in response to the disease. But recent research has confirmed that inflammation actually contributes to the disease process. One clue was a report that people treated with anti-inflammatory drugs for arthritis had a lower incidence of Alzheimer's. This has now been backed up by large genetic studies.

Normally, the brain's inflammatory cells help to prevent damaging build-up of amyloid- β by clearing it away, and it's thought that mutations in inflammatory genes hamper this process. Inflammation is a sign of the immune system kicking into gear, and in the initial stages of disease, this is beneficial. However, in the case of Alzheimer's,

when the disease becomes more advanced, chronic inflammation can set in and add to the toxic insult the brain receives. The brain's immune response to inflammation is therefore believed to play two critical roles in developing Alzheimer's disease.

RESEARCH FOCUS

Researchers such as Professor David Fairlie at UQ's Institute for Molecular Bioscience are investigating how to stop inflammation and the diseases it can cause, including dementia. Dr Rodrigo Medeiros at QBI's Clem Jones Centre for Ageing Dementia Research (see page 32) is also trying to find biomarkers that signpost the initial inflammatory response. From this he hopes to identify promising compounds that could help stop chronic inflammation.



PROFILE

DORIS YOUNANE

AUSTRALIAN ACTRESS DORIS YOUNANE'S MOST CHALLENGING ROLE WAS CARING FOR HER MOTHER, WHO HAD DEMENTIA.

Actress Doris Younane is better known for her roles in McLeod's Daughters and Seachange, but possibly her most challenging role to date was as her mother's carer throughout her journey with dementia.

Doris's mother was diagnosed with dementia 12 years ago and sadly passed away late last year.

"The initial sign of Mum's dementia came when she suddenly pulled up in the middle of a roundabout whilst driving and didn't know where she was going. We went to the specialist and the first thing he did was say, 'Give me your driver's licence,' and then proceeded to cut it up in front of her," says Doris.

The diagnosis was a devastating for Doris's entire family—she and her six siblings had no knowledge of dementia.

"It was a foreign thing to the entire family. Mum locked herself in her bedroom when she found out and, coming from an Arabic background we found it difficult, as it wasn't part of her nature to talk openly about these things."

Doris's biggest regret is not explaining to her Mum what was happening to her.

"It was such a scary period of her life and initially she cried a lot, but in the final six years she became this amazing affectionate person – a beautiful, gentle, old soul who we loved to be around."

"We were in the dark but contacted Dementia Australia who were incredible and helped us navigate the unknown territory of dementia. The experience is different for everyone and we found we were

constantly experimenting with ways to keep Mum connected with the world."

Doris believes she was fortunate, as with the support of her six siblings, she was able to care for her mother at home.

"The cost of keeping Mum at home was phenomenal but my dream is to now find an affordable way for all those with Alzheimer's to continue a life at home."

"With an ageing population, we need to find

"With an ageing population, we need to find a cure for Alzheimer's while also making the community at large more attuned with it."



a cure for Alzheimer's while also making the community at large more attuned with it."

"Education is paramount in removing the stigma that still surrounds dementia despite the high number of people it affects."



MORE INFORMATION

National Dementia Helpline: 1800 100 500



WIKIMEDIA

A brief history of dementia research

The concept of dementia has been around since early civilisations.

Ancient philosophers viewed mental decay as a normal part of ageing. The prevalence and study of dementia increased as the lifespan of humans extended. In the late 1800s, with advancements in medicine and the ability to look inside the brain, the medical community realised that diseases could cause this deterioration. The most

common dementia was named, in 1910, after Alois Alzheimer, a German psychiatrist.

In 1906, Alzheimer, who looked at post-mortem brains of affected younger people, published the first case - a 50-year-old woman with dementia symptoms. After her death, Alzheimer saw the microscopic plaques and tangles now known as hallmarks of the disease. At the same time another German psychiatrist, Oskar

Fischer, studied the brains of older people, and he, too, saw plaques and tangles. Both contributions furthered the understanding of the condition, but the naming of Alzheimer's disease by prominent psychiatrist Emil Kraepelin and the occurrence of World War II relegated Fischer's name into obscurity.

As medical technology improved, so has the understanding of dementia and its causes.

HISTOLOGY

New staining methods let scientists see microscopic plaques and tangles

1906
1907
1910

Alzheimer described first patient

Fischer published description of plaques

Alzheimer's disease named

BIOCHEMISTRY

1960s

1970s

1980s

Electron microscope can zoom in on plaques and tangles.

Alzheimer's recognised as the most common form of dementia and different from the mild cognitive decline associated with ageing. CT scan shows shrinkage of diseased brains.

Molecular and biochemical advances see tau and amyloid- β identified as components of tangles and plaques.

GENETICS

1990s

Genetic mutations in Alzheimer's disease identified. Risk factors identified. Stages of dementia categorised. Brain imaging improves.

Biological understanding of processes that cause dementia better understood - genetics, molecular biology, brain imaging.

BRAIN IMAGING

2000s

2020

Effective treatment?

CHAPTER 3. Understanding dementia

SIMPLY OLD AGE OR DEMENTIA?



As we age, our cognitive abilities decline gradually, but dementias are a fork off that path. Determining whether mild symptoms are due to normal ageing, mild cognitive impairment (MCI) or a progressive disease is difficult; a person may have the underlying biology of dementia (see page 9), but not exhibit obvious symptoms. Cognitive tests and scans can

be normal in early stages. It's thought that the disease process may occur for up to 20 years before signs appear.

NORMAL COGNITIVE DECLINE IN AGEING

As we age, our cognition – mental processes – naturally declines. The most notable change may be cognitive slowing, with one study showing that a 20-year-old is 75% faster than a 75-year-

old at substituting symbols for numbers. With regards to language, vocabulary and verbal skills remain largely unchanged, but the ability to find a particular word can decline. Memories formed many years ago remain quite stable, but forming new memories can be difficult, and working memory (e.g. recalling a phone number to dial it) is particularly affected. The ability to focus on a single

task is largely unchanged but there is increased difficulty with multitasking or switching attention.

These changes reveal a pattern: although our general knowledge and 'crystallised intelligence' (the ability to use skills and knowledge) are mostly unaffected, our fluid intelligence (the ability to think on the fly and solve new problems) suffers.

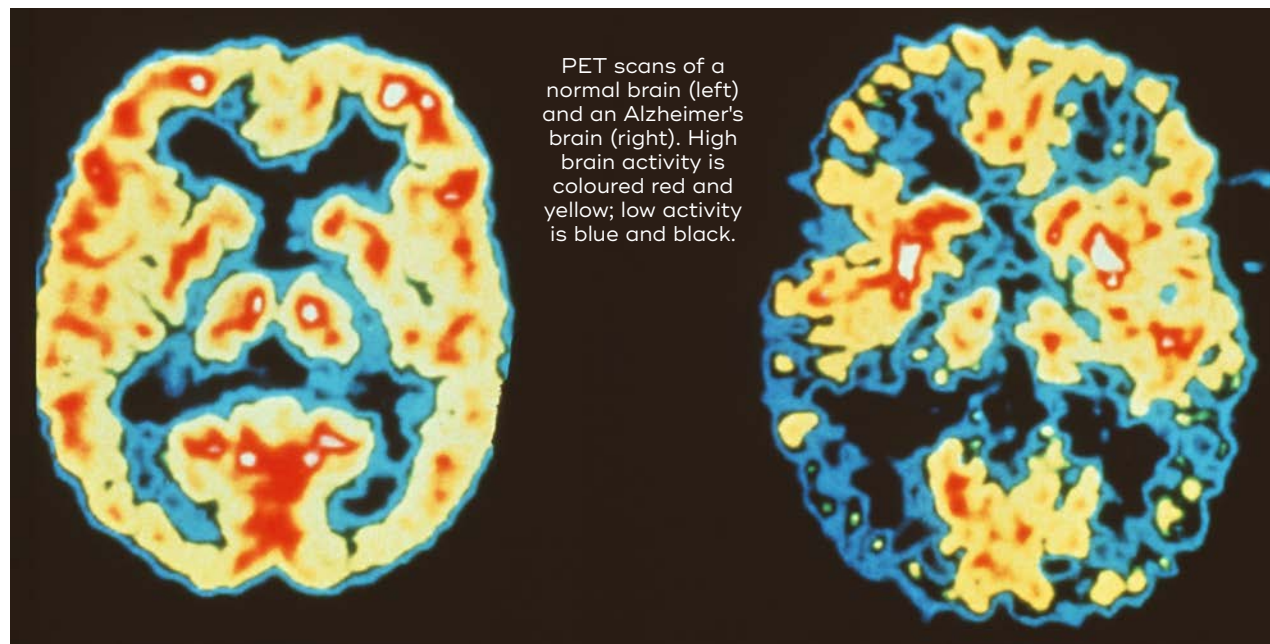
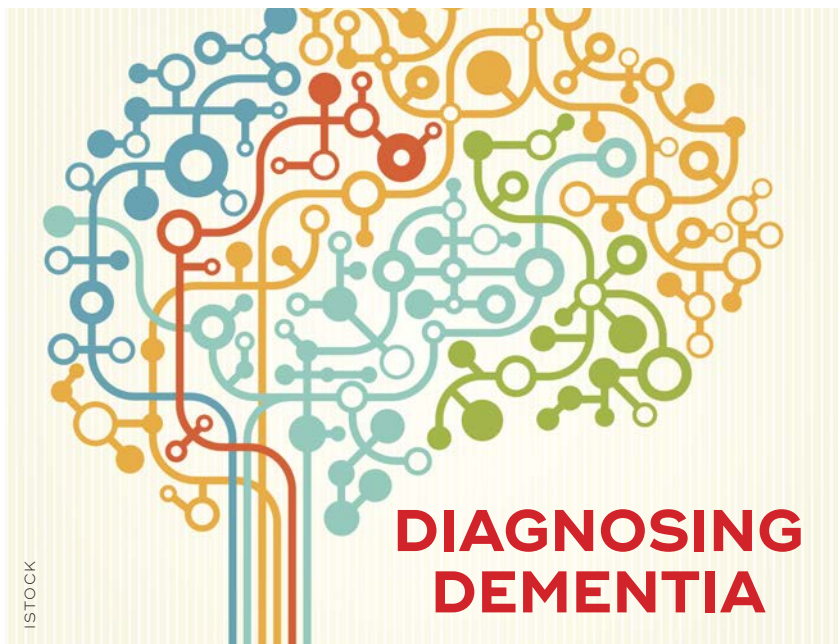
MILD COGNITIVE IMPAIRMENT

MCI exists in a transitional or grey zone between normal cognitive decline and dementia. The symptoms are similar to those of dementia – forgetfulness, impulsivity, irritability and some difficulty maintaining a train of thought – except that they are not serious enough to interfere with a person's independent function or overall cognitive state, as a person is still able to do complex tasks. MCI is a risk factor for developing dementia and a proportion

of people with MCI go on to develop dementia.

DEMENTIA: WHEN COGNITIVE DECLINE AFFECTS DAILY FUNCTIONING

In dementia, the features of cognitive decline become amplified. Rather than simply forgetting that a meeting was on, someone with dementia might not remember the meeting was ever planned. Personality changes, confusion, problems navigating familiar environments, and difficulty performing everyday tasks are common challenges. Inside the brain, the accumulation of deposits, such as amyloid- β and tau in the case of Alzheimer's disease (see page 9), cause damage to neurons. While these deposits may signal a neurodegenerative disorder, they can sometimes be found in cognitively normal people.



When signs of cognitive decline and changes in personality or social behaviour can no longer be ignored, a GP visit is often the next step. The doctor will take a patient's history, assess their physical and mental abilities, order investigations and, if necessary, refer to a specialist geriatrician, neurologist or psychiatrist. Standardised cognitive tests are used by both GPs and other specialists. Examples are the Mini Mental State

Examination (MMSE) and the clock-drawing test. Some states also have early memory assessment clinics.

BRAIN SCANS

Imaging technologies such as CT or MRI, which reveal the structure of the brain, can detect changes in the features of vascular dementia, and the shrinkage of brain tissue caused by degeneration. Other types of scans, such as PET, fMRI (functional MRI) and SPECT, show localised changes

in brain activity and can be used together with cognitive and behavioural symptoms to aid diagnosis. A new imaging method called PiB-PET is being investigated for use in showing amyloid- β plaques.

An abnormal scan alone, however, is not a diagnosis. It is important to note that imaging tests can fail to detect abnormalities, especially in a person with early dementia, and scans can be lengthy, unpleasant and expensive. Currently,

scans are mostly research tools and not used for diagnosis and management in the general community.

BIOMARKERS

Other research is looking at whether lab tests of biomarkers, such as the level of amyloid- β and tau in blood or cerebrospinal fluid, can predict a susceptibility to dementia. However, the work is complicated by the fact that different forms of amyloid- β and tau exist.

The key is to correctly identify the toxic forms.

Finding biomarkers of dementia will be critical in early diagnosis and treatment. One large-scale study looking to do this is the Australian Imaging, Biomarker & Lifestyle Flagship Study of Ageing (AIBL), a longitudinal study aimed at determining what biomarkers, lifestyle choices and cognitive abilities best predict the development of Alzheimer's disease.

📧 aibl.csiro.au

Signs & Symptoms

Dementia symptoms usually develop gradually. Often the earliest signs are recognised in hindsight because they're mistaken for signs of normal ageing.

COMMON EARLY SIGNS OF DEMENTIA

If two or more of these are affecting daily life, it may be time to see a doctor.



Frequent memory loss that affects daily activities



Changes in mood or behaviour



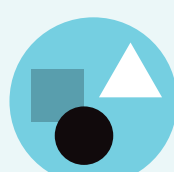
Problems with language – e.g forgetting simple words



Loss of initiative



Misplacing things or putting them in inappropriate places



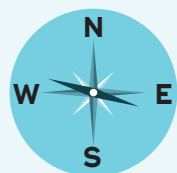
Problems with abstract thinking



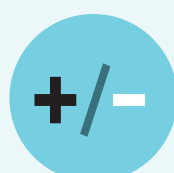
Difficulty performing familiar tasks



Changes in personality



Disorientation with time and place

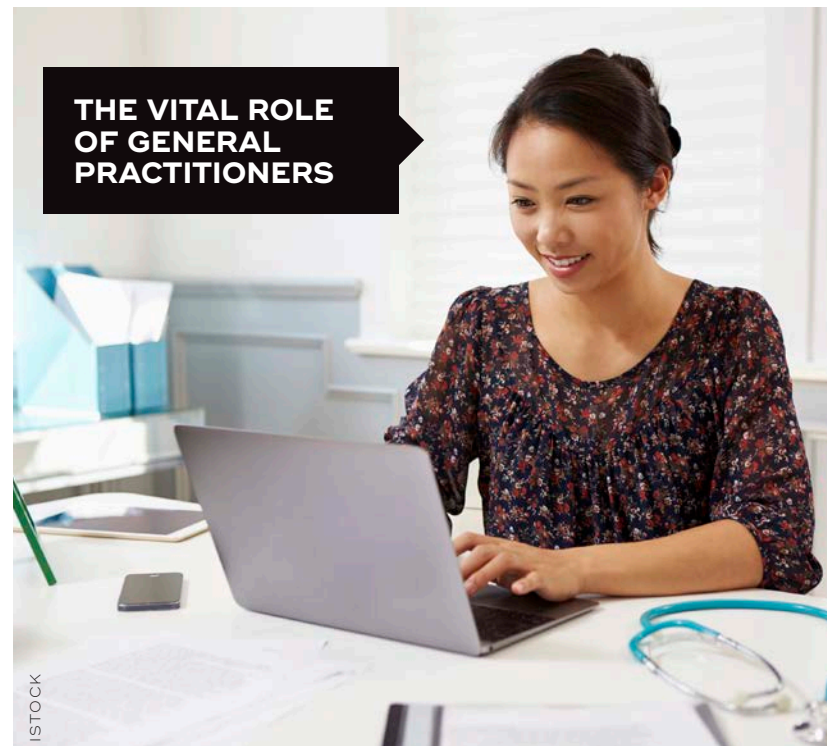


Poor or decreased judgement

The first signs of dementia may vary depending on the type. For instance, memory loss, apathy and depression are common early signs of Alzheimer's disease, whereas impaired judgement and organisational skills are often early signs

of vascular dementia. People in early stages of dementia with Lewy bodies will often display memory loss, sleeplessness and visual hallucinations. Frontotemporal dementia typically causes changes to personality, language and behaviour first.

THE VITAL ROLE OF GENERAL PRACTITIONERS



ISTOCK

General practitioners (GPs) are involved in the care of a majority of people with dementia, from first diagnosis and care at home, through to visiting them in residential care. The GP's role at first presentation is to rule out all other causes for cognitive changes. GPs also rely on aged care assessment teams (ACATs) at their local hospital or community health centre, and support and information from Dementia Australia.

Looking after the carer's emotional and physical

health is also crucial. The GP may organise respite care or community nursing, or support the transition to residential care. For families, the psychological and behavioural symptoms of dementia are often more distressing than the memory loss, and care is typically time-consuming and exhausting.

Doctors have a duty to remind patients and carers about legal and planning issues, such as setting up an enduring guardianship or power of attorney, and an advance care directive, early in the illness.

PROFILE

RACHEL CORBETT

RADIO PRESENTER RACHEL CORBETT SPEAKS OUT ABOUT THE PERSONAL TOLL OF DEMENTIA AND THE HARROWING EXPERIENCE OF HER MOTHER'S ALZHEIMER'S DISEASE.

Rachel Corbett, a writer and media presenter, struck a chord with viewers of *The Project* in early 2017, when she spoke frankly on the panel about her mother's dementia. Rachel's mother was diagnosed with Alzheimer's disease in her late fifties and lived for 10 years with the condition.

In the early years, Rachel's mother hid the diagnosis from her family. After Rachel found out, she realised why: there is still a lot of fear and ignorance about dementia. Her mother could "see people snickering... or making comments about her because she wasn't behaving normally or she was doing things that she couldn't control," she says "That used to kill me to hear that."

"It's really hard for the person to fit into normal life and then on top of that, they feel self-conscious and embarrassed," she says. "You want everybody to feel – especially when it's not their fault – the way that they are is completely okay." Rachel made an effort to take her mother on outings as often as possible "so she didn't feel like she was stuck in a house

and she didn't feel like I was ashamed of her."

As her mother's condition deteriorated, at-home care was no longer possible, but the transition into

residential care was difficult, Rachel says. Her mother had become sleepless and violent – not uncommon symptoms – and her stepfather was constantly being woken in the middle of the night. "She would be bashing him, screaming at him, she would be impossible to calm down, so he was basically calling the ambulance all the time because she just would never sleep."

What Rachel found most saddening about her mother's dementia is the insight she had into her own condition. "I think the worst

"It amazes me that so many people are affected by it, and will be affected by it, and yet we just don't really talk about it."



thing about her situation was that she knew it was happening the whole way along."

Rachel started speaking out about dementia in response to what she saw as public misconceptions about the disease. While acknowledging that each case is different, she doesn't sugarcoat the fact that her mother's

Alzheimer's was a difficult experience. "When you're a family member about

to go through something like that, you need to know what you're about to face, because I was certainly blindsided by it."

Confronting uncomfortable truths is important in raising public awareness about dementia, Rachel believes. "I think the only way that people are going...to be invested in it emotionally is if we start having these kind-of icky, uncomfortable conversations that aren't very pretty," she says. "It amazes me that so many people are affected by it, and will be affected by it, and yet we just don't really talk about it."

Risk factors

Risk factors increase the likelihood of disease occurring.

They do not inevitably cause dementia, but have a strong association. Some risk factors can be modified by changing lifestyle behaviours, while others – such as family history, age or genetic makeup – cannot be changed.

GENETICS

The genes that seem most significant in diseases that cause dementia are those linked to the aggregation of proteins, which leads to the death of neurons (see page 7).

A family history of dementia is a risk factor for Alzheimer's. Younger-onset Alzheimer's is largely inherited and most cases can be traced to mutations in one of three genes: amyloid precursor protein (*APP*), presenilin 1 (*PSEN1*) or presenilin 2 (*PSEN2*). The presence of one or more of these mutated genes virtually guarantees the development of dementia.

YOUNGER-ONSET ALZHEIMER'S THE GENE FACTOR

Three genes have been identified in playing a role in causing most cases of younger-onset Alzheimer's.

- Amyloid precursor protein (*APP*)
- Presenilin 1 (*PSEN1*)
- Presenilin 2 (*PSEN2*)

Mutations of these genes promote the production of toxic amyloid- β plaques. If these are inherited, a person will almost certainly develop the disease. However, some people still develop younger-onset Alzheimer's even without these genes.

For the most common form – late-onset Alzheimer's disease – a variant of the apolipoprotein E (ApoE) gene known as ApoE 4 increases the risk. People with one copy of ApoE 4 are about three times more likely to develop the disease, and those with two copies of ApoE 4 form are about eight times more likely to succumb.

Half or more of people with Alzheimer's disease have at least one copy of the

ApoE 4 gene – but while it means that the chances are higher of developing the disease, it is not inevitable.

Studies have identified about a dozen other genes that may increase the risk of developing Alzheimer's.

However, the known contribution of genetics in causing Alzheimer's disease – combining younger-onset and late-onset forms – remains small.

The genetic contribution to other dementias is also

relatively minor. About 10% of dementia with Lewy bodies cases are inherited. And in frontotemporal dementia, about 10-15% of cases are inherited, while a further 25% have a family history of neurodegenerative disease.

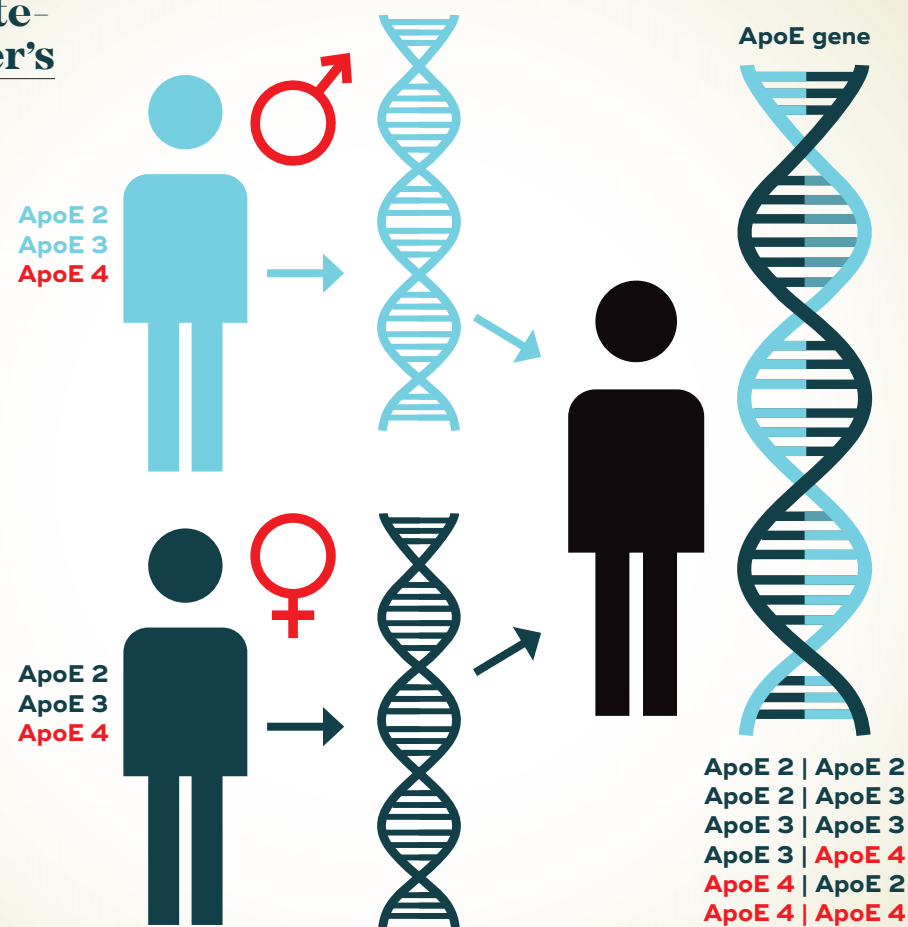
Key genes in late-onset Alzheimer's

RISK GENES

Everyone receives two copies of the ApoE gene, one from your mother and the other from your father. ApoE has three common variants and you can inherit any two of these:

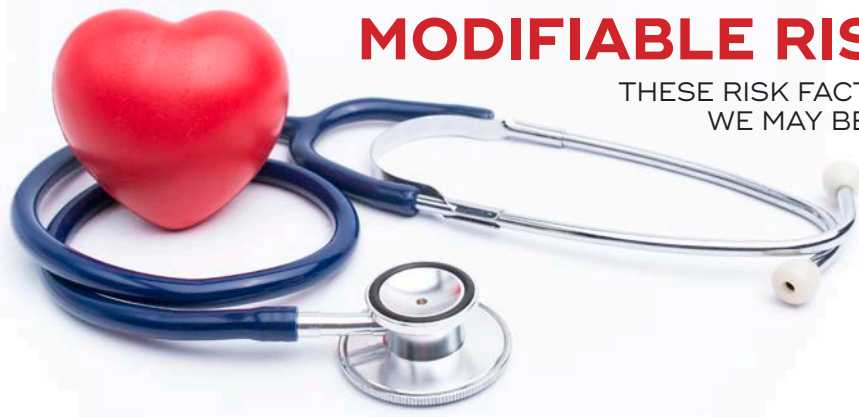
- **ApoE 2** – rare, and may protect against Alzheimer's
- **ApoE 3** – common and seems to play a neutral role
- **ApoE 4** – the risk gene. One copy increases the risk 3-fold. Two copies increases the risk 7-8-fold

There are almost a dozen other potential risk genes for Alzheimer's that have been identified.



MODIFIABLE RISK FACTORS

THESE RISK FACTORS INCLUDE THE ONES WE MAY BE ABLE TO CHANGE



ISTOCK

CARDIOVASCULAR HEALTH

This has one of the strongest links to dementia, particularly Alzheimer's disease and vascular dementia. High blood pressure, high cholesterol levels, diabetes, stroke and heart disease all increase the risk. The connection seems easy to understand – our circulation supplies vital nutrients for the brain, and if something interferes with that, our neurons will suffer. In reality, we're still trying to figure out how these changes might cause build-up of toxic aggregates.

LIFESTYLE CHOICES

Smoking, drinking, inactivity, and limited social

and mental stimulation may increase the risk of dementia. Some of these may be linked to poor cardiovascular health, and methods to increase physical activity in older patients are being investigated to see if they can delay dementia.

HEAD INJURIES

There is now evidence that head injuries – even mild, repeated concussions – can be associated with the development in later life of a kind of degenerative disease called chronic traumatic encephalopathy (CTE). One recent study reported that an incredible 110 out of 111 former NFL (American National Football League)

players, whose brains were donated to researchers, showed signs of CTE. This disorder has many of the same physiological hallmarks of forms of dementia, particularly the abnormal deposits in the brain of the proteins tau and TDP-43 (see page 11).

SLEEP DISTURBANCES

People with dementia commonly have sleep disturbances, even years prior to experiencing symptoms. As with many risk factors, whether this is a cause or a symptom of dementia is unknown – and it's likely to be both. Alzheimer's disease is known to alter production of

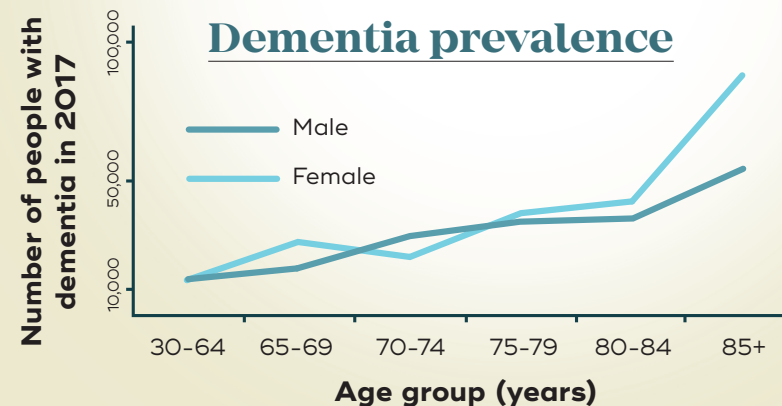
the hormone melatonin by damaging a part of the brain called the suprachiasmatic nucleus, which is responsible for regulating our circadian rhythm, or the sleep/wake cycle. As a result, people with dementia may find it harder to go to sleep and stay asleep; they may sleep for just a few minutes and think they have slept for hours.

Sleep also helps to consolidate memories, and a lack of sleep, or the

right kind of sleep, can impact memory recall. A recent study linked one night of sleep deprivation (of slow-wave, or deep sleep) to increased levels of amyloid- β , the main compound in plaques that hasten neuron death. Chronic sleep deprivation was also linked to an increase in tau, a key protein that forms tangles inside neurons, leading to their death (see page 10).

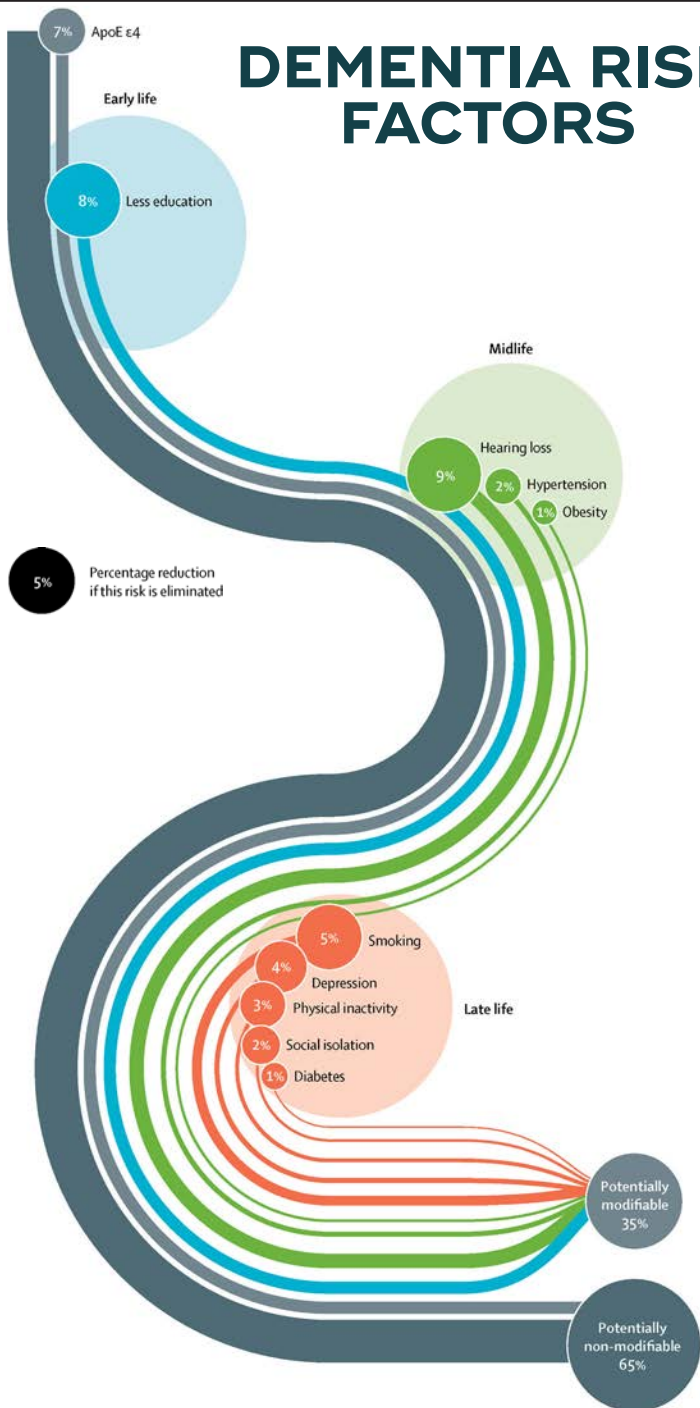
The age risk

Age is the greatest risk factor for developing dementia. As with our genes, we unfortunately can't do anything to overcome ageing! However, there are environmental factors that seem to influence the likelihood of dementia and could account for about one-third of the overall risk of developing dementia (see page 21). There is some evidence to suggest we can take steps to lessen the impact of these factors.



NATSEM CALCULATIONS USING ABS POPULATION PROJECTIONS

DEMENTIA RISK FACTORS



RISK FACTORS THAT CAN'T BE CHANGED

- Age
- Family history of dementia (genetics)

MODIFIABLE RISK FACTORS LIFESTYLE

- Smoking
- Chronic alcohol use
- Lower education level
- Physical inactivity
- Social isolation
- Chronic sleep deprivation
- Poor diet



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HEALTH

- Diabetes
- Heart disease
- Hypertension
- High cholesterol
- Head injury
- Hearing loss
- Obesity
- Depression



STUDY

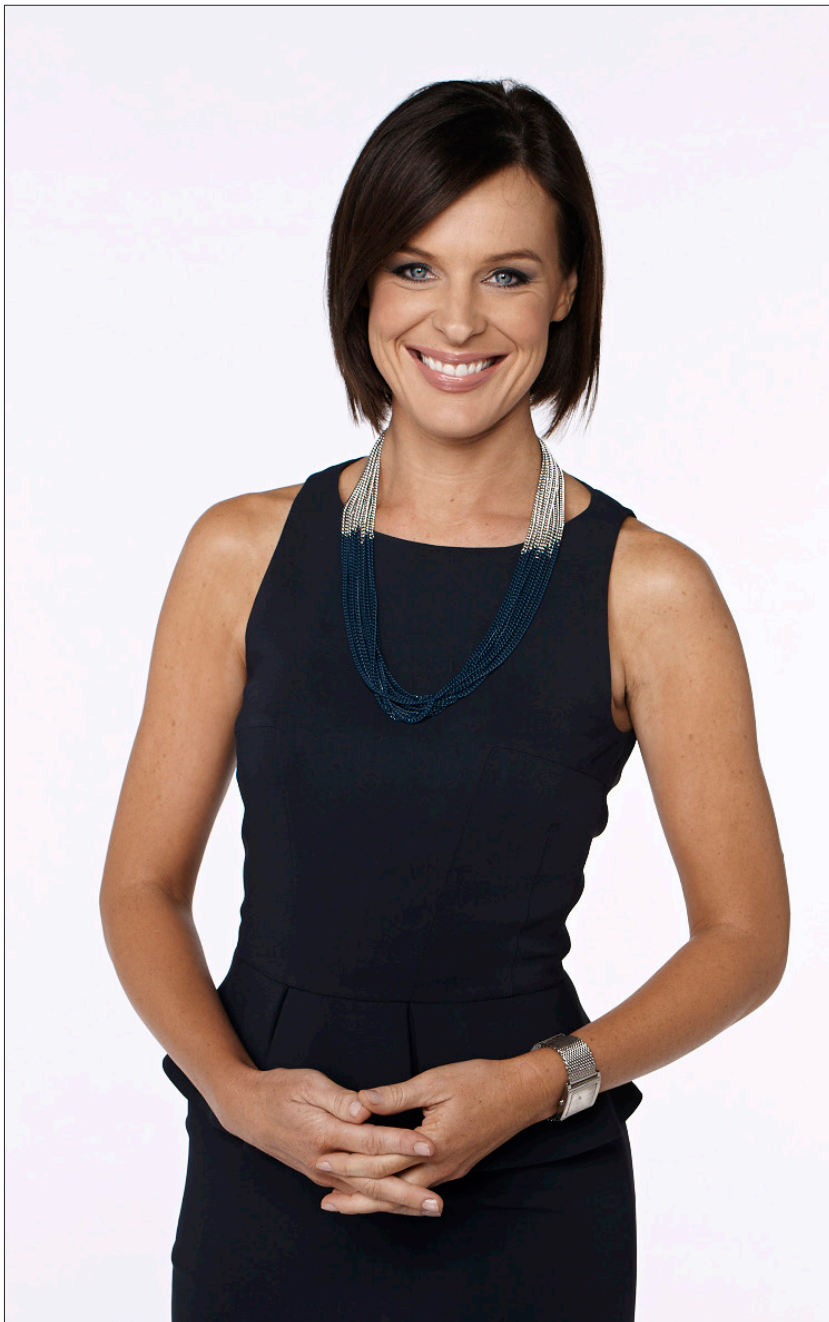
Sleep apnoea study

One of the most common reasons for sleep disruption is sleep apnoea – when upper airways collapse during sleep, resulting in sporadic pauses in breathing that require the person to momentarily wake up to breathe. People who suffer from sleep apnoea are two to three times more

likely to develop Alzheimer’s disease, says Professor Elizabeth Coulson, from the Queensland Brain Institute and the School of Biomedical Sciences at UQ. “This could be because hypoxia – lower levels of oxygen in the blood from poor breathing – causes nerve cell death,” she says. Prof Coulson’s team is conducting a study

that will follow patients aged 55 to 75 with sleep apnoea over an extended period, to determine whether using a continuous positive airway pressure (CPAP) ventilator, which keeps airways open during sleep, protects against brain degeneration and lowers the risk of dementia.

qbi.uq.edu.au/sleepapnoeastudy



PROFILE

NATARSHA BELLING

LOSING A LOVED ONE TO DEMENTIA HAS DRIVEN TV PRESENTER NATARSHA BELLING TO ADVOCATE FOR BETTER SUPPORT NETWORKS.

National television presenter Natarsha Belling knows what it's like to lose a loved one to dementia.

She recounts with sadness her experience when a family member was diagnosed. "She was this most beautifully kind person," says Natarsha. "I was incredibly close to her – she taught me how to sew."

"She was so physically well, but for her mind, it was just absolutely devastating."

Natarsha knows from experience that a new

diagnosis affects more than just the person living with dementia. "Their entire family is affected, and it's also a huge emotional and physical burden on the people who are supporting them."

She emphasises the individuality of each person who has dementia. "They shouldn't all be boxed into one category," she says. "There are varying degrees of dementia and it affects everyone so differently."

"Someone can live with it for only a couple of years and others can live quite

successfully for many more years. Subsequently, there need to be different support networks in place."

After hearing from others living with dementia, Natarsha has become passionate about improving the financial and community support services available for people with dementia, as well as their families.

"Dementia is the greatest cause of disability in older Australians," she says. "We need a much better support network, especially through funding."

Natarsha knows from experience that a new diagnosis affects more than just the person living with dementia.

CHAPTER 4. Living with dementia



STAGES OF DEMENTIA

ISTOCK

It is often helpful to categorise dementia into stages of severity to help doctors formulate a treatment plan, and for the person and their family to consider options for care. Dementia is often divided into early, middle and late stages, but medical professionals use a more detailed seven-stage scale, based on a person's symptoms and assessment of cognitive decline.

Not all of these signs are always present, since dementia can be caused by many underlying conditions, but they represent the typical progression, particularly of the most common form of dementia, Alzheimer's disease.

PROGNOSIS OF DEMENTIA

How does the disease progress and how does it become fatal?

Because dementia is caused by many different underlying conditions, progression will vary. A person's age, physical health and cognitive reserve – how resilient someone is to brain changes – will also affect how fast the disease progresses.

The average time from the appearance of obvious symptoms until death is about 8-10 years for Alzheimer's disease; 4-8 years for Lewy-body and frontotemporal dementias; and 5 years

for vascular dementia.

People may live 20 years or more with dementia, depending on its cause and the age, health and genetics of the person diagnosed. Dementia reduces life expectancy and is not often listed as the direct cause of death. Death is typically caused by complications related to the loss of brain function – infections such as pneumonia (accounting for two-thirds of cases), malnutrition, dehydration or falls.

1 APPEARS NORMAL

Normal, no obvious signs, although brain changes may be occurring.

2 VERY MILD

No noticeable symptoms different to normal ageing. Brain imaging may reveal plaques or degeneration.

3 MILD

Mild cognitive deficits – increased forgetfulness or disorientation, difficulty finding words. Loved ones begin to notice decline.

4 MODERATE

Memory of recent events affected; difficulty with complex tasks and managing personal affairs; may be in denial or withdrawn from family. Decline is obvious to a doctor. Family and friends notice symptoms.

5 MODERATELY SEVERE

Major memory lapses, including significant life events; needs help with daily activities such as dressing or preparing meals; can no longer manage personal affairs.

6 SEVERE

Can no longer care for self; starts to forget names of family members; difficulty finishing tasks; speech affected; incontinence, depression, agitation, delusions may be evident.

7 VERY SEVERE

Full time care is needed; loss of speech; requires assistance with all daily activities, including eating, bathing, toileting; may lose the ability to walk.



ISTOCK

PROFILE

TREVOR CROSBY

67-YEAR-OLD TREVOR CROSBY SHARES HIS EXPERIENCE LIVING A FULL, ACTIVE LIFE WITH DEMENTIA

Trevor Crosby has always led an active life. For 35 years, he ran a farm in rural NSW, as well as two other family businesses. Three years ago, the 67-year-old was diagnosed with Lewy body dementia, something that hasn't stopped him from staying more active than most people his age – if not even younger.

“I’m a bit of a sporting freak,” he says. Aside from doing yoga for over a decade, he sails, plays cricket, golf and lawn bowls and has recently taken up bridge. “Sometimes I wonder if I’ve bitten off more than I can chew,” he chuckles.

Trevor also volunteers with Dementia Australia, speaking at advocacy and engagement events. Having dementia gave him new opportunities, he says, “to do new things, to meet a lot of people I wouldn’t have met if I didn’t have a problem. The fact that I have dementia has increased my quality of life in certain ways.”

His outlook wasn’t always so positive. The initial diagnosis of Lewy body dementia was hard to accept, and came about after his wife Jill

noticed memory problems and changes in behaviour, and urged him to see a GP, who then referred him to a neurologist.

“Shock is an understatement,” says Trevor. “I was dumbfounded...I couldn’t believe there was something that could be wrong with indestructible me. The very first moment that I found out, I tried to speak but I couldn’t. I really understood what the definition of speechless was.”

The diagnosis was followed by a period of helplessness and fear. The turning point in Trevor’s mindset came about after he and Jill took a Dementia Australia program on living well with dementia. “We met up with another dozen people who were floundering around, feeling sorry for themselves, pretty well down in the dumps...in eight weeks there was a total turnaround for us and others.” He now believes that the best thing people with a new diagnosis of dementia can do is to seek information and support from Dementia Australia so that they can be helped and encouraged to live as well as they can with their condition.

While passionate about prevention and quality of life, for Trevor, the future of dementia comes

While passionate about prevention and quality of life, for Trevor, the future of dementia comes down to one key issue: research.



KATHARINE MCKINNON

down to one key issue: research. In light of the huge numbers of people affected and the large economic cost, he strongly believes that funding scientific research into dementia, at present the number two killer in Australia, should be of the highest of priorities. But there’s also a personal reason for Trevor: “I want a cure. I want to continue to live.”



MORE INFORMATION

National Dementia Helpline: 1800 100 500

Delaying dementia and reducing your risk

While scientists are working hard on developing treatments for dementia (see page 29), there is still no cure. Medications can treat some effects of underlying disease, while other therapies help manage the symptoms.

Taking action in the following five areas may help reduce the risk of developing dementia, and delay its onset. yourbrainmatters.org.au

LOOK AFTER YOUR HEART

Keeping blood pressure, cholesterol, Type II diabetes and obesity under control can reduce the impact of vascular dementia in particular. Quitting smoking also falls into this category, and it reduces neurotoxins that could further damage neurons.



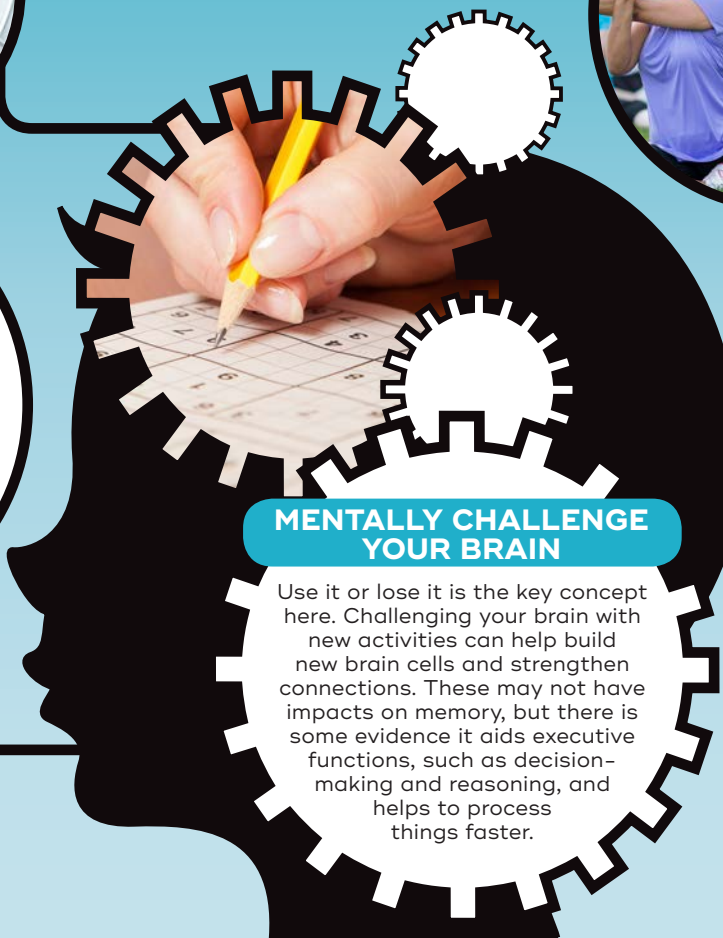
ENJOY SOCIAL ACTIVITY

Social engagement increases mental activity and emotional connections to others and can help strengthen the pathways of memories. Social isolation not only increases the risk of dementia, but also increases the risk of hypertension, depression and coronary heart disease, which are also risk factors for dementia.



MENTALLY CHALLENGE YOUR BRAIN

Use it or lose it is the key concept here. Challenging your brain with new activities can help build new brain cells and strengthen connections. These may not have impacts on memory, but there is some evidence it aids executive functions, such as decision-making and reasoning, and helps to process things faster.



BE PHYSICALLY ACTIVE

Exercise is thought to stimulate the brain to produce new neurons (see page 31) and thereby reduce cognitive decline. Muscle-strengthening activities also help with balance (reducing falls). As well as improving mood, exercise also helps protect your heart by reducing the associated risk factors.



FOLLOW A HEALTHY DIET

Studies have shown that following a healthy diet – eating lots of fruit, vegetables, legumes and nuts; replacing butter with olive oil; eating fish twice a week; adding herbs and spices instead of salt; and limiting red meat – is associated with a reduction in the risk of dementia. Processed foods with high fats and trans fats are associated with an increased risk of dementia.



PROFILE

MAREE MCCABE

FOR DEMENTIA AUSTRALIA CEO MAREE MCCABE, SUPPORTING PEOPLE LIVING WITH DEMENTIA IS BOTH A PASSION AND A JOB THAT SHE IS VERY PRIVILEGED TO DO



“...there won't be a person in Australia who isn't impacted by dementia in some way.”

and educating the community,” she says. “Some people are still fearful of dementia.”

“The day people get the diagnosis, they're no different than they were the day before.

There's a lot of living for people to do and we want them to have the best quality

of life they could possibly have, and remain socially connected and engaged to the people who are important to them and the activities they love.”

The future of dementia concerns her: “It's a public health issue.” Without a medical breakthrough, she says, in three decades' time “there won't be a person in Australia who isn't impacted by dementia in some way. They will have a family member, a loved one, or themselves impacted by dementia. That's the reality. We need a funded Dementia Action Plan to ensure that we do the very best we can for everyone impacted by dementia.”

When you lead one of Australia's largest advocacy organisations, it pays to be passionate about the people you're supporting. When Maree McCabe, CEO of Dementia Australia, talks about the work her organisation does, it's with an inspiring and infectious energy.

“Our role is to empower and enable people who live with dementia, as well as their families and carers, and advocate on their behalf,” she says. In addition to the National Dementia Helpline, Dementia Australia runs counselling services and educational programs, and provides training to the aged care and healthcare sectors.

Some of the training for healthcare professionals includes video-game technology. “We actually simulate for them the experience of what it's like to have dementia,” says Maree. The rationale, she explains, is that the experience would change their attitudes and behaviour, and “improve the outcomes in terms of quality of life and quality of care for people living with dementia.” She adds, “that's exactly what's happening.”

Of the organisation's many outreach activities, their social programs are among the most

popular. “It means that people living with dementia, and their carers, can attend social outings in an environment that really nurtures them,” she says. “They make really great friendships and support each other through their experience.”

Maree also emphasises the carer-focused services that Dementia Australia provides. “Supporting carers is essential for them to support their loved one who's living with dementia.” In turn, early entry into residential care is predictable if that support is not provided, she says, which may not be the desired outcome for loved ones.

Another key program is the Dementia-Friendly Communities project. “It's all about ensuring that communities are aware of the impact of dementia, how to support people living with dementia, how to educate staff, and how to keep people engaged in the community for as long as possible,” she says. “The more engaged people are, the longer they stay well.”

Despite all this, Maree sees Dementia Australia's work as far from done. “There's so much more we need to do in terms of awareness



MORE INFORMATION

National Dementia Helpline: 1800 100 500



ISTOCK

Supporting people with dementia

What should I do if I'm worried about my memory?

Changes in memory and thinking have a number of possible causes besides dementia. These include stress, depression, pain, chronic illness, medication, alcohol, brain tumour and stroke. Major changes in memory are not normal at any age and should be taken seriously. If you're experiencing these kinds of difficulties, it is better to see your doctor sooner rather than later. Early assessment allows early diagnosis and treatment, planning

by family members and consideration of legal and financial issues.

There is no single specific test to identify dementia. A medical diagnosis is made by cognitive testing; talking to relatives or friends to assess the history of changes in memory, thinking and behaviour; as well as a physical examination, blood tests and scans.

I think my loved one has dementia. How do I convince them to see a doctor?

Some people may be resistant to the idea of visiting a

doctor for assessment of their memory. They may not realise, or else deny, that anything is wrong - possibly due to the brain changes that interfere with their ability to recognise or appreciate that issues are occurring. Others, who have retained insight, may be afraid of having their fears confirmed.

One of the most effective ways to overcome this problem is to identify another reason for a visit to the doctor, for a symptom that the person is experiencing, such as headaches or poor eyesight. Any anxiety expressed by

the person is an opportunity to suggest and support them in a visit to their doctor.

What support services are available?

Dementia Australia provides a range of sensitive and flexible services to support people with any type of dementia throughout the illness, as well as their families and carers.

Services provided by Dementia Australia include:

- Information about dementia
- Support and education groups for people who have been diagnosed with dementia as well as for carers and families
- Important information about local services



MORE INFORMATION



Information about support services for dementia are available at: fightdementia.org.au or by calling the National Dementia Helpline on 1800 100 500.

RESEARCH FOCUS

AGEING MIND INITIATIVE

The Ageing Mind Initiative (AMI) is a UQ virtual clinical ageing research group coordinated by Professor Nancy Pachana from the School of Psychology, and Professor Gerard Byrne from Psychiatry in the Faculty of Medicine. AMI provides a focal point for clinical, translational ageing research in a mental health context.

ami.group.uq.edu.au

CARFREEME

CarFreeMe is an evidence-based method to help older people transition from driving. The program is for people with dementia or brain injury and stroke survivors. CarFreeMe works on the basic principles of empowerment, support and understanding.

carfreeme.com.au

EARLY DETECTION OF DEMENTIA

UQ's Centre for Health Services is developing an electronic system to improve early detection of dementia when people go to see their GPs. The research also aims to find ways to support GPs in helping patients to reduce their risk factors and change behaviours.



PROFILE

KATE SWAFFER

KATE SWAFFER, 2017 AUSTRALIAN OF THE YEAR IN SA AND CO-FOUNDER, CHAIR AND CEO OF THE DEMENTIA ALLIANCE INTERNATIONAL, LIVES WITH YOUNGER-ONSET DEMENTIA.

As a 49-year-old married working mother of two teenage sons, when I was diagnosed with younger-onset dementia, I was initially in deep shock. Even though I had been a nurse in a dementia unit, I had no idea younger people could get it. Ten years on, a lot has happened, and I am still living beyond dementia, in spite of the increasing disabilities. Since losing a partner to suicide aged 27, I learned personally the reality of the old saying, “The King is dead. Long live the King”. After some time grieving, decided it is better to live every day as if it is my last, just in case it is.

I’ve become an accidental global warrior for people with dementia, and whilst I still have breath and can use my voice, I will stand up for the rights of us all, including our families. In 2015, the report Addressing Dementia: The OECD Response concluded that “Dementia receives the worst care in the developed world”. This is abhorrent, and obviously includes Australia. As an activist for human rights and access to the Convention on the Rights of Persons with

Disabilities for people with dementia, it is my ambition to ensure global change, with a human rights approach to dementia.

I believe we need research for so much more than a cure, and if we don’t increase research for improving post-diagnostic care – that includes rehabilitation, disability support, timely diagnosis, and research into risk mitigation or even reversal of dementia – we are failing our communities. Not to focus on reducing risk

“...it is my ambition to ensure global change, with a human rights approach to dementia.”

would also herald an economic cost that not even the rich developed countries can afford. A report commissioned by Dementia Australia predicted that with a focus on risk reduction, the potential savings in Australia would be more than \$120 billion. We simply cannot afford not to focus on this, and as the only Australian who is full member of the World Dementia Council (WDC) I can report the WDC also believes this to be very important if we are to manage the costs of dementia globally.

Personally, I have never had a dream for a ‘dementia free world’ as I believe that is an



unachievable notion – you might be interested to know that many others diagnosed feel the same. I specifically want more research into risk reduction, and improving care that is aligned with human rights, in equal proportions to research for disease-modifying drugs or a cure.

CHAPTER 5. Beating dementia



TREATING AND MANAGING DEMENTIA

There is no cure for dementia, and while current treatments manage symptoms, they offer no prospect of recovery. The main therapies available come in the form of medications and social programs.

DRUG TREATMENTS

For Alzheimer's disease, most medications aim to correct the impact to the brain's chemical

messengers – called neurotransmitters – particularly, the cholinergic and glutamate neurotransmitter systems. Drugs known as acetylcholinesterase inhibitors prevent enzymes from breaking down acetylcholine (which is important for memory), meaning more of it is available at the sites where neurons transmit messages.

Cholinergic treatments may be prescribed for people with mild-to-moderate disease. Glutamate blockers prevent excess glutamate destroying neurons and are given to those with moderate-to-severe disease. There's a window for using these drugs; they can improve symptoms in some people, but because of side effects, their use is closely monitored by doctors.

SOCIAL PROGRAMS

Keeping loved ones active with hobbies and interests they enjoyed in the past can be important after a disease diagnosis. Social programs such as music therapy and visits with animals can help stir memories, foster emotional connections with others, lessen anxiety and irritability and make people feel more engaged with life.



DEFINITION Neurotransmitters

Neurotransmitters are the chemical messengers of the body's nervous system. These molecules are released by one neuron and travel to the next, binding to specific receptors on the surface of a neuron and sparking an electrical signal that sends the message down the neuron. Interruption to this communication system – due to too much or too little neurotransmitter – can result in neurons firing too much, not enough or not at all. Neurons are then unable to communicate their messages.

RESEARCH FOCUS

Enhancing Language Learning in Ageing with Exercise

This UQ study aims to understand how exercising affects learning, by training older people to learn new words immediately before or after they exercise. Understanding how exercise affects language learning may lead to new approaches for improving language re-learning in older people with brain conditions.

exercise-ella.com



ULTRASOUND: A NON-INVASIVE TREATMENT

A major problem in treating any brain disorder is the difficulty in accessing the brain itself. Not only is the brain protected by a thick skull and a three-layered protective membrane called the meninges, but the blood-brain barrier prevents most things from leaving the bloodstream and entering the brain.

While it is beneficial for keeping out foreign substances such as toxins or bacteria from the brain, the blood-brain barrier is a huge impediment to drug development for brain disorders. Not surprisingly, vast resources have been devoted to designing drugs with the right properties to get through this almost impenetrable barrier.

An alternative way to overcome the blood-brain barrier is to temporarily open it. Focusing ultrasound waves at specific locations in the brain can temporarily open the tight junctions of the blood-brain barrier that are usually sealed shut. This allows drugs to enter the brain that, because of their size or chemical properties, are normally prevented

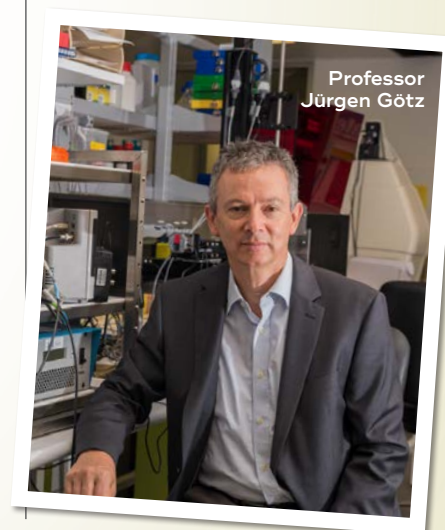
from doing so. Higher brain levels of an appropriate therapeutic drug means more of that drug reaches its target, elevating its effectiveness.

QBI research, from the laboratory of Professor Jürgen Götz, established scanning ultrasound as a method to clear amyloid- β from the brains of Alzheimer's mice and restore memory. Extending this work, he and his team have shown that scanning ultrasound helps deliver an antibody that works against the toxic tau protein.

When mice were given the tau antibody alone, the amount of toxic tau protein decreased and the animals' behaviour improved. Multiple treatments of ultrasound on its own also decreased the levels of toxic tau, and had a positive effect on cognition when the

number of treatments was increased. Most crucially, when ultrasound was combined with the antibody, the therapeutic effects were even greater. To test the safety of using ultrasound to open the blood-brain barrier, this research is moving into sheep, which have a skull thickness similar to human skulls. If successful, the next stage will be to add additional capabilities and proceed to human clinical trials.

📍 qbi.uq.edu.au/CJCADR





Immunotherapy: vaccines for toxic deposits

ISTOCK

Whereas currently available medicines manage symptoms, new treatments are focused on slowing or reversing the disease process itself by using the body's own immune defence system. This approach, called immunotherapy, involves creating artificial antibodies that attach to abnormal aggregates (such as amyloid- β or tau), and mark them for destruction by the immune system. Immunotherapy is experiencing a surge of interest and a number of clinical trials – targeting both amyloid- β and tau – are underway.



DEFINITIONS

Antibody

An antibody is a large protein produced by the body's immune system when a foreign substance (such as bacteria, viruses, or parasites) is detected. Antibodies can tag an invader for destruction by other immune cells, or directly destroy it. Antibodies can be engineered and used as research tools, in diagnostics and for therapy.

Vaccine

A vaccine is an introduced agent that trains the immune system to protect against future exposure to that agent.



ISTOCK

Exercise may be an effective way of decreasing the risk of cognitive decline. Evidence for its direct benefit as a treatment for dementia, however, is lacking. A 2015 review, which analysed multiple studies into the effects of exercise on people with pre-existing dementia, found some evidence that exercise could help with daily living activities, but no clear cognitive benefits were found. Other studies show that people who exercise regularly are less likely to have dementia.

Recently, QBI Founding Director Professor Perry Bartlett successfully used exercise to improve cognition in older mice. He is now leading a human clinical trial, along with Dr Mia Schaumberg, from the UQ School of Human Movement and Nutrition Sciences, to find the amount, intensity, and type of exercise that might lead to cognitive improvement in elderly people. It's thought that exercise boosts the production of new neurons in the brain, which might improve cognition. qbi.uq.edu.au/exercise-study



Where to next for dementia? More than a century since Alzheimer’s disease was first described, we still lack an effective treatment and the same is true for other dementias. The obvious question is, when are they coming and will there be a cure? It’s likely dementia, like cancer, will never be completely preventable, but we should be able to delay its onset, and limit its damage.

The large impact that dementia currently has on society has led to generous

support for basic research, from both governments and philanthropists. In 2013, the Australian Government set up the National Institute for Dementia Research to coordinate funding and priority research projects on dementia in Australia. Both the Queensland Government and Australian Government have committed funding to dementia research.

A WORLD-LEADING RESEARCH CENTRE

Around the same time, with funding from the

Queensland Government and generous support from the Clem Jones Foundation, QBI established Australia’s first dedicated research centre for dementia – the Clem Jones Centre for Ageing Dementia Research (CJCADR).

In just a few years, CJCADR has become a global leader in dementia research, with 10 research groups and more than 90 scientists working to understand what causes dementia and how it can be treated. Directed by Professor Jürgen Götz, the Centre’s

work is driven by the belief that fundamental, basic research is needed to solve the increasing challenges posed by Alzheimer’s disease and other dementias. This aligns with international initiatives such as the UK Dementia Research Institute and the German Centre for Dementia Research.

A range of issues are being addressed to understand and combat this devastating condition, from the molecular and cellular changes that underlie disease, to the development of new antibodies and therapeutic approaches.

The ultimate objective is to help the community by coming up with new treatments and ways to monitor and diagnose

dementia. QBI scientists are keen to translate basic research findings into clinical trials, as demonstrated by their exercise trial (see page 31) and portable ultrasound project (see page 30). If the ultrasound research goes according to plan, this will also help the more than one-third of people with dementia who live in rural and regional locations where access to medical facilities is difficult.

To help communicate its research and to connect with patients and carers impacted by dementia, QBI hosts an annual Public Dementia Forum, bringing together scientists, clinicians, carers, community groups and the general public to promote knowledge exchange across the dementia community.





Our vision

QBI researchers are working to develop a safe, portable, drug-free treatment for dementia patients.

Help us help those you love.

qbi.uq.edu.au/donate



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